HEALTH EFFECTS OF
PROJECT SHAD
BIOLOGICAL AGENT:

SERRATIA MARCESCENS

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Health Effects of *Serratia marcescens*
This report deals primarily with the biological health challenges engendered by the agent that is the subject of the report. Nevertheless, this report also incorporates, by reference and attachment, a supplement entitled "Psychogenic Effects of Perceived Exposure to Biochemical Warfare Agents".

The supplement addresses and describes a growing body of health effects research and interest centered upon the psychogenic sequelae of the stress experienced personally from actual or perceived exposure to chemical and biological weaponry. Because awareness of exposure to agents in Project SHAD logically includes the exposed person also possessing a perception of exposure to biochemical warfare agents, the psychogenic health consequences of perceived exposure may be regarded as additional health effects arising from the exposure to Project SHAD agents. This reasoning may also apply to simulants and tracers. Therefore, a general supplement has been created and submitted under this contract to address possible psychogenic effects of perceived exposure to biological and chemical weaponry.

Because such health effects are part of a recent and growing public concern, it is expected that the supplement may be revised and expanded over the course of this contract to reflect the actively evolving literature and interest in the issue.
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I. EXECUTIVE SUMMARY

*Serratia marcescens* (formerly *Bacillus prodigiosus*, -is, -um), is a facultative anaerobic, motile Gram-negative rod-shaped bacterium. It belongs to the *klebsiella-enterobacter-serratia* division of the family *Enterobacteriaceae*. A saprophyte, it can be normally found in water, soil, sewage, foodstuffs, and in animals like rabbits, horses, deer and water buffalo. In Project SHAD, it was disseminated in an aerosolized form in order to evaluate the effect of solar radiation on its viability.

*Serratia marcescens* has a historical background that may be described as literally colorful. Many strains yield a red pigment, called prodigiosin. Prior to the scientific age, the organism appears to have been the causative agent for a celebrated appearance of red fluid on communion bread in a Catholic Mass. Regarded as the miraculous appearance of blood, it became a factor in the adoption of the theological doctrine of the transubstantiation of communion bread and wine into the body and blood of Christ. This episode and others like it may also have led to incidents of anti-Jewish violence as the appearance of what was taken for blood on communion hosts was sometimes attributed to the false anti-Semitic accusation of Jewish ritual desecration of Christian communion.

The microbe was first identified in modern times by an Italian pharmacist, Bartolomeo Bizio, in 1819. Human conflict appears not to have escaped the history of *S. marcescens* even then. The genus name that Bizio gave it, *Serratia*, was from the name of an Italian physicist Bizio believed did not get adequate credit for the invention of the commercial steamboat.

The secreted red pigment allowed *S. marcescens* to become a popular marker for tracing bacterial activity. At one point it was literally exhaled and expectorated into a cleared British House of Commons chamber to investigate the spread of illness among Members of Parliament. In 1920, it was also sprayed on the mouths and hands of African-American soldiers to test bacterial contagion in the washing of Army “mess-kits”.

In the early 1950s, *S. marcescens* was part of a test for the atmospheric distribution of bacterial pathogens. The U.S. Army released bacteria off the coast of California. Years later, reports of an outbreak of nosocomial *S. marcescens* infections contemporar to the release in an area hospital (Stanford University) were discovered. Army tests were suspected to have been the cause, but this was later deemed unlikely after typing of the strains showed they were not the same. Production of the microbe by the military stopped with the termination of the biological weapons program in the late 1960s.

*S. marcescens* was still being used in medical training as a tracer in the early 1970s despite a growing awareness of another aspect -- its pathogenic potential. About the same time, use as a tracer in human systems appears to have been stopped because of the awareness of the pathogenicity of *S. marcescens*. In Project SHAD, it was used as late as 1973 but not reported to be used on human subjects.
*S. marcescens* is most commonly encountered as an opportunistic pathogen in nosocomial settings. It is typically associated with the use of invasive devices or procedures (e.g. surgical wounds, hemodialysis) and with patients whose health is generally compromised. Other associations are poor hygiene in health care facilities and prior unsuccessful treatment of the patient with antibiotics. Heroin addicts are sometimes found to have endocarditis traceable to the pathogen.

Frequent or noted conditions associated with *S. marcescens* infection include compromised/suppressed immunity, recent surgery, diabetes, cancer, burns, alcoholism, and recent corticosteroid therapy. Chronic Obstructive Pulmonary Disease (COPD) is a possible co-factor, or at least one common associated disorder. Being bed-ridden, receiving oral care, receiving mechanical ventilation and manipulative airway procedures have all been found to be risk factors. Age, both elderly and neonatal, may also be a risk factor.

One notable feature of *S. marcescens* infection is the microbe’s powerful, enduring, and adaptable resistance to anti-microbial agents.

Among the devices and reservoirs of *S. marcescens* pathogenesis are intravenous solutions, surfaces of blood packs, bristles on shaving brushes, double distilled water, moistening fluids for umbilical cords, sponges, fiberoptic bronchoscopes, adhesive tape, eyedrops, defibrillators, EDTA blood-collecting fluid, urine bottles, sinks, liquid soap dispensers, polyethylene containers, shower caps, plastic bottle caps, saline solutions and various disinfectant solutions. Flowers, food, sinks, and soil can contain *S. marcescens*. Mouthwash and plastic nebulizers are additional known reservoirs. The human gastrointestinal tract may be a reservoir but probably not for adults. Contaminated blood is a rare source of human infection by *S. marcescens*, however.

One type of therapeutic device notably associated with *S. marcescens* infection is soft contact lenses. The pathogen is able to survive on them and can cause conjunctivitis, infective keratitis with frequent permanent effects on the eye, and corneal opacity. The transmission to the lens is usually via contaminated lens fluids. Other common devices associated with the pathogen are indwelling catheters.

A broad variety of infectious conditions have been traced to *S. marcescens* exposure. The effects of *S. marcescens* infections can involve just about every physiological system. Urinary tract infections (usually associated with indwelling catheters), septicemia, bacteremia, osteoarthritis, septic arthritis, otitis media, empyema, lymphadenitis, soft tissue/skin infections (e.g. necrotizing fasciitis), ocular infections (microbial keratitis, endogenous ophthalmitis), endocarditis, meningitis, peritonitis, and various respiratory conditions like necrotizing pneumonia have been implicated.
Where infection does occur, identification and typing can be done through culturing of body fluids and the use of standard commercial systems like the API 20E system and pulsed-field gel electrophoresis (PFGE).

*S. marcescens* infections can often be lethal. When not, they tend to follow an acute course and go into spontaneous remission as resistance to antibiotic therapy is strong. Chronic cases are not common but long-term local bone infections related to trauma are reported (one lasting 16 years), most of which ultimately resolve despite the failure of anti-microbial therapy. Ocular effects can be devastating, with enucleation required or blindness following infection. Long-term diminution of visual ability is also possible.

In some cases, long periods of incubation may be taking place as there are gaps of months to a few years between the possible onset of exposure and the manifestation of illness.

Psychogenic effects of exposure to the pathogen have not been specifically identified although the historic record from the period prior to scientific understanding of microbes and their action shows that reaction to its pigment appearing mysteriously has caused political and religious tensions.

Prevention of infection is the maintenance of a good hygienic regimen around debilitated persons to avoid the “person-to-equipment-to-person” transmission. Where instances of infection have taken place, isolation of those afflicted from other vulnerable persons is recommended. Treatment is difficult due to the pathogen’s notorious resistance to microbial agents. Most therapy to be supportive in nature and most prevention to be simple conscientious hygienic care. Amputation or other surgery of an infected area may be necessary.

Because of the broad scope of possible infections, it is hard for literature to encapsulate all the risks of *S. marcescens* exposure. Information from the Department of Defense on Project SHAD, while noting the microbe’s pathogenic potential, does not directly point out that infection can be lethal.
II. MICROBE & HISTORICAL BACKGROUND

Microbe

Serratia marcescens

(Shirley Owens and Catherine McGowan, Microbe Zoo Project, Comm Tech Lab, Michigan State University.)
(http://commtechlab.msu.edu/sites/dlc-me/zoo/microbes/serratia.html)

General Description:  S. marcescens is an aerobic (facultatively anaerobic), motile, Gram-negative, enteric saprophytic rod of the klebsiella-enterobacter-serratia division of the family Enterobacteriaceae (Yu 1997, Hejazi 1997, Parment 1997).

Names: Bacillus prodigiosus, -is, - un; Monas prodigiosa,-us;, Chromobacterium prodigiosus. Zaogalactina imetrofa. (Yu 1979; Thayer 1966; Cumming 1920)
Identification code letters “SM” have been used in Project SHAD (Project 112 Tests 2004).

S. marcescens secretes a red pigment called prodigiosin. Although this has been one of the most noted qualities of S. marcescens, actually less than 10% of its strains produce the pigment (Yu 1997). S. marcescens secretes DNAase, a lipase and gelatinase. It also secretes exoenzymes, chitinases, and many extracellular proteases. Most strains secrete catalase, nitratalase, lysine, and decarboxylase. S. marcescens also produces acetoin. It does not, however, secrete oxidase (Theccanat 1991; Parment 1997; Hejazi 1997; Hertle 2001).

S. marcescens can survive and even thrive under anaerobic conditions with only a very low amount of organic material necessary. Although it can grow well under aerobic and semi-aerobic conditions, oxygen may be toxic when a low-nutrient condition exists (Hejazi 1997). Varied motility for different strains results from the existence of different types of S. marcescens flagettal cells. Non-flagettal strains move quickly on low-agar media surfaces (Hejazi 1997). The SS-1 strain secretes an extracellular surfactant that decreases the surface tension of water (Wei 2004).

S. marcescens is highly resistant to antibiotics and over time the species has continued to adapt to later generations of antimicrobial agents and to seek out new ecological niches. Variable cell wall permeability and the secretion of beta-lactamases (non-plasmid-
mediated in \textit{S. marcescens}) are considered to be factors in its resistance (Carbonell 2003; Hejazi 1997). The microbe is also able to thrive on dry plastic and in non-hydrous fluids (Parment 1997).

\section*{History}

Throughout pre-modern history there have been reports of “blood” appearing on bread. These incidents have had some substantial impact on significant episodes of history. It is probable that many of the incidents involved the activity of \textit{S. marcescens}. The secretion of red dye by strains of \textit{S. marcescens} has thus given the microbe an especially interesting history. Even after scientific awareness of the microbe grew, it still managed to insert itself into noteworthy places and events (Yu 1979).

Pythagoras observed red fluid emerging from bread as far back as the 6\textsuperscript{th} century BC. In 331 BC, Alexander the Great’s forces in the Levant took heart from an omen of what appeared to be blood appearing on grain. In 541 AD, the discovery of what was assumed to be blood on bread was said to foretell the defeat of the Lombards (Yu 1979).

In the later Middle Ages, the appearance of what was taken for blood on bread would directly affect art, religion, and an ancient prejudice. The “Miracle of Bolsea” was a famous Renaissance painting by Raphael commemorating the mysterious appearance of blood on a communion host during the earlier Middle Ages. That and other apparent “miracles” fueled the Catholic theological concept of the “Real Presence,” or transubstantiation, of the elements of bread and wine into the actual body and blood of Christ. The appearance of red fluid on communion hosts also validated in many medieval minds one form of “blood libel” against Jews – that they ritually desecrated Christian communion hosts. This helped impel anti-Semitic persecutions in Europe (Yu 1979).

A more scientific approach to the phenomenon of red fluid appearing in grain came in 1819 when an Italian pharmacist Bartolomeo Bizio identified what he thought was a fungus on bread that was mysteriously exuding a blood-like fluid. He named the organism \textit{Serratia marcescens}. \textit{Marcescens} is a derivation of a Latin verb meaning “to decay” and it reflects the secreted dye’s tendency to lose its original hue rapidly after exposure to light. The genus name \textit{Serratia} is derived from a more recent communal tension: Bizio wanted to immortalize the name of an Italian pioneer of steam sea vessels, Serafino Serrati who, he felt, had been slighted in favor the American entrepreneur Henry Fulton for the public acclaim of having produced the first commercially utilizable steam-powered boat (Yu 1979).

Bizio’ efforts included two other science-promoting points of note. He duplicated the dye secretion in the house of a priest, putting to rest the then-prevailing superstition that the mysterious red secretions could only occur in the house of a sinner. Bizio’s efforts also constituted the first example of using solid media to cultivate chromogenic bacteria (Yu 1979).
In the 19th century, the name of the organism was changed to *Monas prodigiosa* and later *Bacillus prodigiosus, -is*. Prodigosin became the common name for the red secretion. By the 1920s standardization in bacterial taxonomy led to the revival of *Serratia marcescens*, though the alternate names *B. prodigiosus* and *Chromobacteria prodigiosus* have persisted (Yu 1979; BMJ 1969; Cumming 1920). In 1957, “pseudohemoptysis” became the formal name given to false observations of blood engendered by the secretion of *S. marcescens*. (Yu 1979; Thayer 1966).

By the early 20th century, the potential of the microbe’s pigment as a tracer for the route and presence of microorganisms became apparent. No less distinguished a site than the British House of Commons became a locus of the microbe’s forensic use as a tracer when in 1906 M.H. Gordon read Shakespeare aloud in an empty chamber after gargling *S. marcescens* and distributing agar plates. The aim of the exercise was to determine and demonstrate the aerial risks of microbial infection during an influenza epidemic (Yu 1979).

Over the 20th century, the popularity of *S. marcescens* as a tracer grew. As late as the early 1970s, *S. marcescens* would remain a standard academic display tool for students to show how microorganism are transmitted via handshakes. A relatively harmless uncontrolled appearance of *S. marcescens* occurred in the mid-1950s, when for several months diapers of babies in a nursery turned mysteriously red, giving rise to a phenomenon called the “red diaper syndrome” (Yu 1979).

As early as 1919, the burgeoning role of *S. marcescens* as a tracer tool in military use and testing of microorganism behavior was becoming established. In that year, *S. marcescens* was administered to African-American US Army soldiers to test the hygienic risks of mess-kits and their handling (Cumming 1920). In 1950-1952, *S. marcescens* was distributed in the air over the Pacific Ocean off the coast of California to trace and assess the bio-vulnerability of the United States (Yu 1979). In Project SHAD, it was used through 1973 in aerosolized form to test aerosol microorganism decay rate data (Project 112 Tests 2004).

In 1976, reports of the earlier California ocean test led to some public examination of the possibility of the test being the cause of outbreaks of *S. marcescens* infection in the San Francisco area. Later testing by the Centers for Disease Control (CDC) showed that different strains of *S. marcescens* from the ones used in the ocean biowarfare tracer experiments were responsible for the infections. Nevertheless, the concern highlighted another aspect of *S. marcescens* that also emerged more clearly, though more recently, over the course of the 20th century – its role as dangerous, even lethal, pathogen (Yu 1979; Acar 1986; Parment 1997).

The relatively harmless uses of *S. marcescens* as a tracer had eclipsed a growing awareness over most of the 20th century of the pathogenic potential of *S. marcescens*. “It is difficult to realize how benign it was once considered to be, and how recently” (Yu 1979). Even before the 20th century, in 1896, Professor Schuerlen at the University of
Strasbourg warned, to little effect, that *S. marcescens* was potentially “more deadly than many pathogens” (Hejazi 1997). In 1913, the first clinical report of its pathogenic nature emerged when red dye from *S. marcescens* was found in the sputum of patients with bronchiectasis (Yu 1997). Reports of meningitis in 1943 and an outbreak of septicemia in a British hospital in the 1960s were among other stray clinical reports of serious health effects caused by *S. marcescens* (Thayer 1966; BMJ 1969).

In 1966, Harley Thayer of the Veterans Administration in Memphis, Tennessee, warned his fellows in the dentistry profession against using *S. marcescens* as a tracer of bacterial activity. He cited earlier reports of its pathogenicity (Thayer 1966). By 1968, the US military had ceased using *S. marcescens* as a biomarker (Project 112 Glossary 2004). It is reported that its pathogenic potential was recognized by the military by 1968, causing its military use as a biomarker agent to stop, although it was apparently used in Project SHAD in 1973 in a controlled environment but not on human subjects (Project 112 Glossary; Project 112 Tests 2004).

As mentioned above, the microbe continued to be used as a biomarker in some academic exercises, but since the 1970s, increased awareness of the presence of *S. marcescens* as an opportunistic infection has taken place, particularly in hospitals and other health care centers.
III. PATHOGENESIS & DIAGNOSIS

Pathogenesis: General

Infection by *S. marcescens* is typically associated with the patient having some kind of associated health debilitation and/or undergoing an invasive procedure. Exactly which factors are independent co-factors is not always clear. In general, however, *S. marcescens* has appeared as an opportunistic nosocomial pathogen with a conspicuous ability to resist antibiotic therapy.

Outbreaks of *S. marcescens* infections in hospitals are increasingly commonly reported worldwide. In 1991, it was suspected as an agent of 8% of hospital urinary tract infections (Hejazi 1997). In the 1980s, *S. marcescens* accounted for as much as 2-5% of all nosocomial infections (Acar 1997; Acar 1986). *S. marcescens* is now one of the more frequently isolated pathogens in hospital infections; it is responsible for about 1.7% of hospital bloodstream infections in the USA (Acar 1997; Wisplinghoff 2004). ICU’s are a noted area of associated risk, and multiple isolates can usually be found there in a single outbreak (Howland 2000). One common population of non-nosocomially-afflicted individuals has been heroin addicts (Reisberg 1979).

Only one case of an apparently totally healthy (though elderly) patient with no prior invasive treatment or associated disability condition who acquiring disease (necrotizing fasciitis) from *S. marcescens* has been found. The effects were fatal in that case (Liangpunsakul 2001).

Pathogenesis: Reservoirs & Risk Factors

*S. marcescens* infection has been described as being usually acquired from a “person-to-equipment-to-person” pathway (Takahashi 2004). One of the most emphasized reservoirs in the literature has been the unhygienic hands and related carelessness of hospital workers (Hejazi 2000). A single anesthesiologist appears to have caused a major hospital outbreak in Ontario, Canada in 1999 (Henry 2001). The cell surface hydrophobicity of *S. marcescens* permits it to survive and thrive on plastic and thereby ultimately turn health care centers and medical procedures into zones of danger (Hejazi 1997). The survivability of *S. marcescens* in fluids, anaerobic environments, and its capacity to resist anti-microbial agents adds to this risk greatly (Hejazi 1997).

The list of demonstrated sources of contamination is long and probably not exhaustive of all possibilities. Among them are medical equipment and fluids. Intravenous solutions, surfaces of blood packs, bristles on shaving brushes, double distilled water, moistening fluids for umbilical cords, sponges, fiberoptic bronchoscopes, adhesive tape, eyedrops, defibrillators, EDTA blood-collecting fluid, urine bottles, polyethylene containers, shower caps, plastic bottle caps, saline solutions and various disinfectant solutions have all been identified as sources of infection. A liquid soap dispenser have also been implicated in spread (Takahashi 2004; Parment 1997; Hejazi 1997; Yu 1979). Flowers,
food, sinks, and soil can contain *S. marcescens*. Mouthwash and plastic nebulizers are additional known reservoirs. The human gastrointestinal tract may be a reservoir but probably not for adults (Yu 1979; Parment 1997; Hejazi 1997; Su 2003). Contaminated blood is a rare source of infection by *S. marcescens*, however (Hejazi 1997).

Outside the hospital environment, contact lens solutions (particularly with chlorhexide) have become an increasingly important reservoir for *S. marcescens* ocular infections. *S. marcescens* adheres well to hydrogel lenses (Parment 1997). 50% of chlorhexidine solutions have been found to be contaminated within 7 days in doctors’ officers (Farris 1990).

Invasive/surgical procedures or conditions are key risk factors. Local infections tend to be associated with local invasive/surgical procedures having been done by contaminated devices or with contaminated fluids. A very significant source of infection are indwelling catheters of various types. Urinary tract infections are associated with bladder catheters and systemic infections with intravenous catheters (Lau 2004; Yu 1979; BMJ 1969). Contact lenses become vehicles for infection when they are neglected, eroded or spoiled. This may enable infection through the presence of puncturing needle-like crystal deposits formed on the surface of the spoiled lens. In 1989, the Food and Drug Administration (FDA) declared *S. marcescens* to be a challenging organism for the safety of contact lens solutions (Parment 1997).

Surgical wounds and drainage can yield soft tissue and other local or systemic infections; manipulative airway procedures can cause upper respiratory infections by *S. marcescens*, etc. (Hejazi 1997). Laser in situ keratomileusis (LASIK) eye surgery has been associated with *S. marcescens* ocular infection as has keratoplasty suture abcess. (Munoz 2004; Su 2003).

Surgical lumbar puncture enables nervous system infection. Dialysis and intravenous catheters also appear to serve as pathways for local and systemic infections (Parment 1997).

Debilitated health conditions and related treatment are commonly associated with *S. marcescens* infection. In fact, prior unsuccessful anti-microbial treatment is itself a significant risk for infection to the highly resistant and adaptable pathogen (Brarcos 1991). Frequent or noted health conditions associated with *S. marcescens* infection include heroin addiction, compromised/suppressed immunity, diabetes, cancer, burns, alcoholism, and recent corticosteroid therapy (Parment 1997; Yu 1979). Chronic Obstructive Pulmonary Disease (COPD) is a possible co-factor, or at least one common associated disorder (Theccanat 1991). Being bed-ridden, receiving oral care, receiving mechanical ventilation have all been found to be risk factors (Takahashi 2004). Age may also be a risk factor. Outbreaks among neonates occur often (Berthelot 1999). The debility of advanced age may be also enable infection to develop (Su 2003; Takahashi 2004; Liangpunsakul 2001).
Pathogenesis: Biologic Action

Although study of *S. marcescens* infection is growing, the full nature of its pathogenicity is not understood. It is known that *S. marcescens* produces at least 24 somatic (O-type lipopolysaccharide) antigens. (Hejazi 1997) Phagocytosis and complement killing appear to be ineffective against the microbe. *S. marcescens* survives inside human polymorphonuclear lymphocytes after phagocytosis (Equi 2001).

Recent study has been focused upon the pathogen’s ability to form pore-forming toxins (Alouf 2001). Two hemolysins, ShlA and ShlB, seem to play an important role in that process. ShlB serves to activate ShlA when it reacts with phosphatidylethanolamine. ShlA proceeds to form pores in erythrocytes, fibroblasts, and epithelial cells (Hertle 2001). One *S. marcescens* cytotoxin, distinct from the hemolysins, will begin to induce host tissue cell rounding and nuclear compaction within 15 minutes at a concentration of 0.54 µg/ml (Carbonell 2004; Carbonell 2003).

30 organisms are sufficient to start exogenous ocular colonization and inflammation. Tear fluid, however, is believed to be able to wash away the microorganism, preventing infection unless the corneal stroma is penetrated (Hejazi 1997). If penetration takes place, the toxins secreted by *S. marcescens* are believed to be able to induce acute liquefactive necrosis on the cornea (Munoz 2004).

Reinfection, but only by a different strain of *S. marcescens*, has been found in cases of infection associated with the condition Chronic Granulamitous Disease (Guide 2003). No cases were found of persons who fully recovered but then acquired same-strain *S. marcescens* infection anew from an identifiably new source of infection.

Pathogenesis: Incubation/Latency

Tests on a human volunteer indicate that ill-effects may begin within a few hours of aerosol exposure (Thayer 1966). The speed at which *S. marcescens* cytotoxins can act has been noted above (15 minutes). Some studies, however, suggest that the time between exposure and effects can be very long-term, with onset in some cases ranging from 8 months to 3 years after the possible initial exposure (Svennson 1987; Huang 2001).

Diagnosis

Standard commercial methods are effective at identification. The API 20E system is commonly used, though reservation is expressed as to its precision (Hejazi 1997). Pulsed-field gel electrophoresis (PFGE) is also commonly employed for identification. Cultures can usually be readily taken from the appropriate bodily fluids – blood, urine, sputum, vitreous/aqueous humors, cerebrospinal fluid (CSF), etc (Hejazi 1997) Many
different clinical isolates can often be found in a single outbreak at a single location (Sekisuchi 2004; Howland 2000).
IV. HEALTH EFFECTS

Overview

*S. marcescens* infections can affect a wide variety of physiological systems. In many cases infection can be lethal. This is true even with aggressive treatment since *S. marcescens* is notoriously adaptably resistant to anti-microbial drugs while persons afflicted often have other serious health debilitations which render them especially vulnerable (Yu 1997; Hejazi 1997).

The spectrum of observed clinical effects of *S. marcescens* infection is broad and chiefly includes the following: septicemia, bacteremia, urinary tract infections (UTIs), osteoarthritis, septic arthritis, otitis media, empyema, lymphadenitis, soft tissue/wound/skin infections, ocular infections (microbial keratitis, endogenous ophthalmitis), endocarditis, meningitis, peritonitis, and various respiratory tract conditions like sinusitis or necrotizing pneumonia (BMJ 1969; Yu 1979; Acar 1986; Parmet 1997; Hejazi 1997).

The course of the infections is typically acute and complete recovery can be without outside intervention. Although local effects may predominate, generalized symptoms of infection can appear – fever, chills, aches, nausea, tachycardia, etc. (Liangponsukal 2001; Huang 2001; Svennson 1987; Henry 2001). Sometimes the infecting strain can prove vulnerable to one or another antibiotic, or on occasion, a combination of them (Aygun 2000; Hejazi 1997).

Note on Long-Term/Chronic Effects

Discussion of incubation and periods of latency appeared in the previous section. Cases where the timing of the precise onset of infection is uncertain indicate that 8 months to 2-3 years can exist between exposure and onset of symptoms (Svennson 1987; Huang 2001).

Long duration of an *S. marcescens* infection and the existence of non-lethal permanent effects do occur but are not typical. Some cases of infection and disease have proven refractory over periods of months and years, the longest found in the literature was about 16 years in a case of osteoarthritis following a surgical implant (Svennson 1987). Ocular infections pose a substantial risk of local permanent effects ranging from diminished vision to permanent blindness from the progress of the disease or from enucleation (Parmet 1997). A single case of chronic meningitis is reported (Koo 1989).

The following discussions expand upon the major different effect types.
**Septicemia/Sepsis/Bacteremia**

Bacteremia and sepsis tend to be secondary to an abdominal infection (Yu 1997; Acar 198, Marinella 1998). Different studies suggest a mortality rate of 33-40% over the years (Takahashi 2004; BMJ 1969). Fever, rigors, respiratory distress, cyanosis, oliguria, shock, convulsions, temporary deafness and blindness have presented in the progress of these conditions. Debilitated conditions existing when the condition occurs have included diabetes, malignancy, burns, and alcoholism. Indwelling catheters and prior unsuccessful antibiotic regimens are also commonly associated (BMJ 1969; Takahashi 2004).

**Ocular Effects**

Ocular effects of *S. marcescens* bacterial exposure are frequently the result of contaminated contact lens solutions and spoiled contact lens surfaces that puncture the corneal epithelium. Keratitis and conjunctivitis are common results. Endophthalmitis is also a noted but rarer effect and can occur endogenously via blood transmission from another infected area. It can also occur exogenously due to ocular treatment (Acar 1986; Marinella 1998; Parmet 1997).

Laser in situ keratomileusis (LASIK) surgery appeared to have helped induce ulcerative keratitis, resulting in pain, visual loss, purulent damage, photophobia, monocular diplopia, and partial vision loss (Munoz 2004).

Recovery from bacterial keratitis generally can be slow, requiring a year or more of time and the use of corrective lenses. Suboccipital corneal haze lasting over a year occurred in a case of purulent keratoconjunctivitis. Permanent effects are rare but enduring “night haloes” have been reported (Munoz 2004).

Endophthalmitis from *S. marcescens* infection manifests itself acutely with general symptoms of fever, chills, tachycardia, and edema. Elevated intraocular pressure, pain, redness, a swollen eyeball, hypopyon (including dark hypopyon), have been elicited by *S. marcescens* infection in the eye. Chronic renal failure, and diabetes are common associated debilitations. Outcomes are poor with a high risk of progressive blindness or enucleation (Parmet 1997; Equi 2001).

Orbital infections are possible, and likely to be associated with ocular surgery, contaminated contact lens solutions, and an alloplastic orbital implant. Enucleation, evisceration, and diminished eyesight are common outcomes. Death has also occurred though rarely (Equi 2001).

**Central Nervous System (CNS)/Meningitis**

Acute meningitis is the most common CNS effect of *S. marcescens* infection, though it is generally rare in adults. A single case of chronic meningitis is reported (Koo 1989; Huang 2001). Most cases are associated with neurosurgery and invasive techniques or devices. Mortality can run as high as 30% from meningitis. Hydrocephalus, seizures,
and CSF rhinorrhea are reported sequelae of CNS infection. Focal suppurations have included brain abscess, cranial and spinal epidural abscess, and cranial subdural abscess (Huang 2001). Infected lumbar pseudomeningocele is another effect of *S. marcescens* invasion of the nervous system and can be associated with the chronic form of meningitis (Koo 1989).

Right ear surgery is reported to have precipitated a lethal episode of *S. marcescens* meningitis and reveals the downward progress of a fatal case. The condition initially presented as a slight fever with a stiff neck and proceeded to alternate episodes of agitation and non-responsiveness. Finally, cardiac arrest occurred leading to death. Post-mortem examination revealed purulent exudate covering the leptomeninges, the concavities of both cerebral hemispheres, the base of the brain and the ventricular system. The exudate consisted of lymphocytes and monocytes (Theccanat 1991).

**Endocarditis**

Endocarditis from *S. marcescens* is often associated with intravenous drug abuse, a compromised immune system, or the presence of prosthetic heart valves (Huang 2001; Ewart 1992; Acar 1986). In the 1970s, 14% of drug addicts in the San Francisco Bay area had *S. marcescens* endocarditis (Reisberg 1979). The endocarditis infection also induces a risk of septic embolization that leads to occlusion of arteries and lower extremities. The prognosis is poor, without surgery and antibiotic therapy death is the typical result (Takahachi 2004).

**Respiratory Tract Involvement**

Infection of the respiratory tract by *S. marcescens* is usually associated with manipulative airway procedures (Yu 1997). Sometimes an infection can arise endogenously from another infected area (e.g. a urinary tract infection) (Yu 1997). *S. marcescens* has also been a cause of superinfection in chronic bronchitis patients (Acar 1986).

Various forms of pneumonitis are common effects. Necrotizing pneumonitis has proven fatal (Acar 1986). Sinusitis has been reported. (Hejazi 1997) Biologic effects of respiratory infection can include bronchospasms, bronchiectasis, diffuse infiltrates, pleural effusion, and empyema (Acar 1986)

**Osteomyelitis**

Osteomyelitis from *S. marcescens* infection is often associated with heroin addiction and with prior antimicrobial therapy. The pathogen usually arrives at the site hematogenously. There is also a substantial association of *S. marcescens* osteomyelitis with surgery/devices applied to bone fractures, such as arthrodesis. Effects can be complicated by multiple infections and draining fistulae (Svennson 1987).

A noteworthy factor is some cases is the long period between the possible time for initial exposure and the subsequent long duration of the manifestation of symptoms. In a series
of cases, infections often did not manifest for 8 months to two years and the *S. marcescens* infections proved resistant to antibiotic treatment resulting in chronic recurrences of symptoms over months to years. In one case local effects continued to recur over 16 years (Svennson 1987).

Effects were usually local (joint/bone pain) but they could persist, advance and spread over the long term (e.g. tinnitus and cochlear degeneration). General systemic symptoms include fever and adrenal insufficiency. Outcome is often spontaneous remission (Svennson 1987).

**Septic arthritis**

Septic spread of infection to joints can occur. One study shows a strong association of the condition with heroin addiction (Brancos 1991). Axial joints are most affected. Hips, shoulder, and sacroiliac joints are common areas of infection. There seems to be relatively good response to antimicrobial treatment for this form of infection (Brancos 1991).

**Soft-Tissue/Skin Infections**

Cellulitis is a common condition following *S. marcescens* challenge to connective tissue (Marinella 1998; Bornstein 1992). Much of *S. marcescens* involvement in soft tissue proceeds from infected surgical wounds. Necrotizing fasciitis can also occur in association with chronic conditions like leg ulcers, renal failure, and diabetes. A history of local trauma is an important association as well (Huang 1999; Liangpunsakul 2001).

One reported case is significant in that except for age (66 years) the person who was afflicted had no factor in her personal history that suggested debilitation, trauma, or other invasive experience (surgery, medical device use). The patient eventually died after presenting first with left leg pain that spread from ankle to bone. Tachycardia and temperature changes followed. The soft tissue became swollen and the patient grew lethargic and disoriented. Bullae formation followed with focal areas of suppuration. Aggressive antimicrobial therapy and surgical amputation was undertaken but the patient deteriorated into a hypotensive state. Finally in a matter of days she died after multiorgan failure. The origins of her infection were obscure (Liangpunsakul 2001).

A fatal epiglottitis occurred in a 59 year old who was immunocompromised (total absence of granulocytes) and undergoing predisolone therapy in relation to his general affliction with lymphatic leukemia. Fever, sore throat, and a swollen epiglottis progressed to pneumonia despite aggressive antibiotic therapy. The patient died several days after the infection first appeared (Parment 1986).
V. PSYCHOGENIC EFFECTS

Studies or reports of psychogenic effects resulting specifically from exposure to S. marcescens have not been found. In section II, above, the psychosocial impact of red pigment from the microbe appearing on grain throughout history was discussed. Reactions included the imputation of theological or predictive significance of a mystical, moral, or supernatural kind. They also included popular false imputations of desecration and evil towards an outside group.

General psychogenic effects of perceived exposure to agents of biological (and chemical) warfare are examined in the supplement “Psychogenic Effects of Perceived Exposure to Biochemical Warfare Agents.”
VI. TREATMENT/PREVENTION

The key emphasis in prevention of *S. marcescens* infection is good hygienic practice. In hospitals the simplest but more critical step is proper hand-washing by personnel. Effective decontamination of the physical environment has been demonstrated in a Taiwan hospital following the use of 0.6% sodium hypochlorite solution and air drying (Su 2003). Replacement of contact lens solutions and proper care and cleaning of contact lenses is important in limiting the spread of *S. marcescens*. The use of polyaminopropyl biguanide (PAPB) as a preservative in hydrogel contact lens solutions has proven able to neutralize *S. marcescens* at a concentration of 15 ppm.

Where outbreaks have taken place in hospitals, certain general reactive steps have been recommended. These include reviewing lab and other infection control data; performing efficient genotyping of the pathogen; reinforcing and supplementing the number, and hygienic training, of staff (with special emphasis on hand-washing); neutralizing likely reservoirs of infection by removing indwelling catheters and isolating infected patients (Su 2003; Howland 2000).

The well-observed progressive, variable, and powerful resistance to antibiotics shown by *S. marcescens* makes any therapeutic treatment difficult. In one 1991 hospital outbreak, *S. marcescens* proved fully or partly resistant to all antibiotics except imipenem (Su 2003). Imipenem nevertheless was ineffective in a 1997 study which found that a combination of beta-lactam antibiotics and aminoglycosides resulted in rapid killing of the pathogens. (Beta-lactamase IMP-1 was found to be the agent that specifically neutralized imipenem (Hejazi 1997)).

Combination therapies involving different and hopefully synergistic types of antibiotics have been more and more recommended as a strategy to meet *S. marcescens* resistance. Amikacin and the aminoglycosides have shown some synergistic antimicrobial action. (Hejazi 1997; Equi 2001, Acar 1986). Nevertheless, the difficulty presented by the tenacity of the microbe in the face of drug therapy has meant that care is often reduced to palliative care for the disease’s duration.

Surgical intervention is often required in cases of intractable and advanced infection. Where infections have been sufficiently advanced, this has meant removal of distal members and of organs. Ocular enucleation has been the outcome of cases of endoophthalmitis (Marinella 1998; Parment 1997; Equi 2001).
VII. SECONDARY SOURCE INFORMATION

Secondary source literature generally recognizes the pathogenic nature of *Serratia marcescens*. The descriptions in the Department of Defense *DeploymentLink* sites on Project SHAD, however, do not address the notable mortality rate of the infections when they do occur (Project 112 Glossary 2004; Project 112 Tests 2004).
VIII. BIBLIOGRAPHY WITH ABSTRACTS

{Unless otherwise noted, the abstracts for the following references are rendered verbatim as provided by the original publication or as made available in a standard print or electronic catalogue, or database. Errors, omissions, or other defects of language, style, or substance are strictly those of the original source or its transmission.}


The emergence of resistance to fluoroquinolones in virtually all species of bacteria was recognized soon after the introduction of these compounds for clinical use more than 10 years ago. Various resistance mechanisms, often interdependent, may explain different levels of resistance. Epidemiological factors, local antibiotic policies, patients’ characteristics, origin of the strains, and geographic location are among the factors contributing to highly variable resistance rates. During the last several years, resistance to fluoroquinolones has remained very high among methicillin-resistant Staphylococcus aureus strains and in intensive care unit patients, and it has increased among nosocomial isolates of Klebsiella pneumoniae, Serratia marcescens, and Pseudomonas aeruginosa. More worrisome are recent reports of an overall increase in resistance to fluoroquinolones among bacteria responsible for community-acquired infections, such as Escherichia coli, Salmonella species, Campylobacter species and Neisseria gonorrhoeae.


Contract No. IOM-2794-04-001
Health Effects of Serratia marcescens
Serratia marcescens is a well-known cause of nosocomial infections and outbreaks, particularly in immunocompromised patients with severe underlying disease. An outbreak due to *S. marcescens* infection was detected from 13 to 22 February 2001 at the intensive care unit (ICU) of our institution. We used pulsed-field gel electrophoresis (PFGE) typing to analyse the outbreak strains involved. METHODS: A total of 25 isolates were included in this study: 12 isolates from infected patients, nine isolates from insulin solution, one isolate from sedative solution (midazolam and morphine infusion) and one isolate from frusemide solution. Two isolates from other wards which were epidemiologically-unrelated were also included. RESULTS: The *S. marcescens* from patients, insulin solution and sedative solution showed an identical PFGE fingerprint pattern. The isolate from the frusemide solution had a closely-related PFGE pattern to the outbreak strain with one band difference. Attempts were made in the present study to identify the environmental reservoir of *S. marcescens* during the outbreak. We found that the insulin and sedative solutions used by the patients were contaminated with *S. marcescens* which was proven to be the source of the outbreak. CONCLUSION: Using PFGE, we showed that the outbreak in the ICU of our hospital was due to the clonal spread of a single strain of *S. marcescens*.


Antibodies that lyse trypomastigotes in a complement-mediated reaction are believed to be the main participants in the protection against virulent *Trypanosoma cruzi*. Antibodies with a specificity for alpha-galactosyl-containing determinants--generally called antiGal--were studied to determine their role in the lysis of trypomastigote forms. The titers of antiGal markedly increase in Chagas's disease. In the present study we demonstrate binding of this antibody to *T. cruzi* and the complement-mediated lysis of trypomastigotes by antiGal. Lysis of metacyclic trypomastigotes by whole Chagasic (Ch) serum or isolated antiGal fractions was equally inhibited by alpha- but not by beta-galactosides. Most of the lytic power of the Ch antiGal as well as of the whole Ch serum was removed by absorption on Synsorb-linked Gal alpha 1, 3Gal beta 1, 4GlcNAc followed by rabbit erythrocyte absorption. The Ch antiGal had a lower affinity for melibiose bound to agarose than for the trisaccharide linked to Synsorb, and was several times more effective in the immunolysis of trypomastigotes than the corresponding antiGal from normal human serum. Lytic antibodies were partly absorbed by Serratia marcescens but not by Escherichia coli O111. A human volunteer immunized with an *S. marcescens* vaccine elicited a specific antiGal response that was lytic to trypomastigotes (70% lysis). We suggest that in vivo high-affinity antiGal antibody clones, as occur in Ch patients, may significantly contribute to the destruction of the parasite, whereas low-affinity antiGal clones are much less effective in the protection against *T. cruzi* infection.


Contract No. IOM-2794-04-001
Health Effects of *Serratia marcescens*

An outbreak of Serratia marcescens infection occurred in a special neonatal unit. The epidemic involved seven newborns, one of whom died. Contaminated hand-washing brushes were implicated in the epidemic; their removal resulted in a dramatic elimination of the infection.


To determine if antimicrobial synergism might affect the results of treatment of gram-negative rod infections, 444 bacteremias from 1972 through 1974 were studied. On these, 173 were treated with two antibiotics to which the infecting organisms were sensitive. Clinical responses were observed in 80% of 83 cases where antibiotic activity was synergistic, as defined by a minimum inhibitory concentration (MIC) of each antibiotic in combination being one-fourth or less than the MICs of individual drugs. This response rate was significantly better than the 64% response seen in patients treated with nonsynergistic combinations (p less than 0.05). Synergism correlated with significantly better clinical responses in those patients with “rapidly fatal”; and “ultimately fatal”; underlying disease (p less than 0.005), neutropenia (p less than 0.001), shock (p less than 0.01) and Pseudomonas aeruginosa infections (p less than 0.05). These results suggest that the use of antibiotic combinations to treat patients with gram-negative rod bacteremia who have the poorest prognosis is clinically justified and the improved results may be related to the synergistic activity of antimicrobial agents.


OBJECTIVES: To determine risk factors for Serratia marcescens infection or colonization, and to identify the source of the pathogen and factors facilitating its persistence in a neonatal intensive-care unit (NICU) during an outbreak. DESIGN: Retrospective case-control study; review of NICU infection control policies, soap use, and handwashing practices among healthcare workers (HCWs); and selected environmental cultures. SETTING: A university-affiliated tertiary-care hospital NICU. PATIENTS: All NICU infants with at least one positive culture for S marcescens during August 1994 to October 1995. Infants who did not develop S marcescens infection or colonization were selected randomly as controls. RESULTS: Thirty-two patients met the case definition. On multivariate analysis, independent risk factors for S marcescens infection or colonization were having very low birth weight (<; 1,500 g), a patent ductus arteriosus, a mother with chorioamnionitis, or exposure to a single HCW. During January to July 1995, NICU HCWs carried their own bottles of 1% chloroxylenol soap, which often were left standing inverted in the NICU sink and work areas. Cultures of 16 (31%) of 52 samples of soap and 1 (8%) of 13 sinks yielded S marcescens. The 16 samples of

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Health Effects of *Serratia marcescens*
soap all came from opened 4-oz bottles carried by HCWs. DNA banding patterns of case infant, HCW soap bottle, and sink isolates were identical. CONCLUSIONS: Extrinsic contamination of soap contributed to an outbreak of S. marcescens infection. Very-low-birth-weight infants with multiple invasive procedures and exposures to certain HCWs were at greatest risk of S. marcescens infection or colonization.

Serratia meningoencephalitis is often a fatal disease that causes widespread destruction of brain tissue despite aggressive antibiotic treatment. The autopsy findings of 2 cases are described. In a case caused by S. liquefaciens, previously not reported as the causative organism of meningoencephalitis, suppurative meningitis, ventriculitis, vasculitis, and extensive necrotic process of the brain matter were found. In the other case, caused by S. marcescens, the findings were those of acute and subacute abscesses with hemorrhagic necrosis.

Arroyo et al. 1981. Clinical, epidemiologic and microbiologic features of a persistent outbreak of amikacin-resistant Serratia marcescens. Infect.Control. Vol. 2(5): 367-372. This article describes a prolonged outbreak (January 1977 to February 1980) of amikacin-resistant Serratia marcescens (ARSM) urinary infections and the methods used for its control. Significant factors predisposing to ARSM urinary tract infection included an extended hospital stay, being in the urology ward, and undergoing urologic surgery. There had been on prior administration of amikacin or of other aminoglycosides in 20 of 27 patients with ARSM urinary tract infections. Chronically infected patients who required multiple hospitalizations represented a major reservoir for the perpetuation of the outbreak, overshadowing the importance of aminoglycoside use. Traditional control measures and even a major change in the inanimate environment were only partially effective in controlling the outbreak, but treatment of bacteriuric patients in the urology unit with “second and third generation” cephalosporins interrupted patient-to-patient transmission. No new cases of ARSM bacteriuria appeared in the urology unit in the ensuing 12 months.

Sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE) profiles of bacterial proteins have been successfully used for taxonomical purposes. More recently this technique has been applied to epidemiological investigations in respect of various micro-organisms including Neisseria meningitidis, Staphylococcus aureus and Clostridium difficile. The main limitations of the methods so far described are lack of standardisation in extraction and separation as well as in the analysis of results. Although reproducibility in the same laboratory has been shown to be satisfactory, comparison of results among laboratories is still difficult. Moreover, assessment of differences and/or similarities among chromatograms or autoradiographs showing many bands depends upon qualitative descriptions. Interpretation of densitometric scannings is laborious and time-consuming. In this paper we present our experience of a completely standardised,
Fully computer-controlled procedure for SDS-PAGE (AMBIS System) in analysing 35S-methionine-labelled total proteins. The methodology proved very useful in monitoring a hospital outbreak of Serratia marcescens. It allowed us to make quantitative comparison in a shorter time as well as to handle easily a great amount of data and usefully integrate it with those obtained with other systems such as serotyping. Furthermore, when the two systems are used together, more precise information can be gained. In this epidemic, serotyping indicated the presence of two groups which would have been missed by PAGE analysis alone. Electrophoretotyping, however, focused on similarities of cellular proteins among the epidemic strains. This allowed us to distinguish them from epidemiologically unrelated strains of the same serogroup. (ABSTRACT TRUNCATED AT 250 WORDS)


Three selective isolation media and the paraffin baiting technique were compared with conventional culture (Sabouraud dextrose agar without antibiotic supplement) for the ability to grow and detect nocardiae from simulated sputum specimens. Modified Thayer-Martin medium, incorporating vancomycin, colistin, nystatin and trimethoprim as selective agents, produced the highest recovery rate and with the greatest suppression of normal respiratory tract flora. A clinical evaluation using a screening programme devised for a busy diagnostic microbiology laboratory was performed on 1600 sputum specimens. Inoculating sputum on modified Thayer-Martin medium and extending the initial incubation period of 3 days at 35 degrees C under 10% carbon dioxide to a further 3 weeks at room temperature in a candle jar, led to the diagnoses, which otherwise would have been missed, of pulmonary nocardiosis in 3 patients and pulmonary infections due to Neisseria meningitidis, Pseudomonas cepacia, and Serratia marcescens in a further 22 patients.


OBJECTIVES: To investigate and describe an outbreak of Serratia marcescens in a neonatal intensive care unit (NICU) and to report the interventions leading to cessation of the outbreak. SETTING: A 2,168-bed, tertiary-care, university teaching hospital in Vienna, Austria, with an 8-bed NICU. DESIGN: We conducted a case-control study to identify risk factors for colonization and infection with *S. marcescens*. A case-patient was defined as any neonate in the NICU with a positive culture for *S. marcescens* between October 1, 2000, and February 28, 2001. Polymerase chain reaction was applied to type isolates. METHODS: During unannounced observations, the NICU was examined and existing policies were reviewed. Staff were re instructed in hand antisepsis and gloving policies. Admissions were halted on December 27. During previously planned technical maintenance of the ward, the NICU was closed for 10 days and thorough aldehyde-based disinfection of the NICU was performed. RESULTS: Ten neonates met the case
definition: 6 with infections (among them 3 with cerebral abscesses) and 4 with asymptomatic colonization. Previous antibiotic treatment of the mothers with cefuroxime was the single significant risk factor for colonization or infection (P = .028; odds ratio, 17; 95% confidence interval, 1.3 to 489.5). CONCLUSIONS: \textit{S. marcescens} can cause rapidly spreading outbreaks associated with fatal infections in NICUs. With aggressive infection control measures, such outbreaks can be stopped at an early stage. Affected neonates themselves may well be the source of cross-infection to other patients on the ward. Antibiotic treatment of mothers should be reevaluated to avoid unnecessary exposure to antibiotics with the potential of over-growth of resistant organisms.


The number of band differences in DNA macrorestriction profiles required to distinguish unrelated strains from an index strain varies in an outbreak with the species and restriction enzyme used. In order to define this difference for epidemiological studies of \textit{Serratia marcescens}, we produced DNA fingerprints from 57 isolates of the organism using the restriction enzyme \textit{XbaI} and pulsed-field gel electrophoresis (PFGE). The isolates were selected on the basis of their epidemiology, serotype and phage-typing patterns to include 28 unrelated strains and 29 representatives from 2 distinct outbreaks. One of the outbreaks was prolonged, lasting for several years. Electrophoretic profiles consisting of 20 or more clearly resolved bands were obtained for all isolates. Twenty-six of the unrelated strains had unique profiles with over 10 band differences from all other strains, while 27 of the outbreak representatives could be assigned to the appropriate outbreak with confidence. The majority of the outbreak isolates had none or 2 band differences from the index profile, although 3 isolates differed by 5-7 bands. The 2 exceptions among the unrelated strains differed by 4 bands, and 3 phage typing reactions, and were isolated from London and Berlin 3 years apart, while the 2 exceptions among the outbreak collection had clearly unique profiles with over 20 band differences from each other and the outbreak profiles. Cluster analysis using Dice coefficient and UPGMA gave cut-off values of 75-78% similarity overall for related isolates, while the closest similarity for unrelated strains was 70%. The results of this study together with those of the 6 previous reports of PFGE for \textit{S. marcescens} (which used either enzymes \textit{XbaI} or \textit{SpeI}) confirm that this technique is of value for this species and that with \textit{XbaI} at least, most epidemiologically related strains will only differ by 3-4 bands. However, on occasion up to 7 band differences can be found within an apparent outbreak, which may be suggestive of genetic drift.


Since 1984, 13 patients were entered into our study and 12 patients have completed one or more cycles of treatment with mixed bacterial vaccine (MBV), a natural biologic response modifier derived from \textit{Streptococcus pyogenes} and \textit{Serratia marcescens}. Eight patients with refractory malignancy were treated with MBV only (0.1 ml intravenously [IV]) twice weekly for 3-16 weeks (colorectal cancer, pancreatic cancer, chronic melanoma, breast cancer, lymphoma, chronic lymphocytic leukemia).

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lymphatic leukemia, hepatoma [two patients], sarcoma [three patients]). Four patients with advanced non-small cell lung cancer were treated with MBV in combination with low-dose cyclophosphamide, day 1; cisplatin, day 15; and MBV, 0.1 ml IV, days 5, 7, and 9. Two patients in this study received cyclophosphamide and cisplatin alone. The cycle was repeated every 28 days. Plasma interferon levels, interleukin-2 production by peripheral lymphocytes, and lymphocyte subpopulations were monitored. Interferon levels and interleukin-2 production showed increased or sustained values in general. In some patients, B-cells and helper T-cell populations increased, whereas T-suppressor cell numbers declined. With one exception, side effects were mild and consisted of fever greater than 37.8 degrees C (nine of 13), chills (11 of 13), increased respiratory rate (nine of 13), minor changes in blood pressure (seven of 13), and nausea (three of 13). One patient with non-small cell lung cancer had a partial response. Two patients with non-small cell lung cancer and one patient with refractory malignancy had stable disease and performance status at the end of 8 weeks of treatment; one patient with refractory malignancy was stable at the end of 4 weeks of treatment. In this pilot study, cancer patients treated with MBV showed objective evidence of immune stimulation with acceptable toxicity.

As smaller babies survive in neonatal intensive care units, late-onset septicemia with unusual pathogens appears. Between 1 January and 31 December 1998, in Hacettepe University Ihsan Dogramaci Children's Hospital Neonatal Intensive Care Unit, seven infants had S. marcescens isolates. Four babies had septicemia with the microorganism. The case fatality rate was 50 percent in infants with S. marcescens septicemia. The combination of ceftazidime or imipenem with amikacin appears appropriate for the treatment of newborns with Serratia infection.

We investigated an outbreak of Serratia marcescens in the adult intensive care unit of the University Hospital of Napoli. The outbreak involved 13 cases of infection by S. marcescens over a nine-month period and was caused by a single pulsed-field gel electrophoresis clone. The epidemic strain was multiply antibiotic resistant, producing an inducible Amp C-type beta-lactamase enzyme and carrying the trimethoprim-resistance gene and the adenyltransferase gene, which confers resistance to streptomycin and spectinomycin, within a class 1 integron. Antimicrobial therapy with beta-lactams was associated with S. marcescens acquisition in the intensive care unit.

The incidence and etiology of infections in 210 acute leukemias at the University of Mississippi Medical Center between 1962 and 1978 were reviewed. Infections episodes occurred 269 times in 148 patients. In 193 infections, potential pathogens were cultured.
Infection was a contributing cause of death in 89 patients. E. Coli, S. aureus, K. pneumoniae, and P. aeruginosa accounted for 58% of the isolates. No unusual patterns of antimicrobial resistance were observed. The outcome of the infections was related to the absence or resolution of neutropenia. Among 48 patients febrile on first admission, four cases of gram-negative pneumonia, two cases of fungal pneumonia, and two cases of pseudomonas cellulitis were diagnosed. We conclude that the etiology of infections was similar to that of cancer centers; multidrug-resistant gram-negative organisms were not prevalent; absence or resolution of neutropenia indicates a good prognosis for outcome of infection; and untreated acute leukemics may acquire opportunistic infections.


Twenty-four outbreaks of nosocomial bloodstream infection (BSI) were investigated by the Centers for Disease Control from Jan 1, 1977 to Dec 31, 1987. Intravascular pressure monitoring devices (transducers) were the most commonly identified source of bacterial and fungal BSI outbreaks and were implicated as the source of infection in eight (33%) outbreaks. These included outbreaks caused by Candida parapsilosis (2), Serratia marcescens (2), Klebsiella oxytoca (1), Pseudomonas cepacia (1), Acinetobacter calcoaceticus (1), and one polymicrobial bacteremia outbreak due to Acinetobacter, Pseudomonas, Citrobacter, and Enterobacter species. In all eight outbreaks, reusable transducers improperly disinfected or fitted with domes that had been improperly sterilized served as reservoirs for the organism. Compared with nosocomial BSI outbreaks not related to transducers, those in which transducers were implicated as a reservoir involved a larger mean number of patients (24 v 9; P = 0.007), and were significantly more likely to involve intensive care unit patients (23/24 v 3/9; P = 0.025) and to have a longer mean duration (11 v 3 months; P = 0.007). These findings show that the characteristics of transducer- and non-transducer-related BSI outbreaks differ, and that centers using intravascular pressure monitoring devices must be aware of and implement recommended infection control strategies for care and maintenance of these devices.


An outbreak of purulent meningitides in a hospital ward for preterm babies, caused by Contract No. IOM-2794-04-001

Health Effects of *Serratia marcescens*
Serratia marcescens strain of serovar 05/13 with multiple resistance, is described. Data on the results of the long-term observation of the ward showed that during three months preceding the outbreak the consecutive spread of the infective strain and its colonization of the intestine of children occurred. At the moment of the outbreak S. marcescens 05/13 was the dominating intestinal microflora in 37% of children in the ward and constituted 30% of the total aerobic flora in the intestine of the examined children. No S. marcescens strains were isolated from the feces and urine of the medical personnel and mothers. The importance of the observation of microflora colonizing newborn infants in the ward for the evaluation and prognostication of the epidemiological situation is discussed.

A case of metastatic Serratia marcescens (SM) endophthalmitis is described in a 57-year-old diabetic woman, after amputation of her leg above the knee because of peripheral vascular disease. SM cultured from the infected surgical stump was the source of septic emboli to her right eye and lungs, causing endophthalmitis and pneumonia. The ocular infection did not respond to appropriate antibiotic therapy and evisceration was required. SM infection can cause endophthalmitis refractory to antibiotics, and it should be aggressively treated when SM is cultured from any infected site.


OBJECTIVES: To investigate an outbreak of Serratia marcescens in a maternity hospital (November 1994 to May 1995). DESIGN: Retrospective analysis of epidemiological data and prospective study of systematic bacteriological samples from patients and environment, with genotyping of strains by arbitrarily primed polymerase chain reaction. SETTING: A private maternity hospital, Saint-Etienne, France. RESULTS: In the neonatal unit, 1 newborn developed a bacteremia, and 36 were colonized in stools with S marcescens. As the colonization of some newborns was shown to occur only a few hours after delivery, the inquiry was extended to other maternity wards, where 8 babies and 4 mothers were found to be colonized. Environmental sampling led to the isolation of S marcescens from a bottle of enteral feed additive in the neonatal unit and from the transducers of two internal tocographs in the delivery rooms. The genotyping of 27 strains showed two different profiles: a major epidemic profile shared by 22 strains (18 from babies of the neonatal unit, 2 from babies of other units, and 2 from breast milk) and another profile shared by 5 strains (2 from transducers of internal tocographs, 2 from babies, and 1 from a mother). The strain isolated from lipid enteral feeding was not available for typing. Although this source of contamination was removed soon from the neonatal unit, the outbreak stopped only when infection control measures were reinforced in the delivery rooms, including the nonreuse of internal tocographs. CONCLUSIONS: In delivery rooms, the quality of hygiene needs to be as high as in surgery rooms to prevent nosocomial colonization or infection of neonates at birth.

Nosocomial infection cause severe morbidity and mortality in pediatric patients. To find the cause of an infectious disease outbreak, epidemiologists need to determine early on whether a single strain of microorganism is responsible for the majority of cases. Phenotypic characteristics have been widely used in epidemiologic studies. However with most systems poor reproducibility, poor sensitivity have been reported and they do not reliably show enough strain-to-strain variation to be sufficiently discriminative. Molecular approaches like the analysis of the restriction fragment length polymorphism of the total DNA and of the rDNA regions and pulsed-field gel electrophoresis typing have now been applied with success to a large number of bacterial species associated with epidemics.


We report on nosocomial infections caused by Serratia marcescens occurring in a neonatal intensive care unit and a children's ward for cardiac intensive care. According to the plasmid pattern analysis, all isolated epidemic strains belonged to one clone. Multi-drug resistance, even to cephalosporins of the third generation and amikacin, was characteristic for all strains. Certain markers of S. marcescens (haemolysin, proteases, siderophores) which are thought to be related to virulence were studied but will require further investigation.

Serratia marcescens is an infrequent cause of cellulitis with only 5 reported cases. Four of the 5 patients were immunocompromised. Additionally, the cellulitis usually occurred at a site contiguous with a wound. We report a case of S. marcescens cellulitis in a patient with end-stage renal disease on chronic hemodialysis. The initial presentation was a soft tissue infection that progressed to septic shock. Ultimately, the patient responded to antibiotics and surgical debridement of infected tissue. This case serves as a reminder to consider infections due to gram-negative bacilli as a cause of cellulitis in immunocompromised patients regardless of the presentation.

During a 10-week period, 16 patients in a neurosurgery intensive care unit were involved in an outbreak of Serratia marcescens. The epidemic strain was found in several flasks of 1:4 diluted hexetidine solution, an antiseptic used for patient mouth washing. Testing of the bactericidal activity of the diluted antiseptic revealed that all the epidemic strains were able to grow in the diluted antiseptic solution. Strains isolated from clinical samples Contract No. IOM-2794-04-001

Health Effects of Serratia marcescens
and from the antiseptic solution were compared by random amplification of polymorphic DNA. Epidemiologic typing data implicated the diluted antiseptic solution as the single source of this *S. marcescens* outbreak.


**Bouza et al. 1987.** Serratia bacteremia. *Diagn.Microbiol.Infect.Dis.* Vol. 7(4): 237-247. During a 6-yr period, 146 patients at our institution had Serratia bacteremia (3.8% of the total number of episodes of bacteremia), with an incidence of 1.24/1000 admitted patients. We chose a random group of 50 cases for clinical analysis in the present study. The disease was community-acquired in 8% of the cases and nosocomially-acquired in the remaining 92%. The bacteremia was unimicrobial in 84% and part of a polymicrobial bacteremia in 16% of the episodes. The most frequently isolated species of the Serratia genus was *S. marcescens*. Portals of entry, in decreasing order of frequency, were: urinary, unknown, respiratory, and surgical wound infections. Clinically, the most frequent finding was fever (100%). Shock occurred in 28% of the patients, and none of our cases showed evidence of disseminated intravascular coagulation. We found 62% of Serratia isolates resistant to gentamicin. Overall mortality was 38% and factors associated with a poor prognosis were: severity of the underlying disease, critical clinical situation at onset of bacteremia, presence in the intensive care unit (I.C.U.), occurrence of shock or polymicrobial bacteremia, portal of entry in the respiratory tract, and inadequate treatment.

**Bouza et al. 1983.** Evaluation of ceftazidime in the treatment of severe bacterial infection. *J.Antimicrob.Chemother.* Vol. 12 Suppl A153-159. We investigated the clinical efficiency and safety of ceftazidime for treatment of 33 episodes of infection in 30 patients (17 males and 13 females), whose ages ranged from 9 to 92 years (mean 52.5). Fourteen patients had ultimately fatal disease and the remaining 16 had non-fatal diseases. The clinical condition of patients at the beginning of treatment was critical or poor in 16 cases. Episodes of infection treated were: 24 urinary tract infections (eight of them with concomitant bacteraemia), seven wound infections (one with concomitant bacteraemia and three with osteomyelitis), and two episodes of pneumonia. Twenty-nine episodes of infection were monomicrobial and the four remaining ones were polymicrobial. Significant organisms isolated were all aerobic or facultatively anaerobic Gram-negative rods and were responsible for the following episodes of infection: Escherichia coli (14), Pseudomonas aeruginosa (12), Pseudomonas cepacia (1), Proteus mirabilis (5), Serratia marcescens (2), Klebsiella (2), Enterobacter aerogenes (1) and Haemophilus influenzae (1). Total dosage of ceftazidime ranged from 28 to 240 g (mean 82.4 g), and mean duration of therapy was 17 days (range 8 to 44 days). The overall rate of clinical response to ceftazidime was 91%. Local and general tolerance to the drug was excellent. Enterococcal and/or candida colonization occurred in Health Effects of *Serratia marcescens*
12 episodes (36%) and superinfections by the same micro-organisms occurred in three episodes. Ceftazidime seems to be an effective and safe single agent for therapy of many bacterial infections, including those caused by Ps. aeruginosa.


Six cases of neonatal meningitis due to E. coli (3 cases), K. pneumoniae (1 case), P. aeruginosa (1 case) and *S. marcescens* (1 case), and eleven cases of suckling and little child meningitis caused by M. influenzae (10 cases) and N. meningitidis (1 case) were treated with ceftazidime. The susceptibility of agents was qualitatively tested according to the disk-diffusion method, and quantitatively according to biological dilution method on liquid broth. Ceftazidime concentrations in cerebrospinal fluid and sera were determined by the modified microbiological method using diffusion on agar. Efficacy of ceftazidime therapy was assessed by quickness of cerebrospinal fluid “;sterilization”;, duration of antimicrobial therapy and outcome of the disease. In spite of very good agents susceptibility to ceftazidime determined by disk-diffusion method, notable differences were found in quantitatively determined susceptibility (minimal inhibitory and minimal bactericidal concentration). Antibiotic penetrability was various in proportion with individual intensity of blood brain barrier break down. Bactericidal effect and prompt “;sterilization”; of cerebrospinal fluid within 48 hours after the beginning of ceftazidime therapy was achieved in those patients in whom ceftazidime cerebrospinal fluid concentration was 10 and several times higher than the minimal bactericidal concentration (all cases due to H. influenzae, N. meningitidis and E. coli). In these cases the issue of the disease was also favourable and none of the patients died. (ABSTRACT TRUNCATED AT 250 WORDS)


Over a 6-year period (1982 to 1988), 36 episodes of septic arthritis were diagnosed in 35 heroin addicts from Barcelona, Spain. Thirty (86%) were men and five (14%) were women, with a mean age of 24 years (range, 14 to 39). Twenty-nine episodes (80%) were monoarticular and seven (20%) were oligoarticular. The sacroiliac (16 cases), sternoclavicular (8), hip (5), and shoulder (4) joints were most frequently infected. *Staphylococcus aureus* and *Pseudomonas aeruginosa* were the etiological agents in 75% and 11% of episodes, respectively. Response to antibiotic treatment was good in 32 cases (90%), eight patients needed surgical drainage, and none died. We conclude that septic arthritis in heroin addicts localizes predominantly in axial joints. In our geographic area, infection with *S aureus* is more frequent than with gram-negative rods such as *P aeruginosa* or *Serratia marcescens*, which are most frequently found in reports from the United States.

During the period between October 1984 and January 1985, an outbreak of Serratia marcescens took place in the Serlin Maternity Hospital in Tel-Aviv. Four major and six minor infections were noted in newborn and preterm infants. An additional group of 24 neonates were asymptomatic carriers of *S. marcescens*. Extensive control measures were undertaken, including closing the SCBU to further admissions and the opening of a new SCBU. Other measures included maintaining babies in cohort groups, strict handwashing, and use of gloves and gowns. There was also intensified encouragement of breast feeding and thorough cleansing and disinfection of the SCBU and nurseries. After 3 months, the outbreak was controlled. No identified source for the outbreak was detected. We feel that the extensive measures employed were responsible for controlling the outbreak within a relatively short time.


Five geographically separate outbreaks of hospital acquired infection caused by gentamicin-resistant strains of Serratia marcescens occurred in the period October 1977 to January 1980 in southwest England. The patients affected were in wards for general or urological surgery, or in neurosurgical, cardiothoracic or general intensive therapy units. Asymptomatic colonization was more common than symptomatic infection, although deaths and serious infections occurred. Control of spread of the bacteria proved difficult. Most strains were resistant to many currently available antibiotics besides gentamicin; only one strain became resistant to amikacin. Representative isolates where characterized by O serotype, bacteriophage type, antibiotic sensitivity pattern, production of beta-lactamases and amino-glycoside-aminocyclitol (ACAG)-modifying enzymes, and plasmid visualization. Plasmid studies provided information that complemented conventional typing methods in determining epidemiological relationships among the outbreaks.


OBJECTIVE: To describe the epidemiology, interventions, and molecular typing methods used during the investigation and control of concurrent outbreaks of Serratia marcescens and methicillin-resistant Staphylococcus aureus (MRSA) infections in a neonatal intensive-care unit. *Infect.Control Hosp.Epidemiol.* Vol. 19(12): 924-928.
neonatal intensive-care unit (NICU). SETTING: A 206-bed women's and infants' hospital with a 48-bed NICU. DESIGN: A 22-week, prospective, descriptive study of all NICU infants with S marcescens or MRSA infection or colonization. Repetitive polymerase chain reaction (rep PCR) and pulsed-field gel electrophoresis (PFGE), respectively, were applied to the typing of S marcescens and MRSA isolates. INTERVENTIONS: Infants with S marcescens or MRSA infection or colonization were placed in isolation; all other infants were cohorted. A multidisciplinary task force implemented education for all hospital and medical staff regarding policies essential for outbreak control. Changes in physical setting and patient contact procedure were required to promote adherence to existing policies. RESULTS: Two premature infants had S marcescens infection, and five were colonized; rep PCR verified that both invasive and three of five colonizing isolates were related genotypically. Five bacteremic and 10 MRSA-colonized infants were identified; PFGE confirmed that 12 of the isolates had similar electrophoretic patterns. S marcescens infection was eliminated from the NICU 3 weeks after interventions were initiated. MRSA infections also were eliminated, and MRSA colonization fell to below pre-outbreak rates within 8 weeks. Despite a 100% increase in NICU patient days per month during the subsequent 2 years, no further clusters of S marcescens or MRSA infection have occurred. CONCLUSIONS: Concurrent outbreaks of S marcescens and MRSA in an NICU were confirmed by genotyping of strains. Control was achieved by isolation and cohorting of patients and strict adherence to NICU policies and procedures.


Serratia marcescens was isolated from the urine of five patients, two of whom subsequently developed septicaemia with other Gram-negative bacilli. Four of the five patients had undergone urodynamic investigation. An inadequately sterilized re-usable rectal balloon was identified as the source of infection.


The intraphagocytic killing of Escherichia coli, Serratia marcescens, Pseudomonas aeruginosa, and Salmonella typhi by ciprofloxacin (0.1, 1 and 5 microg/ml) within human neutrophils with intact and impaired (by phenylbutazone treatment) O2-dependent killing mechanisms was studied and compared with the extracellular killing in the same medium of the intraphagocytic killing, but omitting neutrophils. The MIC/MBC of ciprofloxacin in vitro (assays performed according to NCCLS specifications) were: 0.015/0.06 for E. coli, 0.12/32 for S. marcescens, 1/16 for P. aeruginosa, and 0.007/0.06 for S. typhi. Ciprofloxacin showed bactericidal activity both extracellular and within phenylbutazone-treated and untreated neutrophils. The minimum concentration of ciprofloxacin to kill 90% of phagocytosed bacteria within neutrophils with normal O2-dependent killing power after 30 min was: 0.1 microg/ml for E. coli, and S. typhi, 1 microg/ml for P. aeruginosa, and 5 microg/ml for S. marcescens. In contrast, exposure for 60 min was required to reach this percentage within phenylbutazone treated neutrophils. The minimum concentration to kill 90% of extracellular bacteria after 30 min was: 0.1 microg/ml for E. coli, P. aeruginosa and S. typhi, and 5 microg/ml, for S. marcescens. A positive interaction between ciprofloxacin and the O2-dependent mechanisms of
phagocytes was found. The reactive oxygen metabolites produced in the respiratory burst did not affect the intraphagocytic activity of ciprofloxacin. Phenylbutazone treatment of phagocytes would be a good experimental model to study the intraphagocytic killing of drugs in situations such as AIDS and chronic granulomatous disease where inefficient oxidative mechanisms of neutrophils exist.


In the present work, in vitro assays were used to investigate the toxicity of Serratia marcescens cytotoxin in cultured Chinese hamster ovary (CHO) cells. The time necessary to detect cellular alterations such as the onset of apoptosis, the perturbation of mitochondrial function, and cytoskeletal changes was assessed. The internalization of the cytotoxin by CHO cells was also examined. Within 10-15 min of exposure to cytotoxin, CHO cells became round, the nucleus shrank, the chromatin became more compact, and cytoplasmic blebs appeared on the cell surface. TUNEL (TdT-mediated dUTP nick end labeling) and propidium iodide staining identified some nuclei with fragmented DNA, and electrophoresis of CHO cell DNA obtained after 30-min exposure to S. marcescens toxin showed a pattern of DNA fragments typically associated with apoptosis. The cells also lost their characteristic actin organization within 10 min of exposure to cytotoxin. Lactate dehydrogenase leakage was detected after 20-min exposure to the cytotoxin and increased with time thereafter. Concomitantly, there was a time-dependent reduction in mitochondrial activity. Fluorescein-labeled S. marcescens cytotoxin was detected only on the surface of CHO cells, even after 30-min exposure to the toxin. These results show that there was no internalization of the toxin by CHO cells, and that, once bound to the cell surface, the toxin was able to induce changes in intracellular metabolism and to trigger cell death by apoptosis.


Serratia marcescens cytotoxin was purified to homogeneity by ion-exchange chromatography on a DEAE Sepharose Fast Flow column, followed by gel filtration chromatography on a Sephadex G100 column. The molecular mass of the cytotoxin was estimated to be about 50 kDa. Some biological properties of the cytotoxin were analyzed and compared with well-characterized toxins, such as VT1, VT2 and CNF from Escherichia coli and hemolysin produced by S. marcescens. The sensitivity of the cell lines CHO, HeLa, HEp-2, Vero, BHK-21, MA 104 and J774 to the cytotoxin was determined by the cell viability assay using neutral red. CHO and HEp-2 were highly sensitive, with massive cellular death after 1 h of treatment, followed by BHK-21, HeLa, Vero and J774 cells, while MA 104 was insensitive to the toxin. Cytotoxin induced morphological changes such as cell rounding with cytoplasmic retraction and nuclear compactation which were evident 15 min after the addition of cytotoxin. The cytotoxic assays show that 15 min of treatment with the cytotoxin induced irreversible intoxication of the cells, determined by loss of cell viability. Concentrations of 2 CD50 (0.56 g/ml) of purified cytotoxin did not present any hemolytic activity, showing that the cytotoxin is distinct from S. marcescens hemolysin. Antisera prepared against S. marcescens cytotoxin did not neutralize the cytotoxic activity of VT1, VT2 or CNF toxin, indicating
that these toxins do not share antigenic determinants with cytotoxin. Moreover, we did not detect gene sequences for any of these toxins in S. marcescens by PCR assay. These results suggest that S. marcescens cytotoxin is not related to any of these toxins from E. coli.


Acute osteomyelitis is the clinical term for a new infection in bone. This infection occurs predominantly in children and is often seeded hematogenously. In adults, osteomyelitis is usually a subacute or chronic infection that develops secondary to an open injury to bone and surrounding soft tissue. The specific organism isolated in bacterial osteomyelitis is often associated with the age of the patient or a common clinical scenario (i.e., trauma or recent surgery). *Staphylococcus aureus* is implicated in most patients with acute hematogenous osteomyelitis. *Staphylococcus epidermidis, S. aureus, Pseudomonas aeruginosa, Serratia marcescens* and *Escherichia coli* are commonly isolated in patients with chronic osteomyelitis. For optimal results, antibiotic therapy must be started early, with antimicrobial agents administered parenterally for at least four to six weeks. Treatment generally involves evaluation, staging, determination of microbial etiology and susceptibilities, antimicrobial therapy and, if necessary, debridement, dead-space management and stabilization of bone.


The frequency, predisposing factors, therapy, and outcome of 45 episodes of bacteremia due to *Staphylococcus aureus* were reviewed in adult cancer patients. A poor performance status (i.e., patients largely bedridden), progressive neoplastic disease, and compromise of the mucocutaneous defense barriers characterized the patients with *S. aureus* sepsis. Seventeen patients died soon after the onset of infection: seven (16%) as direct result of staphylococcal sepsis, seven of factors unrelated to infection, and three of secondary sepsis due to gram-negative bacilli. The data presented here and reported by others indicated that (1) the incidence of staphylococcal sepsis in cancer patients has recently increased from a low point of 5% to a level as high as 30%; (2) breaches in the epithelium are the most important factors determining risk; (3) there are three effective approaches to therapy depending upon the clinical setting; and (4) the outcome appears to be determined by the status of the neoplastic disease and by early institution of appropriate antimicrobial therapy.


An epidemiological survey was carried out which included a dual epidemic of septicaemia and pseudo-bacteremia caused by *Serratia marcescens*. The survey enabled 15 septicaemias and 43 pseudobacteremias to be detected in a regional hospital between March and August, 1983. Two mishandlings were at the origin of the outbreak: citrated tube normally reserved for coagulation tests were severely contaminated by *Serratia marcescens*, and inaccurate samplings had been made. Once the mechanisms of contamination were found, specific preventive measures put an end to the epidemic. The
authors insist on the need for uncontaminated tubes and citrate solutions and for the development of precise sampling methods which are essential to avoid the occurrence of pseudo-bacteremia or septicemia. It is important to detect such epidemics at an early stage by an efficient control of nosocomial infections, thus avoiding their extension.


**Chernin et al. 1997.** Molecular cloning, structural analysis, and expression in Escherichia coli of a chitinase gene from Enterobacter agglomerans. *Appl.Environ.Microbiol.* Vol. 63(3): 834-839. The gene chiA, which codes for endochitinase, was cloned from a soilborne Enterobacter agglomerans. Its complete sequence was determined, and the deduced amino acid sequence of the enzyme designated Chia_Entag yielded an open reading frame coding for 562 amino acids of a 61-kDa precursor protein with a putative leader peptide at its N terminus. The nucleotide and polypeptide sequences of Chia_Entag showed 86.8 and 87.7% identity with the corresponding gene and enzyme, Chia_Serma, of Serratia marcescens, respectively. Homology modeling of Chia_Entag's three-dimensional structure demonstrated that most amino acid substitutions are at solvent-accessible sites. Escherichia coli JM109 carrying the E. agglomerans chiA gene produced and secreted Chia_Entag. The antifungal activity of the secreted endochitinase was demonstrated in vitro by inhibition of Fusarium oxysporum spore germination. The transformed strain inhibited Rhizoctonia solani growth on plates and the root rot disease caused by this fungus in cotton seedlings under greenhouse conditions.

**Choi et al. 2002.** Serratia bacteremia in a large university hospital: trends in antibiotic resistance during 10 years and implications for antibiotic use. *Infect.Control Hosp.Epidemiol.* Vol. 23(12): 740-747. OBJECTIVE: To identify antibiotic resistance trends and risk factors for resistance of Serratia species to third-generation cephalosporins. DESIGN: Retrospective survey of medical records. SETTING: A 2,200-bed, tertiary-care hospital. PATIENTS: One hundred twenty-two patients with Serratia bacteremia between January 1991 and June 2001. METHODS: Infectious disease physicians collected data from medical records regarding patient demographics, underlying disease or condition, portal of entry, microorganism, antibiogram, complications, antibiotics received, and outcome. RESULTS: Among 122 Serratia isolates, 117 (95.9%) were Serratia marcescens and 110 (90.2%) were of nosocomial origin. During the study period, the 122 isolates showed a high rate of resistance to third-generation cephalosporins (45.9%) and extended-spectrum penicillins (56.6%). The resistance rate to ciprofloxacin was 32.0%. The resistance rate to third-generation cephalosporins increased from 31.7% for 1991 to 1995 to 54.9% for 1996 to 1998 and 50.0% for 1999 to 2001. In the multivariate analysis, prior use of a second-generation cephalosporin (adjusted odds ratio [OR], 5.90; 95% confidence interval 1.66-21.1) was an independent risk factor for resistance to third-generation cephalosporins.
interval [CI90], 1.41 to 24.6; P = .015) or a third-generation cephalosporin (OR, 3.26; CI95, 1.20 to 8.87; P = .020) was a strong independent risk factor for resistance to third-generation cephalosporins. The overall case-fatality rate was 25.4% (Serratia bacteremia-related case-fatality rate, 13.1%). CONCLUSION: Prior use of a second- or third-generation cephalosporin was the most important risk factor for bacteremia with Serratia resistant to third-generation cephalosporins, suggesting the need for antibiotic control. The potential role of patient-to-patient spread could not be fully evaluated in this retrospective study.

Chokephaibulkit et al. 2002. The outbreak of Serratia marcescens bacteremia in a pediatric ward, Siriraj Hospital 1997. J.Med.Assoc.Thai. Vol. 85 Suppl 2S674-81. Between October 20 and November 11, 1997, Serratia marcescens bacteremia was identified in 8 patients in a pediatric ward at Siriraj Hospital. The organism was isolated from 17 blood and 3 bone marrow specimens. The only common associated factor in these patients was that they all had received an intravenous fluid infusion. In the attempt to investigate the source of S. marcescens implicated in the outbreak, 108 specimens of intravenous fluid, 3 intravenous fluid bottle caps, 4 specimens from intravenous fluid tubing sets, 21 specimens of antiseptics used on the ward, 28 specimens of rectal swabs from patients on the ward, 1 sample of blood culture media prepared by the hospital for routine use, and 62 environmental specimens including hand swabs of the medical personnel, refrigerator, air conditioning, milk samples, room air, water sink, wooden splint and adhesive tape used to immobilize the intravenous access. Of 227 specimens sent for culture, S. marcescens was isolated from only one specimen collected from the in-use intravenous fluid given to a patient with Serratia bacteremia. S. marcescens was not found in any other surveillance culture. The 8 patients were placed under quarantine in the same room with an exclusive nursing team. With the investigation and intervention including monitoring for meticulous hand washing of the ward staff, the outbreak was stopped within 7 days. Although the investigation failed to discover the environmental reservoir of S. marcescens in this outbreak, the data suggested that intravenous fluid was probably the route of transmission and the medical personnel played an important role in spreading the infection.

Christensen et al. 1982. Epidemic Serratia marcescens in a neonatal intensive care unit: importance of the gastrointestinal tract as a reservoir. Infect.Control. Vol. 3(2): 127-133. Between a March and December of 1979, an outbreak of infections due to multiply antibiotic resistant Serratia marcescens took place in a 50-bed neonatal intensive care unit. Fifteen neonates suffered major infections (sepsis, meningitis and pneumonia) with one death, and 20 suffered minor infections (conjunctivitis, cystitis, wound infections). Epidemiologic investigation failed to reveal a common source; S. marcescens, however, was isolated from an employee's hand, emollient skin cleanser, suction tubing, and three in-use manual infant resuscitation bags. The skin cleanser and equipment-cleaning agents were ineffective against S. marcescens. Asymptomatic, colonized infants were the major reservoir of S marcescens. These infants were identified by daily cultures of the nose, umbilicus and rectum. The rectal swab most commonly (76%) yielded first-positive cultures in previously uncolonized infants, and was ultimately positive in 92% of colonized infants. A control program was begun by: 1) removing all inanimate sources of
S. marcescens; and 2) cohorting patients and staff into a S. marcescens-exposed group and a new patient group. The new patient group of infants was surveyed by daily triple-site cultures for colonization and subsequent transfer to the S. marcescens-exposed group. After four months, the epidemic was controlled and the organism eradicated from the neonatal intensive care unit.


**OBJECTIVE:** Define the applicability of a rapid molecular typing scheme to study the epidemiology of a Serratia marcescens outbreak. **DESIGN:** With the assistance of a simple bacterial lysis technique, isolates of S marcescens from a putative outbreak were genotyped with the polymerase chain reaction technology for which primers were chosen on the basis of previously defined enterobacterial repetitive intergenic consensus sequences. **SETTING:** Pediatric ICU. **PATIENTS:** Intensively monitored patients who were found to yield S marcescens from any body site during the epidemic period. **RESULTS:** Over an 8-month period, 12 ICU patients were either infected or colonized with S marcescens. All of these patients were transiently supported by artificial ventilation. During the epidemiologic investigation, a dilution error in a high-level glutaraldehyde disinfectant, which was being used for some ventilator components, was observed. Rectification of the error was associated with an abrupt termination of the outbreak. Enterobacterial repetitive intergenic consensus polymerase chain reaction was easily applicable to this setting and it defined 4 distinct genotypes among the 12 isolates. **CONCLUSION:** The typing method is easily implemented and offers great promise as an epidemiologic tool. The associated investigation served to emphasize that an outbreak may occur with more than one epidemic strain and that strain heterogeneity itself does not exclude an outbreak.

**Clarke. 1976.** Infection in the intensive care unit. *Aust.N.Z.J.Surg.* Vol. 46(4): 318-321. An epidemic of infection associated with Serratia marcescens and other Gram-negative organisms resistant to aminoglycosides and other chemotherapeutic agents occurred in the Intensive Care Unit, and spread to other areas of the hospital. This paper describes the problems of sepsis in the critically ill patient, outlines the occurrence of organisms in the patients concerned in this epidemic, and discusses the policies adopted to control the incidence of life-threatening infection caused by bacteria resistant to all other agents.


An epidemic of infection associated with Serratia marcescens and other Gram-negative organisms resistant to aminoglycosides and other chemotherapeutic agents occurred in the intensive care unit of St Vincent's Hospital, Melbourne, and spread to other areas of the hospital. This paper describes the problems of sepsis in the critically ill patient, outlines the occurrence of organisms in the patients concerned in this epidemic, and discusses the policies adopted to control the incidence of life-threatening infection caused by bacteria resistant to all other agents.

Recurrent tunnel stenosis of the left ventricular outflow tract following operation for subaortic stenosis and hypoplastic aortic annulus remain a challenge for pediatric cardiac surgeons. We have recently applied a new technique of extended aortic root replacement using an aortic allograft to treat three patients who had previously been operated upon for subaortic stenosis and three who had aortic stenosis with a hypoplastic aortic annulus. This new procedure combines the concept of aortoventriculoplasty with allograft aortic root replacement and coronary artery reimplantation. The valved aortic homograft is used in place of an aortic valve prosthesis and the attached anterior mitral leaflet augments the interventricular septum to relieve the subvalvular left ventricular outflow tract obstruction. The coronary ostia are then reimplanted into the allograft and distal graft to ascending aorta anastomosis completed. Allograft aortic tissue is then used to patch the right ventricular outflow tract. There have been no operative or late deaths. One patient developed Serratia marcescens mediastinitis but recovered uneventfully after mediastinal drainage. Two cases of transient complete heart block reversed spontaneously. A patient with type II hyperlipidemia developed postpericardiotomy syndrome early, which resolved but then required reoperation at six months for stenosis of the distal anastomosis and left main coronary stenosis, both thought to be complications of his underlying disease. Completely benign convalescence and early follow-up has occurred in the last two patients. This modified technique using aortic allograft was very helpful in treating these difficult problems, and the lack of mortality, limited morbidity, and good function results are encouraging.

Seventy isolates of Serratia marcescens were obtained from 30 patients in different units of one hospital between April 1982 and February 1983. No common source was found. Not all isolates were multi-resistant and nearly all that were, fell into two main groups, A and B. These groups were defined by phage typing and cephalosporin sensitivity, all apart from one Group B isolate were multi-resistant, whereas Group A isolates contained multi-resistant and sensitive strains. Plasmid screening, resistance transfer studies and plasmid elimination experiments demonstrated that the multi-resistant phenotype was due to a 120 Mdal transmissible plasmid. Resistance to cephalosporins was chromosomally encoded.

Neutrophilic eccrine hidradenitis (NEH) is a rare dermatosis which usually develops after administration of chemotherapeutic treatments. An infective origin is exceptional. We report a patient, previously operated on for ependymoma, who presented with an eruption typical of NEH even though he had not received chemotherapy. Culture of a skin biopsy revealed Serratia marcescens. The dermatosis improved after antibiotic therapy but recurred twice and culture again isolated S. marcescens; electron microscopy revealed cytoplasmic inclusions within neutrophils, suggestive of bacteria. The disease improved every time with appropriate antibiotic therapy. An infective aetiology for NEH is rare: three such cases have been reported, of which one was due to S. marcescens. The originality of our case is the recurrence of the disease on three occasions with the same
bacterium isolated on each occasion, with disease remission after antibiotic therapy. This case confirms that infections may be a possible cause of NEH and underlines the necessity to search for infective agents, especially in patients immunocompromised by haematopoietic malignancies and/or chemotherapeutic treatments.


An outbreak of amikacin-resistant Enterobacteriaceae (KES) occurred in the Intensive Care Nursery (ICN) of the Louisville General Hospital from January 1978 through March 1978. Epidemic disease and an increased colonization rate in newborn infants due to amikacin-resistant microorganisms has not been documented previously. Three of the 11 neonates died. The organisms isolated were resistant to amikacin and two experimental aminoglycosides, sissomicin and netilmicin. The outbreak was contained following institution of several control measures, including pharyngeal inoculation of an experimental strain of alpha streptococcus in four infants.


Gram-negative bacteremia is a common cause of infection in hospitalized patients. Serratia sepsis is known to cause clinically significant morbidity and mortality. The most common species involved is *Serratia marcescens.* Clinicians have been uncertain as to the role of *Serratia odorifera* biogroup 1 as a human pathogen because most isolates have not been associated with invasive disease. In previous publications, 12 cases have been described in which *S odorifera* biogroup 1 caused sepsis. These observations verify the organism's role as a human pathogen.


Electric fly killers (EFKs) are commonly used to control flying insects that enter food establishments. For establishment of the incidence of pathogen-bearing insects in food establishments, insect samples obtained from EFK trays could be used. The principal difficulty with this approach is that the survival time of microorganisms on or within insect corpses after electrocution is unknown. This study determined the survival of *Serratia marcescens* (as a representative of the enteric bacteria) within houseflies following their electrocution by a commercial EFK. *S. marcescens* was successfully ingested by houseflies and survived on and within the corpses after electrocution for up to 5 weeks. Maximal levels of bacteria were recovered 24 h postelectrocution. The study also demonstrates the ability of ingested *S. marcescens* to out-compete resident microbial flora within houseflies. The findings are intended to pave the way for further research to determine the incidence of pathogen-laden flying insects in food establishments.

Bullous cellulitis is a distinctive form of cellulitis most often caused by beta hemolytic streptococci. This report describes a case of bullous cellulitis caused by Serratia marcescens in an elderly diabetic woman with peripheral vascular disease. A discussion of this ubiquitous, nosocomial pathogen follows.


A nosocomial infection outbreak occurred in the Intensive Care Unit (ICU) of the Instituto Nacional de Pediatria (INP) in Mexico City, during the months of March, April and May in 1988. Serratia marcescens was isolated as the etiological agent for this epidemic. Up to date, the source of contamination, the spreading and the pathogenic mechanisms which were involved in this outbreak remain unknown. In order to study the dynamics of the bacterial population involved in this outbreak, all strains of nosocomial *S. marcescens* isolated during 1988 were collected and studied. Eighty nosocomial strains were analysed. For this purpose we used four different markers: antibiotic susceptibility, presence of plasmids, exoenzyme production and pigment synthesis from a precursor. Using these markers, we were able to establish that five subpopulations of bacteria were present during the ICU outbreak, and that one of these subpopulations, VIII-A, was the most frequently isolated. A short time after this outbreak, we obtained *S. marcescens* isolates with similar properties which proceeded from other hospital units, suggesting intrahospital dissemination of the strain in question. We believe that, eventually, this study will allow us to establish bacterial spreading models within our institution.


The incidence of systemic or local infections due to gram-negative bacilli in an Infant Ward from September 1969 to December 1976 was 7.9%. The 29.34% were septicemia, most of them as epidemic outbreaks caused by Pseudomonas aeruginosa, Klebsiella-Enterobacter and Serratia marcescens. Two facts are to be emphasized: an almost complete disappearance of systemic infections with Pseudomonas starting from 1972, and the global predominance of the group Klebsiella-Enterobacter, particularly evident from 1970 to 1972.


Over a recent 22 month period, 222 patients in two adjacent hospitals became infected with a multiply antibiotic-resistant strain of Serratia marcescens; 13 were bacteremic. Nineteen patients with clinically significant infections received amikacin. Nine of 11 patients with urinary tract infections were cured. In contrast, only one of eight patients with pneumonia or other deep tissue infections was cured and four died. These eight patients were severely ill; many had infections with multiple microorganisms. In four of five patients in whom the infection failed to clear promptly, Serratia strains became increasingly resistant to amikacin during therapy and these strains contributed to the
death of two of these patients. Amikacin proved useful in treating patients with infections due to gentamicin-resistant *S. marcescens* organisms, especially urinary tract infections. However, the capacity of some strains of *S. marcescens* to develop resistance to amikacin may limit the usefulness of this antibiotic in the treatment of deep tissue infections which involve this microorganism.


The cytotoxicity of prodigiosin, an antibiotic and potential trypanocide produced by *Serratia marcescens*, and Benznidazole, a trypanocidal drug, were assayed on V79 fibroblast cell line. Three independent endpoints for cytotoxicity were evaluated; namely, the nucleic acid content (NAC), MTT reduction and neutral red uptake (NRU). IC(50) values of 1-20 microM were obtained for prodigiosin in the NRU, MTT and NAC tests. Prodigiosin had greater trypanocidal activity (IC(50)=5 microM) than Nifurtimox (IC(50)=150 microM) a known trypanocide drug used in Chagas' disease therapy. Benznidazole was less toxic (IC(50)=2000 microM) than prodigiosin (IC(50)=1-20 microM) in V79 cells based on the MTT and NAC assays. Benznidazole stimulated the NRU until 2 mM. Indeed, the cell viability measured with the NRU was higher at all concentrations of benznidazole tested than that measured by MTT reduction and NAC assays.


During an outbreak of *Serratia marcescens* from May to November 1993 43 strains obtained from 27 ICU patients infected or colonized with multiresistant *S. marcescens* were genotypically characterized with random amplified polymerase chain reaction (RAPD-PCR)-fingerprinting. In addition, 43 epidemiologically unrelated control isolates were selected. PCR-fingerprinting identified ten different genotypes of *S. marcescens* among the outbreak related strains. One predominant genotype was demonstrated in 21/43 isolates of 11/27 patients. A cluster of this genotype was found in seven/eight patients on the cardiosurgical ICU. The epidemiologically unrelated strains all showed different genotypes as compared to the predominant type. This survey proved RAPD-PCR to be a highly discriminatory and reproducible method for epidemiological studies of *S. marcescens* strains in nosocomial outbreaks.


Enteroaggregative Escherichia coli (EAiEC) is a distinct category of diarrheal pathogen implicated as the cause of persistent diarrhea. The pathogen exhibits a characteristic “;stacked-brick”; pattern of aggregation when incubated with HEp-2 cells. The outer
membrane protein (OMP) profile of a prototype EAggEC strain (F03) reflected the presence of one major 30-kDa protein. The OMP is expressed in the presence of the 60-MDa plasmid that the strain harbors. Antibodies were raised against the OMP by injecting the protein into a rabbit. The manifestation of an adherence phenotype on HEp-2 cells was observed for F03 and other strains that express OMP in the presence and absence of anti-OMP serum. Clumps of bacteria forming an aggregative pattern were observed in the HEp-2 cell assay in the absence of OMP antibodies, whereas a few bacteria attached to the cells in the presence of OMP antibodies. Mannose-resistant hemagglutination of human erythrocytes observed in the presence of EAggEC strains was inhibited in the presence of anti-OMP serum. Sequence analysis of a peptide generated by protease digestion of OMP exhibited 90% homology to a peptide of flagellin protein encoded by the hag gene of Serratia marcescens. Immunolabeling of the outer membrane by colloidal gold confirmed the protein to be an OMP. Our results suggest that the OMP of EAggEC have common antigenic properties. Antibodies raised against the protein can prevent adherence in vitro and could potentially interrupt the natural disease.

Thirty-one moderately or severely ill hospitalized patients with proved (25 patients) or suspected (six) bacterial infections were randomly allocated to receive imipenem/cilastatin (16) or cefotaxime (15). The median age, sex, duration of therapy, underlying disease, and types of infection were similar in both groups. Nineteen patients with pneumonia, eight with soft tissue infection, and four with acute pyelonephritis were included. The pathogens isolated included Escherichia coli (six), Streptococcus pneumoniae (five), Streptococcus pyogenes (five), Haemophilus species (four), Proteus species (three), Staphylococcus aureus (three), and Serratia marcescens (two). In the imipenem/cilastatin group, 13 patients were cured of their infections and three showed improvement. In the cefotaxime group, nine were cured, three showed improvement, and three showed no improvement. Nine patients treated with imipenem/cilastatin developed phlebitis, as compared with eight treated with cefotaxime. One patient treated with cefotaxime developed diarrhea. During therapy, potential pathogens were isolated from four patients in the imipenem/cilastatin group (Candida species [two] and Pseudomonas maltophilia [two]), as compared with eight in the cefotaxime group (enterococci [two], Pseudomonas aeruginosa [two], Candida species [two], Acinetobacter anitratus [one], and Pseudomonas fluorescens [one]). There were no recognized superinfections.

BACKGROUND: The extraordinary growth properties of most microorganisms in 10% and 20% lipid emulsions has led to the Centers for Disease Control and Prevention recommendation that if lipids are given through an i.v. line, the administration set should be replaced every 24 hours rather than the usual 72-hour interval used for crystalloid solutions, including those used for conventional total parenteral nutrition. For nearly 15 years, parenteral alimentation has been given as a total nutrient admixture (TNA), with
the glucose, amino acids, and lipid mixed within the same bag and infused continuously over 24 hours. METHODS: We prospectively studied in a representative TNA (17.6% glucose, 5% amino acids, 4% lipid; pH 5.6, osmolality 1778) and in a control solution, 5% dextrose-in-water (D5%/W), the growth properties at 4, 25, and 35 degrees C of three isolates each of Staphylococcus epidermidis, Staphylococcus aureus, Enterobacter cloacae, Klebsiella oxytoca, Serratia marcescens, Acinetobacter calcoaceticus, Stenotrophomonas maltophilia, Pseudomonas aeruginosa, Burkholderia cepacia, Flavobacterium spp, and Candida albicans, and two isolates of Staphylococcus saprophyticus, the species that are most likely to contaminate TNA during preparation or administration and that have been implicated in >;95% of all outbreaks and sporadic cases of nosocomial bloodstream infections traced to contaminated parenteral admixtures reported in the world literature. RESULTS: Growth in TNA at 25 and 35 degrees C occurred with only two species, C. albicans and S. saprophyticus, and only after 24 to 48 hours; D5%/W allowed growth at 25 degrees C of two gram-negative species, S. marcescens and B. cepacia. CONCLUSIONS: We conclude that TNA is a poor growth medium for most nosocomial pathogens and is no better than D5%/W. The need to replace administration sets every 24 hours with TNA should be reconsidered and ideally be studied in a prospective randomized trial.

In this open study the efficacy and tolerability of rufloxacin in a single dose of 400 mg the first day and 200 mg the nine consecutive days was studied in 26 patients with an acute exacerbation of chronic bronchitis. Twenty-two patients were evaluable for efficacy. Four patients stopped treatment prematurely after five days because of clinical cure. At the enrollment visit a pathogen was isolated in the sputum sample in 19 of 22 evaluable patients. The predominant pathogens were Streptococcus pneumoniae and Moraxella catarrhalis. In 17 of these 19 bacteriologically evaluable patients the initial infecting organism was eradicated from specimens obtained within 48 hours after the end of therapy. There was one case of persistent infection caused by S. pneumoniae (MIC 4 mg/l), one patient had a superinfection with Serratia marcescens (MIC 1 mg/l) susceptible to rufloxacin and therapy was stopped after five days due to clinical failure. One week after the end of therapy, 15 patients remained free from infection whilst one patient experienced reinfection with Klebsiella pneumoniae (MIC 0.5 mg/l). Clinical cure or improvement was observed in 21 of 22 patients. Mild adverse events were reported by two of 26 enrolled patients. In one patient, complaining of headache and dizziness, the adverse events were considered possibly study drug related. No abnormal laboratory findings were reported. Nadir plasma levels of rufloxacin were measured and no accumulation in plasma was observed during treatment. A ten day course of an oral single dose of rufloxacin proved efficacious and was well tolerated in patients with an acute exacerbation of chronic bronchitis.(ABSTRACT TRUNCATED AT 250 WORDS)

In this retrospective investigation, we documented the bacterial colonization of 79
patients with chronic wounds, who had been treated between January 2002 and May 2003 in an outpatient wound healing clinic of a university dermatology program. We isolated 106 facultative pathogenic bacterial strains of which 56 were Staphylococcus aureus, 19 Pseudomonas aeruginosa, 11 Escherichia coli, 4 Proteus mirabilis, 4 Enterobacter cloacae, 2 Serratia marcescens, 2 Streptococcus group G und 8 further species. 68 of these bacterial strains were gram-positive and 46 gram-negative. Moreover we identified one patient with Candida parapsilosis. Therefore, 70.8% of all patients showed Staphylococcus aureus in their chronic wounds. Determination of the specific resistances showed 17 patients to be colonized with oxacillin-resistant Staphylococcus aureus (ORSA) strain; this corresponds to 21.5% of all patients. Consequently, 30.4% of all Staphylococcus aureus isolates were ORSA strains. All of the ORSA isolates were sensitive to vancomycin. Sensitivity to tetracycline was documented in 15, to amikacin in 13, to clindamycin in 7, to gentamicin and erythromycin in 6 of the ORSA-positive patients. In the case of trimethoprim/sulfamethoxazole, 10 were sensitive and 3 were intermediate in sensitivity. Beside the obligate resistance to oxacillin, penicillin G, ampicillin, cefuroxime and imipenem, none of the ORSA was sensitive to ofloxacin. The results of our investigations demonstrate the actual spectrum of bacterial colonization in chronic wounds of patients in an university dermatologic wound clinic and underline the growing problem of ORSA.


We have evaluated 44 cases of Serratia marcescens bacteremia (SB). Most took place in surgical services (57%) and the ICU (34%). In one occasion, the cases developed as an epidemic outbreak. SB basically developed in patients with underlying diseases (neoplasia in 32%, heart disease in 16%, chronic bronchitis in 14% and miscellaneous in 20%) in whom some invasive procedure had been carried out (98%). The most common complication was septic shock. In 17 cases the infection was polymicrobial. The most common serogroup was 0:5 (41%). 98% of strains were resistant to cephalothin, 78% to ampicillin and 29% to tobramycin. The mortality rate was 39% and the most common cause of death was septic shock. The factors which adversely influenced prognosis were as follows, in order of decreasing importance: leukocytosis, thrombopenia, associated gram-positive infection, age older than 65 years, “non-typable” serogroup, unknown portal of entry, epidemic case and septic shock.


OBJECTIVE: To investigate an outbreak of invasive disease due to Enterobacter cloacae and Serratia marcescens in a surgical intensive care unit (ICU). DESIGN: Pulsed-field gel electrophoresis (PFGE) analysis of restriction fragments was used to characterize the outbreak isolate genotypes. A retrospective cohort study of surgical ICU patients was
conducted to identify risk factors associated with invasive disease. Unit staffing data were analyzed to compare staffing levels during the outbreak to those prior to and following the outbreak. SETTING: An urban hospital in San Francisco, California.

PATIENTS: During the outbreak period, December 1997 through January 1998, there were 52 patients with a minimum ICU stay of ≥ or = 72 hours. Of these, 10 patients fit our case definition of recovery of E. cloacae or *S. marcescens* from a sterile site.

RESULTS: PFGE analysis revealed a highly heterogeneous population of isolates. Bivariate analysis of patient-related risk factors revealed duration of central lines, respiratory colonization, being a burn patient, and the use of gentamicin or nafcillin to be significantly associated with invasive disease. Both respiratory colonization and duration of central lines remained statistically significant in a multivariate analysis. Staffing data suggested a temporal correlation between understaffing and the outbreak period.

CONCLUSIONS: Molecular epidemiological techniques provided a rapid means of ruling out a point source or significant cross-contamination as modes of transmission. In this setting, patient-related risk factors, such as respiratory colonization and duration of central lines, may provide a focus for heightened surveillance, infection control measures, and empirical therapy during outbreaks caused by common nosocomial pathogens. In addition, understaffing of nurses may have played a role in this outbreak, highlighting the importance of monitoring staffing levels.


The new acylampicillin derivatives azlocillin, mezlocillin, and piperacillin have an increased activity against many gram-negative bacilli, especially *Klebsiella pneumoniae*, *Serratia marcescens*, and *Pseudomonas aeruginosa*, when compared with the carboxypenicillins carbenicillin and ticarcillin. The new penicillins show synergistic activity in combination with aminoglycosides but, when combined with other beta-lactams, may be synergistic (piperacillin and moxalactam; mezlocillin and cefoperazone), indifferent, or antagonistic (azlocillin, mezlocillin, or piperacillin and cefoxitin or cefamandole). The in vitro activity of these agents, either alone or in combination, appears to correlate with in vivo efficacy in animal models. The new penicillins are clinically effective for a very broad range of infections, including life-threatening nosocomial infections. Adverse effects with these, as with other semisynthetic penicillins, are minimal. Attention must be paid to the potential for infection by naturally resistant, gram-negative bacilli such as beta-lactamase-producing *Escherichia coli* and for the emergence of resistance during therapy. The granulocytopenic patient should receive these agents only in conjunction with another agent, such as an aminoglycoside; this combination will often result in a synergistic effect when tested in vitro. The carboxypenicillins and the newer penicillins have substantial similarities, and prospective, comparative studies have so far failed to demonstrate significant clinical superiority. However, the increased activity of the acylampicillins may be advantageous for the treatment of infections due to *K. pneumoniae* and *P. aeruginosa*.


A spectrophotometric Limulus amebocyte lysate assay using lysis filtration and
centrifugation has been developed for the detection of gram-negative bacteria in blood. The assay is directed at detection of endotoxin in viable and nonviable bacteria present in the blood-stream and not detection of free endotoxin in plasma. The assay was evaluated in a model of peritonitis in which rats were challenged with an inoculum consisting of sterilized human feces, barium sulfate, and one of eight species of bacteria. This assay was able to detect gram-negative bacteremia due to Escherichia coli, Pseudomonas aeruginosa, Serratia marcescens, Proteus mirabilis, and Klebsiella pneumoniae in the rat model when compared with sham-inoculated uninfected rats. The assay failed to detect bacteremia due to Bacteroides fragilis or Staphylococcus aureus, nor was there a significant rise in absorbance when a pellet containing sterilized feces was implanted in the rat.


Haemophilus ducreyi, the etiologic agent of chancroid, a genital ulcer disease, produces a cell-associated hemolysin whose role in virulence is not well defined. Hemolysin is encoded by two genes, hhdA and hhdB, which, based on their homology to Serratia marcescens shlA and shlB genes, are believed to encode the hemolysin structural protein and a protein required for secretion and modification of this protein, respectively. In this study, we determined the prevalence and expression of the hemolysin genes in 90 H. ducreyi isolates obtained from diverse geographic locations from 1952 to 1996 and found that all strains contained DNA homologous to the hhdB and hhdA genes. In addition, all strains expressed a hemolytic activity. We also determined that hemolysin is expressed in vivo and is immunogenic, as indicated by the induction of antibodies to hemolysin in both the primate and rabbit disease models as well as in human patients with naturally acquired chancroid. Wild-type strain 35000 and isogenic hemolysin-negative mutants showed no difference in lesion development in the temperature-dependent rabbit model. However, immunization of rabbits with the purified hemolysin protein reduced the recovery of wild-type H. ducreyi, but not hemolysin-negative mutants, from lesions. Our study indicates that hemolysin is a possible candidate for vaccine development due to its immunogenicity, expression in vitro and in vivo by most, if not all, strains, and the effect of immunization on reducing the recovery of viable H. ducreyi in experimental disease in rabbits.


An outbreak of urinary tract infections caused by multidrug-resistant Serratia marcescens lasted for 12 months and was found to be related to urologic instrumentation. Thirty-four patients had primary infections; four had cross-infections. Only six patients had indwelling bladder catheters. The median interval between instrumentation and initial isolation of Serratia was six days. Seventy-three percent of patients were symptomatic, two were bacteremic. No common instruments, personnel, or wards were identified, and
environmental cultures failed to reveal the epidemic strain of Serratia. The outbreak ended when the instrument disinfectant was changed. Serotyping was identical in nine of ten isolates. Intraspecies conjugation demonstrated resistance transfer of gentamicin, tobramycin, carbenicillin, chloramphenicol, and co-trimoxazole. The enzyme 6’-N-acetyl transferase was responsible for gentamicin-inactivation in patient isolates and a transconjugate. Although no significant spread of this multidrug-resistance plasmid to other Enterobacteriaceae occurred in the hospital, two instances of apparent in vivo transfer to other bladder organisms occurred.


An antibiotic produced by the scab disease-suppressive Streptomyces diastatochromogenes strain PonSSII has been isolated and partially characterized. The antibiotic is produced throughout culture growth, with maximum amounts accumulating in the broth when the culture is in the early stationary phase of growth. The activity declines within about 30 h after the culture enters stationary phase. Purification techniques included chromatography on Amberlite XAD-2, DEAE Sephadex and SP Sephadex in addition to C18 HPLC with an average yield of 75%. This antibiotic only inhibits pathogenic strains of S. scabies that cause scab disease on potato and other tuberous vegetables and does not affect S. griseus, S. venezuelae, Actinomyces bovis, Nocardia asteroids, Clostridium perfringens, Bacillus subtilis, Staphylococcus aureus, S. epidermidis, Enterococcus faecalis, Micrococcus luteus, Serratia marcescens and Escherichia coli. The antibiotic has a molecular weight of 500 or less, and is stable for weeks at acidic pH but is very labile at alkaline pH conditions.


A 3-year-old male from Bolivia who sustained a full-thickness 80 per cent TBSA burn complicated by smoke inhalation on the 28 March 1995 was admitted to our burn centre on 6 April 1995. On 11 April the patient's wounds were colonized with a Serratia marcescens sensitive only to ciprofloxacin and imipenem. Sputum cultures revealed the same phenotypic *S. marcescens*. Two patients who were admitted days later had the same phenotypic *S. marcescens*. Their TBSA burns ranged from 54 to 80 per cent. Both were injured in early April. Sputum and wound cultures were also positive for *S. marcescens*. Precautionary measures were instituted immediately. All potential reservoirs were cultured. Cultures were negative for *S. marcescens*. Patient therapy was maintained via strict isolation. The first patient died on 17 May. The two remaining patients survived and were discharged colonized with *S. marcescens*. However, the biotype of the initial *S. marcescens* was different from the latter two. Early recognition of a multiresistant *S. marcescens* resulted in negating the spread of this agent to other patients.


Two nosocomial outbreaks of sepsis caused by Serratia marcescens, which occurred in Tokyo were the following cases. CASE A: In July 1999, 10 inpatients admitted to the third floor ward of the General Hospital A, developed sudden onset of high fever, coagulation disorders (disseminated intravascular coagulation), and acute renal failure, of which 5 died. Twenty-one strains of Serratia marcescens were isolated from the inpatient's blood and urine, nurse fingers and environmental samples from floor and cooling tower. Serratia infection was strongly suspected as the cause of sepsis. These cases were defined as “inpatients who developed fever 38 degrees C or more during July 26 to 29 and from whom S. marcescens was isolated by blood culture”.

Ten isolates were detected from the blood. In order to investigate the background of S. marcescens isolation in the hospital and to compare molecular and biochemical characteristics of S. marcescens, cultures were attempted from samples of other inpatients and staffs and hospital environment. Those were classified into 9 groups by various different typings: biotyping with Api Rapid 20; susceptibility typing of antimicrobial agents tested; pulsed-field gel electrophoresis (PFGE) typing of SpeI- or Xba I-restricted chromosome. All 10 isolates causing sepsis were found to be in the same group. CASE B: In January 2002, 24 inpatients, admitted to Neurosurgical Hospital B, developed sudden onset of high fever, of which 7 died. S. marcescens was isolated from a towel, environmental samples and inpatients. These cases were defined as “inpatients who developed fever of 38.5 degrees C and S. marcescens isolated by blood culture”.

Twelve isolates were isolated from the blood samples in 12 cases. In order to investigate the background of S. marcescens isolation in the hospital, cultures were attempted from other inpatient’s urine and environmental samples from medical tape, Tshake and a towel. These isolates were classified into 3 groups by the previous typings; biotyping with Api Rapid 20; susceptibility typing of antimicrobial agents tested; and PFGE typing. All 12 isolates in 12 cases were found to be in the same group. These cases of 2 nosocomial outbreaks of sepsis were defined as “in-patient who developed high fever and S. marcescens isolated by blood culture”. However in both cases transmission routes of Serratia infection remain unknown by field investigation.


CsrS/CsrR is a 2-component system in Streptococcus pyogenes that negatively regulates hyaluronic capsule and several exotoxins. To detect spontaneous mutations in csrRS, mucoid and large colony variants of M1 strain MGAS166 were isolated from experimental murine skin infections. By use of complementation with a csrRS(+) plasmid, relevant mutations were also detected in 7 of 12 human clinical isolates. The presence of spontaneous mutants in mouse infection was associated with larger, more necrotic lesions. Most spontaneous changes in CsrR resulted from single amino acid substitutions, whereas most csrS mutations were frameshift or nonsense mutations. In 2 instances, IS1548 insertions were found in csrS. Experimental inoculation of mixtures of wild-type (wt) and csrRS(-) bacteria yielded larger, more necrotic lesions than did either
strain at twice the inoculum, which suggests that these variants may exhibit pathogenic synergy. Spontaneous emergence of csrRS(-) mutants in vivo enhances the virulence of wt bacteria and increases severity of murine skin infection.


**PURPOSE:** To compare the traditional method of culturing bacterial keratitis (platinum spatula) with the use of a commercially available Mini-tip Culturette (Becton-Dickinson, Cockeysville, MD, U.S.A.).

**METHODS:** An experimental model of bacterial keratitis was created in rabbit corneas by intrastromal injection of bacteria. Cultures were taken of rabbit corneas with both the Mini-tip Culturette and the platinum spatula. Culture results were compared with corneal colony counts. Humans with community-acquired presumed bacterial keratitis were cultured with both the Mini-tip Culturette and the platinum spatula. The sensitivity and specificity of the Mini-tip Culturette method was determined and compared with the platinum-spatula technique.

**RESULTS:** Rabbit keratitis model: 100% of corneas had established infections by colony count. Each ulcer was culture positive with platinum spatula, moist Mini-tip Culturette, and dry Mini-tip Culturette.

**Human keratitis:** Seven patients had culture-negative keratitis with both the Mini-tip Culturette and the platinum spatula. Five patients were culture positive with both the Mini-tip Culturette and the platinum spatula. One of the positive cultures had growth of multiple organisms by using the platinum spatula but not with the Mini-tip Culturette.

The sensitivity of the Mini-tip Culturette was 83.3%. The specificity of the Mini-tip Culturette was 100%. Detected organisms included group A beta-hemolytic Streptococcus, S. aureus, coagulase-negative Staphylococcus, Serratia marcescens, and Pseudomonas aeruginosa. **CONCLUSION:** The Mini-tip Culturette is a highly specific and moderately sensitive method for culturing bacterial keratitis.


A case of endogenous Serratia marcescens endophthalmitis in a patient with diabetes, end-stage renal disease, and an indwelling venous catheter is reported. The patient presented with a tan hypopyon and elevated intraocular pressure. Diagnosis was established by positive blood, vitreous, conjunctival, and catheter tip cultures. After a deteriorating course the eye was enucleated. Gross and histopathologic examination revealed the presence of a dark hypopyon with iris necrosis and pigment dispersion and possible spontaneous globe perforation. This is the eleventh reported case of endogenous Serratia endophthalmitis. Previous association of a pink hypopyon and of pigmented vitreous fluid and Serratia endophthalmitis has been reported. This is the first case of dark hypopyon in endogenous Serratia marcescens endophthalmitis reported in the medical literature. Previous entities associated with dark hypopyon have been limited to intraocular melanoma and Listeria monocytogenes endophthalmitis. Dark hypopyon in the appropriate clinical setting may be useful in aiding diagnostic and therapeutic decisions.
Serratia marcescens was the causative agent of bacterial endocarditis in a 2-year-old Arabian stallion. The horse was treated with broad-spectrum antibiotics for 1 month. The horse died several months after treatment was discontinued. To our knowledge, Serratia marcescens has not been reported as the cause of bacterial endocarditis in horses; however, multiple cases of bacterial endocarditis attributable to Serratia marcescens have been documented in human beings. The bacteria is most commonly isolated in immune-compromised patients.


Infections due to Serratia marcescens were studied in 23 different hospitals. A retrospective study was done in 4 hospitals; all isolates were compared by serological typing, antibiograms, bacteriocin production, and bacteriocin sensitivity. 2 of the hospitals were having cross-infection problems due to antibiotic-resistant strains, but the other 2 had little or no cross-infection. Outbreaks were studied in 19 other hospitals. 9 of these outbreaks were classified as “common source”; since contaminated “sterile solutions” were incriminated as the cause in each. One hospital had a “pseudo-outbreak”; in which Serratia from E.D.T.A. blood-collecting tubes contaminated blood-cultures as they were collected. All 10 of these strains from common-source outbreaks were generally sensitive to antibiotics. Outbreaks in 9 other hospitals resulted from cross-infection and were caused by strains which were very resistant to antibiotics. Guidelines for detecting outbreaks are given and control measures are suggested.

In 1972 there were only 11 genera and 26 species in the family Enterobacteriaceae. Today there are 22 genera, 69 species, and 29 biogroups or Enteric Groups. This paper is a review of all of the new organisms. It has a series of differential charts to assist in identification and a large chart with the reactions of 98 different organisms for 47 tests often used in identification. A simplified version of this chart gives the most common species and tests most often used for identification. The sources of the new organisms are listed, and their role in human disease is discussed. Fourteen new groups of Enterobacteriaceae are described for the first time. These new groups are biochemically distinct from previously described species, biogroups, and Enteric Groups of Enterobacteriaceae. The new groups are Citrobacter amalonaticus biogroup 1, Klebsiella group 47 (indole positive, ornithine positive), Serratia marcescens biogroup 1, and unclassified Enteric Groups 17, 45, 57, 58, 59, 60, 63, 64, 68, and 69.

The practitioner's office can be an unsafe environment for fitting contact lens (CLs),
owing to numerous reservoirs of microbial contamination. These include sinks, trial lenses, solutions, lens cases, multidose dropper bottles, and storage trays. Microbes may also be introduced to the eyes via the practitioner's fingers, the patient's lashes or lids, or cosmetic residues on the ocular adnexa. Because sterility is difficult to achieve in an office, CL fitters must accept the more realistic goal of disinfection. Periodic cultures are necessary to monitor the effectiveness of office hygiene and disinfection. Cultures are especially important, considering that the panel of organisms routinely used to test lens care solutions may not reflect those in office settings, which may become resistant to preservatives. It has been shown, for example, that 50% of chlorhexidine-preserved solutions used in offices can become contaminated with *Serratia marcescens* within 7 days of bottle opening. At present, it appears that contamination is best avoided by using solutions containing 15 ppm of polyaminopropylbiguanide (PAPB). Frequent replacement of solutions, trial lenses, and lens cases may also help to reduce the likelihood of microbial contamination in the office.


Morphological-cultural and physiological-biochemical properties of 24 strains of microorganisms agents of pyo-inflammatory complications of different localization in patients with hemophilia have been studied. Microorganisms strains presented by the following species: Staphylococcus aureus, S. epidermidis, S. saprophyticus, Proteus vulgaris, P. morganii, Hafnia alvei, *Serratia marcescens*, have been identified. It was found out that in monoculture staphylococci prove to be the leading etiological agent (60.9%), gram-negative enterobacteria (52.2%) and bacterial associations (8.7%) occur more rarely. Special attention was paid to the study of resistance of antibiotics, circulation and pathogenicity factors that had a direct effect on the main disease severity. It was ascertained that high activity of enzymes and presence of pathogenicity factors were the peculiarities of microorganisms isolated from pyo-septic sites in patients with hemophilia. All the strains possessed multiple resistance to antibiotics.


Extremity tourniquets are widely used to achieve bloodless dissection in the surgical field. Excision of venous stasis ulcers (VSU) is aided by tourniquet use because of large dilated veins associated with venous stasis disease. We present 3 patients with hypotensive shock occurring 10 to 15 minutes after tourniquet release after excision of venous stasis ulcers. All patients had long histories of venous stasis changes and two-thirds had prior histories of deep vein thromboses and pulmonary embolism. Mean tourniquet inflation time was 34 minutes and there were electrocardiographic changes in two-third of the patients. All patients responded rapidly to standard resuscitation measures and in all 3 postoperative testing for pulmonary embolus and myocardial infarction was negative. Wound cultures revealed no organisms in 1 patient, mixed Gram-positive cocci in another, and greater than 10(5) *Serratia marcescens* in the third patient. Although small decreases in blood pressure and blood pH, and increases in blood lactate, PaO2, and creatinine phosphokinase, are normally associated with the use of extremity tourniquets, hypotensive shock has not been reported. The combined effect of
tourniquet ischemia and venous stasis changes may cause hypotensive shock by (1) an endotoxic bolus upon tourniquet release, (2) pulmonary microembolization of platelet, fibrin, and leukocyte aggregates causing vasoactive substance release, and (3) synergistic effects of platelet-activating factor, a known mediator of endotoxic shock. The untoward events noted in these patients may be prevented by (1) proximal to distal dissection of the ulcer with initial ligation of large veins, (2) pretreatment with steroids and/or platelet-activating factor antagonists, and/or (3) slow release of the tourniquet.


**BACKGROUND:** The first Spanish outbreak of bacterial strains showing resistance to third generation cephalosporins and due to the presence of the extended spectrum betalactamase SHV-2 is reported. This outbreak was observed in Madrid during the years 1988-1990 and involved the San Carlos University Hospital with the same type of isolates at the Ramon y Cajal University Hospital. **METHODS:** The screening for extended-spectrum beta-lactamases was performed by the double-disk synergy test. Analytical isoelectric focusing and susceptibility tests were performed in all the strains showing a presumptive extended-spectrum beta-lactamase. **RESULTS:** Fifty-nine strains belonging to four bacterial species (Klebsiella pneumoniae, 61%; Serratia marcescens, 31%; Klebsiella oxytoca, 5%, and Escherichia coli, 3%) showed a beta-lactamase of point isoelectric 7.6; the susceptibility tests demonstrated more resistance to cefotaxime and ceftiraxone than to ceftazidime and aztreonam. **CONCLUSIONS:** The biochemical, kinetic, and isoelectrofocusing parameters demonstrated the presence of a SHV-2 enzyme. The blind application of NCCLS breakpoints would lead to false “susceptibility” results in over 40% of the cases.


**OBJECTIVE:** To study the microbiology of cystic fibrosis in our hospital for the period from 1985 to 1992. **MATERIAL AND METHODS:** The number of samples analyzed totalled 1,034, most of which were sputum and nasopharyngeal aspirates belonging to 113 patients (49 women and 64 men). The average age was 10 years (range: 15 days-33 years). **RESULTS AND DISCUSSION:** Only 1.7% of the samples were negative. Normal flora were found in 10.8% and one or more potentially pathogenic microorganisms were found in the remaining 87.4%. Colonies were over 10^6 UFC/ml in size in 77.8% of the quantified cultures. The most frequently identified microorganisms in the population overall were P. aeruginosa (53.9%), S. aureus (30.3%) and H. influenzae (22.0%). In patients less than 12 months old, however, the most common isolations were of S. pneumoniae and B. catarrhalis; cultures from patients older than 16 years old most often yielded filiform fungi, mainly Aspergillus spp. We found no strains of Legionella spp. and P. cepacia was found in only 3 cases, in which the clinical outcome was good. In addition to the 3 most common organisms, we recorded several consecutive isolations of Proteus mirabilis, Xanthomonas maltophilia and Serratia marcescens in patients older than 11 years old; this finding suggests that given the improved survival of cystic fibrosis patients over the coming years and the antibiotic
pressure placed on them, there may be slight changes in the bacterial ecology typical of this disease. No strain of S. aureus proved resistant to methicillin, but P. aeruginosa was shown to be resistant to gentamycin (58.2%) among the aminoglycosides and also to some of the beta-lactams considered to be effective, as follows: 25.2% to piperacillin, 22.6% to ceftazidime and even 19.8% to aztreonam. There was slight resistance of ciprofloxacin (6.3%).


Using a broth microdilution technique, the in vitro susceptibility of bacterial isolates from the equine respiratory tract to trimethoprim, sulfadoxine, sulfadimethoxine, and combinations of these compounds was determined. The bacterial strains (n = 88) isolated recently from horses with respiratory symptoms belonged to the following species: Streptococcus equi subsp. zooepidemicus (n = 34), Streptococcus equi subsp. equi (n = 22), Staphylococcus aureus (n = 9), Klebsiella pneumoniae (n = 7), Rhodococcus equi (n = 4), Pseudomonas spp. (n = 3) and Escherichia coli (n = 3). In addition, two isolates of Enterobacter spp. and one isolate of Streptococcus equisimilis, Staphylococcus intermedius, Proteus mirabilis and Serratia marcescens were examined. For determination of susceptibility of an organism the following minimal inhibitory concentrations (MIC) were fixed as limiting values: Trimethoprim < or = 0.5 microgram/ml, sulfadoxine < or = 32 micrograms/ml, sulfadimethoxine < or = 32 micrograms/ml, trimethoprim/sulfadoxine < or = 0.5/32 micrograms/ml, trimethoprim/sulfadimethoxine < or = 0.5/32 micrograms/ml. As expected, Rhodococcus-equ-i isolates were resistant to the antimicrobials tested. However, most of the clinically more common isolates showed a high degree of susceptibility to the combinations. The fractional inhibitory concentration (FIC) indices indicated synergism of the combination-partners in a wide range. According to these in vitro results, application of trimethoprim/sulfonamide combinations for the initial therapy of equine respiratory tract infections can be recommended.


Regarding the adjuvant activity of gram-negative bacteria we have to distinguish at least 4 different potencies, i.e., 1) increase in the production of circulating antibodies during the primary and secondary immune responses; 2) induction of susceptibility to systemic anaphylaxis; 3) prompt production of experimental “allergic” diseases, and 4) increase in resistance to infections. Although all gram-negative bacteria contain several structural components with adjuvant potencies, the immunopotentiating effectiveness of the corresponding whole bacteria becomes--with the exception of killed cells of Bordetella pertussis--only detectable to a weak degree.

In patients with severe underlying disease and in polytraumatized patients, clinical signs of septicemia caused by infections with gram-negative bacteria are observed
postoperatively with increasing frequency. Using a photometric LAL test, a longitudinal assessment of LAL reactivity on 41 intensive care patients was performed. Postoperatively, all patients developed a septicemia of different severity with body temperatures greater than 38.5 degrees C. Dividing the individual disease course, related to body temperatures, into three phases (A-C) it was found that independent of the severity of septicemia, the majority of patients (38/41) yielded a positive LAL reactivity. In phase B (body temperature greater than 38.5 degrees C) more plasma samples contained LAL-reactive material than in phase A and C (body temperature less than 38.5 degrees C). A decline of fever (phase B to C) correlated significantly (P less than 0.05) with the change from positive to negative LAL reactivity. In patients with high leukocyte counts (15-50 X 10(9)/l) a positive LAL reactivity was found more frequently. The majority of patients (21/27) who survived were transferred with negative LAL reactivity to the general wards. The results suggest that single determinations of LAL reactivity are of limited clinical validity. Using the individual profile of LAL reactivity gained through a longitudinal assessment, data upon the development of the disease course can be obtained.


Fisher. 1977. A polyvalent human gamma-globulin immune to Pseudomonas aeruginosa: passive protection of mice against lethal infection. J.Infect.Dis. Vol. 136 SupplS181-5. As a means to development of guidelines for therapeutic application to human disease, preparations of human polyvalent gamma-globulin immune to Pseudomonas aeruginosa (PG) were studied in acute infections in mice. PG was highly effective in controlling lethal infections induced in mice by the major immunotypes of P. aeruginosa; greater than or equal to 10 microgram of of gamma-globulin per mouse protected against challenge with less than or equal to 10(6) 50% lethal doses of P. aeruginosa. PG was less than or equal to 57 times more effective than normal human gamma-globulin. The active antibody component is specific for each immunotype; it is of the IgG type and undoubtedly is directed against the O-antigen. PG was not protective against challenge with Escherichia coli, Enterobacter cloacae, Proteus mirabilis, or Klebsiella pneumoniae; a low degree of cross-protection was seen against Serratia marcescens. In a model infection involving mice in a terminal stage of advanced P. aeruginosa infection, human plasma immune to P. aeruginosa proved ineffective, but the gamma-globulin component showed moderate activity. The apparent irreversibility of this late-stage infection is not clearly ascribable to a toxin. It is postulated that the successful treatment of advanced P. aeruginosa infections in humans would require multiple therapeutic approaches, including passive immunization with a high-potency, specifically immune globulin.

We investigated an outbreak of Serratia marcescens in the neonatal intensive care unit (NICU) of the University Hospital of Zurich. *S. marcescens* infection was detected in 4 children transferred from the NICU to the University Children's Hospital (Zurich). All isolates showed identical banding patterns by pulsed-field gel electrophoresis (PFGE). In a prevalence survey, 11 of 20 neonates were found to be colonized. *S. marcescens* was isolated from bottles of liquid theophylline. Despite replacement of these bottles, *S. marcescens* colonization was detected in additional patients. Prospective collection of stool and gastric aspirate specimens revealed that colonization occurred in some babies within 24 hours after delivery. These isolates showed a different genotype. Cultures of milk from used milk bottles yielded *S. marcescens*. These isolates showed a third genotype. The method of reprocessing bottles was changed to thermal disinfection. In follow-up prevalence studies, 0 of 29 neonates were found to be colonized by *S. marcescens*. In summary, 3 consecutive outbreaks caused by 3 genetically unrelated clones of *S. marcescens* could be documented. Contaminated milk could be identified as the source of at least the third outbreak.


A human intravenous IgG preparation (Anti-LPS IgG) rich in antibodies to different lipopolysaccharides (LPS) and a normal human intravenous IgG (NlgG) were investigated for their ability to confer passive immunity. Both preparations were given at the time of infection (prophylaxis) or during sepsis (therapy) to burned mice with lethal infection induced by various clinically relevant gram-negative bacteria. When given at the time of infection both IgG preparations (5 mg/mouse) inhibited lethality induced by some bacteria (Pseudomonas aeruginosa serogroup G and B), but not others (Serratia marcescens, Klebsiella pneumonia, Proteus mirabilis), indicating a protection by by strain-specific antibodies. However, no significant protection was seen when mice were treated during sepsis. The range of specific antibody titers to the whole live bacteria and heat-killed (LPS-preserved) bacteria in the NlgG paralleled that of Anti-LPS IgG; however, the magnitude of the antibody titers did not accurately reflect the protective capacity in vivo. Thus, the exact specificity of the protective antibodies is still unknown. The protective effect of both IgG preparations was dose-dependent; at low IgG doses (0.5 mg/mouse) better protection was obtained with Anti-LPS IgG, whilst at higher doses (> or = 1 mg/mouse) both preparations exhibited identical effects. Low doses of either IgG preparation in combination with subtherapeutic doses of piperacillin significantly enhanced early survival (day 2 for NlgG and day 2 + 3 for Anti-LPS IgG) against *P. aeruginosa*, but the protective effect waned thereafter. We conclude that a strain-specific antibacterial effect in a compromised mouse infection model can be obtained by early passive immunization with human IgG from large plasma pools. It is suggested that Anti-LPS IgG or NlgG may be of benefit in some cases of gram-negative sepsis when administered as prophylaxis together with proper antibiotic treatment.
Fox et al. 1981. Nosocomial transmission of Serratia marcescens in a veterinary hospital due to contamination by benzalkonium chloride. *J.Clin.Microbiol.* Vol. 14(2): 157-160. During a 1-year period, Serratia marcescens was isolated from 50% of all contaminate intravenous catheters from dogs and cats in a large veterinary hospital. *S. marcescens* was also isolated from respiratory tracts, genitourinary tracts, skin, and other sites in hospitalized animals. A total of 55% of the clinical isolates and 66% of the intravenous catheter isolates had the same API biochemical profile. The source of the *S. marcescens* was determined to be aqueous benzalkonium chloride (0.025%) sponge pots located in the intensive care unit, surgery rooms, and outpatient clinic areas of the hospital. Of the 11 *S. marcescens* isolates submitted to the Centers for Disease Control for serotyping (6 from aqueous benzalkonium chloride sponge pots, 5 from intravenous catheters), 8 were identified as serotype O10:H11. All *S. marcescens* isolates tested for antibiotic susceptibilities were multiply resistant; isolates were most frequently resistant to streptomycin, cephalothin, and ampicillin. This study demonstrates that improper use of disinfectants plays an important role in the nosocomial transmission of *S. marcescens*.


Friedman et al. 2003. Spontaneous dermal abscesses and ulcers as a result of Serratia marcescens. *J.Am.Acad.Dermatol.* Vol. 49(2 Suppl Case Reports): S193-4. Serratia sp have only rarely been reported as isolates from leg ulcers. We describe the case of a middle-aged man with a medical history significant for alcohol-induced cirrhosis who presented with rapidly progressive skin ulcers initially starting as purple nodules. These skin ulcers and underlying dermal abscesses were found to be a result of *S. marcescens*, with the presumed portal of entry being a toe-web infection.


Gaston et al. 1986. A comparison of strains of Serratia marcescens isolated from neonates with strains isolated from sporadic and epidemic infections in adults. *J.Hosp.Infect.* Vol. 8(1): 86-95. As a result of the increased number of outbreaks of Serratia marcescens in special care baby units in the UK, a study was undertaken to compare strains isolated from outbreaks of neonatal infection with strains isolated from outbreaks of infections in adults and with isolates from sporadic infections. None of the biochemical, serological, bacteriological markers examined could distinguish the three groups of strains. When considered as groups there was no difference in the ability of the strains to survive desiccation on hands. Strains from neonatal and sporadic infections were more sensitive to antibiotics than adult epidemic strains. The feature common to all of the neonatal strains tested was
the ability to agglutinate one or more species of erythrocytes in the presence of mannose. Only one strain in each of the other two groups possessed mannose resistant haemagglutinins.


Five hundred forty-three episodes of nosocomial bacteremia were prospectively followed in a large Spanish university hospital. The commonest isolates were Staphylococcus epidermidis, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, and Candida species. The most frequent sources of infection were intravenous lines, urinary tract, and lower respiratory tract. Overall mortality was 18%. A step-forward logistic regression analysis defined eight variables independently influencing the outcome: shock, underlying rapidly fatal disease, high-risk source of bacteremia (intraabdominal, lower respiratory tract, or not identified), age more than 70 years, hospitalization in intensive care or medical units, inappropriate antibiotic treatment, infection due to a high-risk microorganism (P. aeruginosa, Serratia marcescens, Klebsiella, Bacteroides, or Candida), and development of septic metastasis. The identification of those factors independently influencing the outcome and their possible modification may represent a further step in the control of nosocomial bacteremia by improving its prognosis.


Bacteremia due to multiply-antibiotic-resistant Serratia marcescens occurred within 1 week in four patients who were in adjacent beds in an intensive care unit. The strains were serotyped as O14:H12 and were nitrate negative. This unusual biochemical marker was useful in the investigation of the outbreak.


We made an open, noncomparative evaluation of ofloxacin, 400 mg orally bid for 10 days, in 98 subjects with community-acquired pneumonia or pathogen-confirmed bronchitis. Thirty-nine (40%) of the subjects were treated in the hospital and 59 (60%) were treated as outpatients. The mean age of those treated was 56.2 years; 73 (74%) of the subjects either were more than 60 years old or had a history of chronic obstructive pulmonary disease, or both. There were 95 organisms initially isolated in sputum, aspirate, or lavage fluid; all were susceptible to ofloxacin, and none acquired resistance during therapy. Haemophilus influenzae was the most common pathogen (19 isolates), followed by Streptococcus pneumoniae (18) and Staphylococcus aureus (10). Clinical responses included cure in 70 patients (71%), improvement in 26 (27%), and failure in two (2%). After 10 days of therapy, pathogens persisted in two cases; in one case, Streptococcus salivarius was isolated, though it remained susceptible to ofloxacin, and in the other, Klebsiella pneumoniae was accompanied by superinfection due to a resistant strain of Serratia marcescens. We included in this study three confirmed cases of atypical pneumonia successfully treated with ofloxacin, two of them due to Mycoplasma pneumonia and one to Legionella pneumophila. Ofloxacin was well tolerated. Our data
indicate that ofloxacin is effective and safe as specific and empiric treatment for many lower respiratory tract infections.


**Glatman et al. 1994.** Genetic and molecular R-plasmid analysis of Enterobacteriaceae hospital strains at Children's Hospitals of the former USSR. *J.Chemother.* Vol. 6(3): 155-162.

R-plasmids from Enterobacteriaceae clinical strains, mainly Klebsiella and Serratia, isolated at different neonatal and children's hospitals of different cities of the former USSR for 10 years, were studied for their possible influence on the bacterial host phenotype. Hospital R-plasmids of stable inheritance persisted in hospitals from 2 to 7 years and were disseminated among strains of different genera (Klebsiella, Serratia, Enterobacter) and among different units. The data showed a possibility of long-term molecular rearrangements of R-plasmids in the hospital settings and an acquisition of genetic determinants encoding enterotoxin production. A novel R-plasmid encoding cytotoxicity to HEp-2 cells involved in two nosocomial outbreaks due to K. pneumoniae strains was reported. K. pneumoniae population heterogeneity was evaluated by using the plasmid parameters of strains. Their heterogeneity of a bacterial population was significantly lower during nosocomial outbreaks than in interepidemic periods.


Antibiotic sensitivity of 38 strains of enteric bacteria, such as Serratia marcescens Klebsiella pneumoniae and others and Ps. aeruginosa isolated during an outbreak of meningitis in a premature infant resuscitation department was studied. It was shown that all the isolates were multiple resistant, most frequently to 7 antibiotics. All the resistance markers were transferred on conjugation, segregation of some markers being observed. Investigation of the plasmid composition of the clinical strains and transconjugants of E. coli revealed the presence of 2 plasmids with the molecular weights of 40 and 60 Md or one of them. The restriction analysis demonstrated that the plasmids with the same molecular weights isolated from different strains were identical. It was suggested that such plasmids originated from the same source and were distributed by conjugation. The possible part of R plasmids in epidemiological analysis of hospital infections is discussed: the possible part as an additional marker in determination of the infection source and the possible part through its ability to change the host cell phenotype, including the phage and bacteriocin types.


After nearly 10 years of fluoroquinolone usage for a wide range of bacterial infections, a striking difference has been observed in the incidence of bacterial resistance to fluoroquinolones between bacteria responsible for community- and hospital-acquired infections, respectively. Resistance is only rarely encountered among common pathogens. In most studies, 97 to 100% of all pathogens are fully susceptible to fluoroquinolones. In contrast, resistance to fluoroquinolones has emerged and increased among bacteria responsible for nosocomial infections. The incidence of resistance to fluoroquinolones varies between bacterial species, clinical settings and countries, and is related to local epidemic spread of a few clones. The highest incidence of resistance is observed in Pseudomonas aeruginosa, Acinetobacter spp., Serratia marcescens and, particularly, methicillin-resistant Staphylococcus aureus (MRSA): some investigators have reported 95 to 100% fluoroquinolone resistance among MRSA. Follow-up of trends in the resistance to fluoroquinolones based upon surveillance programmes are needed.


In a patient with Serratia marcescens bacteraemia, a variant resistant to cefotaxime and amikacin was isolated in a blood culture under combined treatment with cefotaxime and amikacin. In addition, in vitro selection on cefotaxime and/or amikacin yielded resistant mutants from the sensitive parent strain. These mutants displayed the same type of cross-resistance as the clinical strain to all beta-lactam and aminoglycoside antibiotics. The mechanism for this resistance was a decrease in the permeability of the cell. To our knowledge, the isolation of such strains from blood cultures and the mechanism responsible for this “broad-spectrum resistance”; have not been previously described.


Antibodies levels against Gal alpha 1,3 Gal epitopes were studied in 407 human sera (92 chagasic and 315 non-chagasic), by means of hemagglutination with rabbit erythrocytes reactivity of serum having high titres of anti-Gal antibodies in presence of Escherichia coli and Serratia marcescens antigen was studied by immunoelectrotransference. Finally, using a purified anti-Gal antibody, Gal alpha 1,3 Gal epitopes were identified in metacyclic forms from 12 high Andean Chilean strains of Trypanosoma cruzi. Among the chagasic sera, it was demonstrated that in 63 (68.5%) were detected antibodies anti-Gal at the same or higher titer than 1:1,600; while i the non chagasic sera only 49
(15.6%) showed an anti-Gal response at similar titers. Immunelectrotransference showed that the sera of people infected with T. cruzi recognize antibodies present in E. coli and S. marcescens, which reinforces the idea that at least in part, these bacteria would be capable of stimulating these responses. The autoradiographic analysis using purified anti-Gal antibodies, showed differences in the Gal alpha 1,3 Gal epitopes expressed in the different strains of T. cruzi. These results suggest that anti-Gal antibodies could have a real significance on the natural immunity mechanisms and protection of human infection with T. cruzi.


Serratia marcescens isolates from 164 patients with suspected nosocomial infection in several hospitals in the greater Paris region were investigated by analysis of the electrophoretically demonstrable allelic variations of gene loci coding for five esterases and five other enzymes. All the loci were polymorphic and the mean number of alleles per locus was 6.1. A total of 72 distinctive electrophoretic types (ETs) representing multilocus genotypes was distinguished. The isolates were divided into two groups according to their resistance to antibiotics: 82 multiresistant isolates (MRI) and 82 relatively susceptible isolates (RSI). Seventy-two MRI (88%) were in four genetically related ETs: ET1, ET2, ET8 and ET9; ET1 was found in 48 isolates, whereas the remaining MRI were in 10 ETs, and all RSI in 61 ETs. Three ETs contained both MRI and RSI. The mean coefficients of genetic diversity for the 10 enzyme loci among ETs and isolates were smaller for MRI than for RSI, while the modal ET of MRI resembled that of RSI. The epidemiological significance of isolates varied according to their ET. Thus, isolates belonging to ET1, ET2 and ET8 were responsible for outbreaks or for sporadic infections, whereas isolates of other ETs were responsible for only sporadic infections. The temporal distribution of ET1 isolates among hospitals identified seven outbreaks in seven clinical departments.


During a hospital epidemic of infections with gentamicin-resistant Serratia marcescens (GRS), we studied the relation between receiving antibiotics and acquiring GRS. In a five-month period, 22 patients acquired GRS, whereas 18 patients acquired gentamicin-sensitive Serratia (GSS). When compared with patients with nosocomial GSS infection, patients with nosocomial GRS had been in the hospital ($p = 0.04$) and the intensive care unit ($p = 0.003$) longer before infection and more had received gentamicin ($p = 0.001$) or ampicillin ($p = 0.02$) before infection. To control for the influence of underlying disease, we matched all 12 ICU patients with GRS infection and 12 patients without GRS infection for underlying illness and duration of intensive care. Use of any antibiotic ($p = 0.04$), or a combination of gentamicin plus ampicillin or cephalosporin ($p = 0.047$) was
more common among patients with GRS infection. The hospital had not significantly increased the use of aminoglycosides from the previous year. We conclude that for the individual patient antimicrobial therapy, especially with gentamicin or ampicillin, creates a risk for later infection by GRS that is independent of the severity of the underlying illness.

The cell wall component of Pseudomonas solanacearum that induces disease resistance in tobacco was highly heat stable at neutral or alkaline pH but highly labile at acid pH. Activity was unaffected by nucleases and proteases but destroyed by a mixture of beta-glycosidases. Washing of bacterial cell walls released a lipopolysaccharide (LPS) fraction with high inducer activity. Purified LPS, extracted by a variety of procedures from whole cells, isolated cell walls, and culture filtrates of both smooth and rough forms of P. solanacearum, induced disease resistance in tobacco at concentrations as low as 50 microgram/ml. The LPS from the non-plant pathogens Escherichia coli B, E. coli K, and Serratia marcescens was also active. Cell wall protein, free phospholipid, and nucleic acids were not necessary for activity. Moreover, since LPS from rough forms was active, the O-specific polysaccharide of the LPS was not required for activity. Hydrolysis of the remaining core-lipid A linkage or deacylation of lipid A destroyed inducer activity. When injected into tobacco leaves, purified LPS attached to tobacco mesophyll cell walls and induced ultrastructural changes in the host cell similar to those induced by attachment of whole heat-killed bacteria.

A new technique for simultaneously measuring the phagocytic and bactericidal capacity of human leukocytes is proposed. The method uses 14C labelled bacteria and is based on the principle that only viable intra-cellular bacteria incorporate 3H-thymidine. Phagocytosis is measured by the ratio intra-cellular 14C/extra and intra-cellular 14C and the bactericidal capacity of leukocytes by the difference between the 3H-thymidine incorporation of the ingested and non-ingested bacteria. Results in normal subjects and in a case of chronic granulomatous disease show the validity of the method which is easier and quicker than the methods previously used.

Laboratory surveillance of clinical isolates for Serratia spp. revealed a sudden increase from babies in the Special Care Baby Unit (SCBU). It was established that breast-milk pumps on the post-natal wards were being disinfected inadequately, resulting in contamination of milk and cross-infection within the SCBU. Thirty babies were colonized and no deaths were attributable to the organism. Rectal carriage by the babies was common and often prolonged. The outbreak was brought under control when the method of disinfection of the pumps was changed from soaking in hypochlorite solution to washing at 80 degrees C.
Between 1983 and 1988 we observed altogether 222 cases of neonatal septicemia and/or meningitis in our Department of Neonatology. The incidence was 8.46 per 1,000 liveborn infants. The case fatality rate amounted to 45.9%. The most frequently isolated causative agents were Escherichia coli (23.4%) followed by group B Streptococci (16.7%), Staphylococcus aureus (9.9%), Klebsiella pneumoniae species (8.8%), Serratia marcescens (7.9%), Pseudomonas aeruginosa and coagulase-negative Staphylococci each 5.9%. The report includes information about serotypes of Escherichia coli, group B Streptococci and plasmid patterns of Serratia marcescens. The latter was responsible for an outbreak of septicemia and meningitis with high mortality. The changing infection pattern reflects changes in the newborn population, especially in the patient structure of the neonatal intensive care unit, changes in the antibiotic policy and organizational problems.


The infectious complications of 31 orthotopic heart transplants in 27 patients performed between 1982 and 1987 were reviewed. Fifteen patients (56%) are alive 704 to 1829 days posttransplantation. Five of the 27 patients died within the first week posttransplantation of noninfectious causes. Infection occurred in 17 of the remaining 22 patients and was the major cause of death in 3 of the 12 fatalities. There were 10 proved and 4 probable bacterial infections. Three of the 10 proved bacterial infections were cases of sepsis with focal complications (two Pseudomonas aeruginosa, one Serratia marcescens) resulting in 2 deaths. The cases of sepsis occurred within 12 days of transplantation. There were 11 viral infections. Cytomegalovirus accounted for 7 of these including 1 fatal and 2 nonfatal episodes of disseminated disease. The mean time of onset of cytomegalovirus infection was 33 days. Two cases of fungal disease were identified at autopsy. One additional patient who received intense immunosuppression because of chronic rejection developed Pneumocystis carinii pneumonia. The most frequent site of infection was the lung with early pneumonias caused by Gram-negative bacteria and later episodes by viral (cytomegalovirus or respiratory syncytial virus) agents.

Sixty-four patients with malignant diseases from whom Serratia marcescens was isolated from various sources were studied regarding their antibody responses to somatic O antigens of this microorganism. Antibodies were titrated by the passive hemagglutination test. An antibody response was considered present when either a fourfold or greater rise in antibody titers between two consecutive serum specimens was demonstrated, or when elevated titers (greater than or equal to 40 for serogroup O14 and greater than or equal to 160 for all others) were present in the first available specimen. Overall, 31% of subjects
mounted an immune response, but there were differences depending upon the infection site. Seventy-one percent of patients with *S. marcescens* bacteremia responded immunologically; whereas the percentage for patients with Serratia present in the respiratory tract was only 22%, in the urinary tract, 31%, and in wounds, 26%.

Documentation of an immune response to the patient's own infecting strain of Serratia aids in the differentiation between infection and contamination and possibly also between clinical disease and colonization. In addition, immunoglobulin samples collected in different decades were examined to determine whether the background level of antibodies to *S. marcescens* had changed in the general population over the years. No difference in antibody titers to 13 O antigens was observed in immunoglobulin preparations from 1951, 1962, 1971, and 1975.


Chronic granulomatous disease (CGD) is characterized by severe recurrent infections with *Staphylococcus aureus*, certain gram-negative rods, *Nocardia* species, and fungi. When infections with the same species recur, they may represent relapses or new infections. We collected organisms from infections that occurred between 1992 and 2000 in patients with CGD and determined the biochemical phenotypes, in vitro antibiotic susceptibility patterns, and pulsed-field gel electrophoresis (PFGE) patterns of the organisms causing the initial and recurrent infections. Recurrence of infection with *Burkholderia cepacia* or *Serratia marcescens* was caused by a new strain in 9 of 10 cases (P=.001). Recurrent *S. aureus* infections were caused by new strains in 7 of 8 cases (P=.006). In patients with CGD, recurrence of infection with the same bacterial species after appropriate antibiotic therapy usually represents new infection.


The in-vitro activity of Sch 34343 was compared with that of cefotaxime, ceftazidime, latamoxef (moxalactam), aztreonam and ampicillin. Against pneumococci, Sch 34343 was as active as ampicillin, whereas against the other streptococci it was less active than ampicillin but significantly better than the other antibiotics against enterococci. With clinical isolates of Enterobacteriaceae resistant to cefotaxime, Sch 34343 had MICs generally less than 2 mg/l. After introduction of plasmid-mediated beta-lactamases into *Escherichia coli* Cla. there were no significant changes in the MICs of Sch 34343. Mutants of Enterobacter cloaceae, Citrobacter freundii and Morganella morganii with derepressed cephalosporinases had susceptibilities equal to or less than 1 mg/l, which were generally lower than those of the other compounds tested. Comparison of parental strains and permeability mutants of *E. coli*, Ent. cloaceae, and *Serratia marcescens* showed
that the increase in MICs of Sch 34343 were lower than those found for the other antibiotics.


**BACKGROUND:** Serratia bacteremia is an uncommon illness in hospitalized patients. The aim of this study was to determine how frequently this disease occurs nosocomially and to discover the most common portals of entry and the underlying disorders.

**METHODS:** Fifty-six cases of Serratia bacteremia documented by blood culture (17 cases over a 4-year period in a community hospital in Gainesville, Florida, and 39 cases over a 3-year period in three community hospitals in Dayton, Ohio) were reviewed. Comparison was made with 60 control cases of general bacteremia from three Dayton hospitals.

**RESULTS:** Of the 56 study cases of Serratia bacteremia, 45 (80.4%) were classified as nosocomial, compared with 13 (21.7%) of the controls. Twenty-seven (48.2%) of the 56 Serratia cases occurred in intensive care units. The cases were evenly distributed over the two study periods, and no outbreaks on specific units were noted. The most common portals of entry for Serratia organisms were, in descending order, lung, genitourinary tract, unknown, intravenous line, gastrointestinal tract, and skin. The most common underlying disorder for Serratia bacteremia was malignancy, followed by renal failure (acute or chronic) and diabetes mellitus. Most of the Serratia organisms tested were sensitive to carbenicillin, trimethoprim/sulfamethoxazole, ceftizoxime, ceftriaxone, ceftazidime, cefotetan, aztreonam, ticarcillin/clavulanate, and ciprofloxacin. The organisms were largely resistant to ampicillin, tetracycline, cefazolin, cephalothin, and cefuroxime. Twenty-five percent of the patients with Serratia bacteremia died, compared with 13.6 of the bacteremic controls. CONCLUSION: Serratia bacteremia is often acquired nosocomially. The mortality rate among the study population was surprisingly low for this opportunistic bacteremia, but was higher (though not significantly so) than that of the controls.


**OBJECTIVE:** The National Nosocomial Infections Surveillance (NNIS) System personnel report trends in antimicrobial-resistant pathogens. To validate select antimicrobial susceptibility testing results and to identify test methods that tend to produce errors, we conducted proficiency testing among NNIS System hospital laboratories. SETTING: NNIS System hospital laboratories in the United States.

**METHODS:** Each laboratory received five organisms (ie, an imipenem-resistant Serratia marcescens, an oxacillin-resistant Staphylococcus aureus, a vancomycin-resistant Enterococcus faecalis, a vancomycin-intermediate Staphylococcus epidermidis, and an extended-spectrum beta-lactamase (ESbetaL)-producing Klebsiella pneumoniae). Testing results were compared with reference testing results from the Centers for Disease Control and Prevention. RESULTS: Of 138 laboratories testing imipenem against the Serratia marcescens strain, 110 (80%) correctly reported minimum inhibitory concentrations (MICs) or zone sizes in the resistant range. All 193 participating laboratories correctly reported the Staphylococcus aureus strain as oxacillin resistant. Of the 193 laboratories,
169 (88%) reported correct MICs or zone sizes for the vancomycin-resistant Enterococcus faecalis. One hundred sixty-two (84%) of 193 laboratories demonstrated the ability to detect a vancomycin-intermediate strain of Staphylococcus epidermidis, however, disk diffusion performed poorly when testing both staphylococci and enterococci with vancomycin. Although laboratory personnel correctly reported nonsusceptible extended-spectrum cephalosporins and aztreonam results for K. pneumoniae, only 98 (51%) of 193 correctly reported this organism as an ESbetaL producer. CONCLUSION: Overall, NNIS System hospital laboratory personnel detected most emerging resistance patterns. Disk diffusion continues to be unreliable for vancomycin testing of staphylococci and must be used cautiously for enterococci. Further education on the processing of ESbetaL-producing organisms is warranted.

A case report is presented on an 18-month-old boy who suffered from recurrent infections from early infancy. He was hospitalised for osteomyelitis in the left elbow; differential diagnosis also raised the possibility of a Ewing sarcoma. We were, however, able to eliminate this possibility on the basis of clinical data. Together with the immunologist, we discovered a malfunction of the granulocytes, consisting essentially in the fact that certain bacteria, although phagocytised, cannot be killed off within the cells. This has therapeutic consequences, which are discussed in this paper together with questions of prognosis.


BACKGROUND: The role of hands in disease transmission is well established, and the importance of handwashing is recognized. However, the exits of paper-towel dispensers used in hand drying may be contaminated, and the functionality of handwashing equipment increasingly is being questioned. OBJECTIVES: We sought to study the transfer and cross-contamination potential between hands, towels, and dispenser exits if one or more is contaminated using bacteria representative of the skin's flora.
MATERIALS AND METHOD: A generic wall-mounted paper-towel dispenser and a range of different paper towels were used. Volunteers with either clean or contaminated hands were asked to remove, using a range of protocols, towels from dispensers which themselves were either clean or contaminated. Previously clean surfaces were then microbiologically tested. RESULTS: Recoverable bacterial transfer rates from a contaminated hand to clean dispenser exits ranged from 0.01% to 0.64% depending on the bacteria used with an even higher transfer rate for clean towels. The reverse transfer (ie, from contaminated exits to clean hands) was between 12.4% and 13.1%.
CONCLUSIONS: The results indicate that zig-zag transfer of bacteria between paper-towel dispensers and hands can take place if either one is contaminated. This potential should be considered in the design, construction, and use of paper-towel dispensers.

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Health Effects of *Serratia marcescens*


A biological response modifier, mixed bacterial vaccine (MBV), derived from Streptococcus pyogenes and Serratia marcescens was used as a single agent in the treatment of 11 patients with refractory malignancies. MBV's effect on interleukin-2 (IL-2) production, plasma interferon (IFN) and tumor necrosis factor (TNF) levels was monitored. Most patients' peripheral blood mononuclear cells continued to produce baseline to elevated levels of IL-2, in spite of age and disease status. Several patients maintained moderate to high IFN levels. In general there was little correlation between IL-2 and IFN levels or with the response to therapy. One of 11 patients had minor response, 1 of 11 had partial response, 4 of 11 had temporary stabilization of disease, and 5 of 11 had progressive disease. A patient with AIDS and Kaposi's sarcoma experienced a dramatic improvement in performance status and disease stabilization. In all patients side effects occurred only following i.v. and not i.m. administration and included fever and chills. No adverse hepatic, renal or hematologic effects were observed. MBV is a well-tolerated biological response modifier with modest activity in advanced human tumors.


Clinical evaluation of ceftibuten (CETB, 7432-S) was performed in 20 patients with acute bronchitis. They were consisted of 10 males and 10 females aged from 20 to 80 years old. CETB was given orally in daily dose of 300 mg (18 cases) or 600 mg (2 cases) in three divided portions. The duration of administration was 3 to 14 days. Especially they were given for 7 days in 16 cases. A total of 11 strains comprising 4 strains of Staphylococcus aureus, 2 strains of beta-Streptococcus and 1 strain each of Streptococcus pneumoniae, Branhamella catarrhalis, Klebsiella oxytoca, Serratia marcescens, Acinetobacter Iwoffii were identified from sputa before administration. All of the above bacteria were eradicated but, in 1 case, a strain of Streptococcus pyogenes appeared after the treatment (eradication ratio = 100%). The clinical efficacy rate was 100%: Responses were excellent in 3 cases and good in 17 cases. There was no side effect and no abnormal changes in laboratory test results. From the above results, it is concluded that CETB is effective, safe and useful new oral cephem on acute bronchitis.


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Health Effects of *Serratia marcescens*
Epidural abscess is a rare complication of fistulizing Crohn's disease (CD), potentially appearing as neurologic symptoms or back and leg pain. We report a case of a large epidural abscess resulting from uncontrolled fistulizing CD, which was rapidly defined using gadolinium-enhanced magnetic resonance imaging (MRI). Whenever caudal neurologic symptoms, back pain, and fever arise in CD patients, diagnostic MRI of the pelvis in addition to conventional computerized tomography should be considered to identify perirectal fistulization to the spine.

Over the 8 year period 1988-1995, 1367 isolates of *Serratia marcescens* were isolated from 582 patients on 12 different wards of a large Dublin hospital and were particularly associated with the surgical intensive care unit. The annual incidence was over 200 isolates from 1990 to 1992 but fell to below 100 following the opening in April 1992 of a replacement surgical hospital incorporating a new intensive care unit on the same site. The most common source of *S. marcescens* was sputum from patients. Strain identities were determined by serotyping and phage typing at least one isolate from each of 311 of the 582 patients. The results showed that a single epidemic strain of serotype O14:K14 was present in 69% of these patients, and persisted throughout the hospital for the whole of the eight-year period. This strain was recovered from a variety of clinical specimens, including blood cultures. A minor outbreak involving a serotype O16:K28 strain also occurred and this strain also persisted from at least 1989 to 1994. Extensive surveillance failed to reveal an environmental source or faecal carriage. The likely mode of transmission appears to have been via staff hands from both symptomatic and asymptomatic patients acting as reservoirs of the organism, as has commonly been reported for this species.

Over the last 30 years, *Serratia marcescens* has become an important cause of nosocomial infection. There have been many reports concerning the identification, antibiotic susceptibility, pathogenicity, epidemiological investigations and typing of this organism. Accurate identification is important in defining outbreaks. The API 20E system has been used widely, but is not individually satisfactory. The growth of *S. marcescens* in the environment has been investigated in relation to water, disinfectants and plastics such as blood bags. Certain extracellular products are unique to *S. marcescens*. Pigment (prodigiosin) biosynthesis by *S. marcescens* has been investigated fully since the emergence of the organism as a cause of infection. Many other aspects of the pathogenicity and virulence of *S. marcescens* have been studied, including adherence and hydrophobicity, lipopolysaccharide (LPS) and extracellular products. Two modes of adhesion to host epithelial surfaces have been suggested. These are mannose-resistant (MR) pili and mannose-sensitive (MS) pili. LPS, which is responsible for the biological activity of endotoxin, has been investigated fully and 24 somatic antigens have been described. The production of different enzymes by *S. marcescens* as virulence factors has also been reported, including chitinase, lipase, chloroperoxidase and an extracellular protein, HasA. Antibiotics used to treat *serratia* infection include beta-lactam agents, aminoglycosides and fluoroquinolones and a variety of different resistance mechanisms.
have been demonstrated. Typing methods used to study the epidemiology of *S. marcescens* include biotyping, bacteriocin typing, phage typing, plasmid analysis, polymerase chain reaction amplification of enterobacterial repetitive intergenic consensus sequences (ERIC-PCR) and ribotyping. Serological typing has also been used and this method seems to be a suitable first-line typing method for *S. marcescens*, although some strains remain untypable. RAPD-PCR has also been applied to a small number of isolates and seems to be a promising method, especially for rapid monitoring of an outbreak and tracing the source of initial infection.

**Heltberg et al. 1993.** Nosocomial epidemic of *Serratia marcescens* septicemia ascribed to contaminated blood transfusion bags. *Transfusion.* Vol. 33(3): 221-227. Two cases of transfusion-related *Serratia marcescens* bacteremia prompted extensive epidemiologic investigations in three independent hospitals. Test tubes and plasma from donors whose blood was drawn into bags from a single production batch were cultured. Analysis of the ribotype of *S. marcescens* isolates was performed. For comparison, a strain from the production plant and eight other, unrelated bacteremia isolates were examined. In addition, a retrospective national survey was carried out. *S. marcescens* was cultured from 11 (0.73%) of 1515 blood units, and an additional (third) bacteremic patient was identified. The clinical isolates from three patients, the three units of blood transfused, and the plant-derived strain shared a unique ribotype. The incident is interpreted as a sporadic, bacterial contamination of blood bags with the *S. marcescens* epidemic strain, occurring during the manufacturing or packaging. A similar incident has not previously been reported. Attention is drawn to the possibility of significant contamination during the complex production of multiple-bag blood collection systems. Guidelines for improved registration and handling of transfusion complications in wards are suggested. Manufacturers should be encouraged to provide blood packs with sterile exteriors, in appropriate, single, outer packages.

**Henry et al. 2001.** An outbreak of *Serratia marcescens* associated with the anesthetic agent propofol. *Am.J.Infect.Control.* Vol. 29(5): 312-315. **BACKGROUND:** In October 1999, 7 patients with postoperative infections caused by *Serratia marcescens* were identified at a community hospital in Ontario, Canada. We describe the investigation of this outbreak. **METHODS:** We undertook a case-control study to determine risk factors associated with infection. Case subjects consisted of patients who had undergone surgery and acquired bacteremia or wound infections that, when cultured, grew *S marcescens*. Control subjects were selected from the cohort of patients who underwent surgery at the same hospital during the outbreak period. Chart reviews were conducted for case and control subjects. Environmental samples were taken from medications and liquids in the operating rooms and from one health care professional who was involved in all the cases. *S marcescens* isolates were forwarded to a reference laboratory for pulsed field gel electrophoresis. **RESULTS:** We identified 7 case subjects and 29 control subjects. Five patients had bacteremia and 2 patients had wound infections. Two patients with bacteremia died. All patients with bacteremia or wound infections were exposed to a single anesthetist (anesthetist A) and were administered the anesthetic medication propofol. These patients were more than 40 times more likely to have had anesthetist A administer their anesthetic (OR 41.6, 95% CI 3.6-1120) and 22
times more likely to have received propofol (OR 22, 95% CI 2.1-550) than were control subjects. None of the environmental samples or cultures from anesthetist A were positive for S marcescens. Six of the 7 human isolates had an identical pulsed field gel electrophoresis pattern, and the seventh was untypeable. CONCLUSIONS: This outbreak of postoperative infections was very strongly linked to the use of propofol by one anesthetist. Health care professionals must follow strict aseptic techniques when using propofol and should review these techniques regularly.

The footpad swelling reaction induced by local injection of *S. marcescens* lipopolysaccharide was found to be inhibited in mice given a transplantable tumor (TA3) or cell-free ascitic fluid from tumor-bearing mice. The tumor was shown to contain LDH virus, which is known to cause inapparent persistent infections in mice. Monoclonal antibodies directed against protein VP3 of the LDH virus could partially abrogate the anti-inflammatory effect of the TA3-ascitic fluid, and, conversely, the anti-inflammatory effect could be obtained by LDH virus isolated from the tumor and reproduced by serial passage of cell-free fluids. Inhibition of the footpad reaction was seen in the acute but not in the chronic phase of LDH virus infection, suggesting that the anti-inflammatory effect might be due to endogenous interferon (IFN) which, similarly, was only detectable in the acute phase. Newcastle disease virus, another potent interferon inducer, had a similar inhibitory effect on the footpad reactivity. Moreover, the inhibitory effect of LDH virus infection could partially be abrogated by administration of a polyclonal antibody directed against murine IFN-alpha,beta. Finally, passively administered natural murine IFN-alpha,beta or recombinant murine IFN-alpha 1 (but not recombinant murine IFN-beta) was found to cause inhibition of the footpad reaction. Since Gram-negative bacteria and their lipopolysaccharides have the ability to induce a systemic interferon response, our findings suggest that this interferon may play a modulatory role in local inflammation caused by these bacteria. Our findings also open a new perspective for interferon therapy of certain inflammatory reactions to bacterial infections.

Mice given lipopolysaccharide (LPS) intravenously developed lung edema, which was maximum after 6 h. Tumor necrosis factor, interleukin 12 (IL-12), IL-6, and interferon-gamma (IFN-gamma) appeared in the serum, and levels of nitrogen oxide (NO) derivatives were increased in serum and bronchoalveolar fluid. Mice pretreated with neutralizing anti-IFN-gamma antibodies had lower serum levels of IFN-gamma, and fewer died. However, levels of other cytokines and NO derivatives as well as lung edema were unchanged. If IFN-gamma and LPS were given together, pulmonary edema was less, but levels of cytokines and NO derivatives in serum were raised, and the mortality was greater. IFN-gamma receptor knockout mice had more edema after LPS, but were less sensitive to the lethal effects. Treatment with anti-IL-12 antibody inhibited IFN-gamma induction and reduced mortality, but had no effect on the lung edema; exogenous
IL-12 also failed to affect edema, but boosted serum cytokine levels and increased the mortality. Aminoguanidine, an inhibitor of NO synthase, protected against pulmonary edema, but did not modify the lethal effects of LPS. Clearly, in this model, early pulmonary edema and lethality are not directly related, and induced IFN-gamma has no role in causing early lung edema, but augments other events that result in death.


We describe a serious outbreak of infection caused by a strain of Serratia marcescens in two Dublin hospitals which occurred over an 11 week period and affected a total of 15 patients. A contaminated bed-pan macerator in the Intensive Care Unit of one hospital was identified as the possible source of infection and spread of the organism probably occurred via hand transmission by hospital personnel and via patient transfer to a second hospital. All isolates of S. marcescens involved in the outbreak had the same antimicrobial susceptibility pattern, with reduced susceptibility to gentamicin, cefotaxime and ciprofloxacin. Epidemiological typing revealed that the strains of S. marcescens isolated in the outbreak were of an uncommon serotype, O21:K14, and using pulsed-field gel electrophoresis, Xbal DNA macrorestriction profiles clustered at 90% similarity. The DNA patterns of the outbreak strain were also highly similar to S. marcescens isolates of the same serotype recovered from a separate Dublin hospital during the same time period as the outbreak described here. In addition, the isolates clustered at 82% similarity with strains of the same serotype from a retrospective collection of S. marcescens isolates from various hospitals in the Dublin area, indicating that these may be genetic variants of the same strain. Although the outbreak was brought under control following implementation of infection control measures, a significant number of similar O:21 isolates of S. marcescens have since been identified in four Dublin hospitals. These results suggest the unique spread of a single strain of S. marcescens in Dublin hospitals.

Both the inactive and active conformations of the hemolysin/cytolysin of Serratia marcescens (ShlA) binds membranes of erythrocytes, but only active ShlA is able to form pores. ShlA is unable to lyse prokaryotic membranes. To determine the receptors of the binding and pore-forming domains of active cytolysin on eukaryotic membranes, artificial large unilamellar vesicles (LUVs) of various membrane compositions were examined. In the current study, it is shown that significant pore formation and lysis was achieved with binary phosphatidylcholine/phosphatidylserine (PS) liposomes. No proteinaceous receptor was needed for either binding or pore formation by ShlA. Membrane integration and pore-forming activity were enhanced by addition of phosphatidylethanolamine. Phosphatidylserine is negatively charged at physiologic pH and is almost absent in prokaryotic membranes. Hence, membrane binding and insertion of ShlA are highly dependent on phosphatidylserine, which targets the toxic activity to

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eukaryotic cell membranes without any need of a proteinaceous receptor. This may explain why prokaryotic membranes were found to be resistant against ShlA in a previous study.

Hertle. 2000. Serratia type pore forming toxins. Curr Protein Pept Sci. Vol. 1(1): 75-89. The Serratia marcescens hemolysin represents a new type of hemolysin and has been studied in great molecular detail with regard to structure, activation and secretion. It has nothing in common with the pore forming toxins of E. coli type (RTX toxins), the Staphylococcus aureus alpha-toxin or the thiol activated toxin of group A beta-hemolytic streptococci (Streptolysin O). Studies on erythrocytes, eukaryotic cells and artificial black lipid membranes, have shown that the mechanism of pore formation of ShlA is different from other pore forming toxins. The S. marcescens hemolysin proteins ShlB and ShlA exhibit protein sequence homologues in Proteus mirabilis, Haemophilus ducreyi, Edwardsiella tarda and Erwinia chrysanthemi. Furthermore, sequence motifs present in ShlA and Shlb have been shown to be important for activity and secretion of the S. marcescens hemolysin. Thus, the S. marcescens hemolysin forms the prototype of a new class of hemolysins and of a new secretory mechanism. The uniqueness of this new mechanism is underlined by the fact that activation of ShlA by ShlB strictly requires phosphatidylethanolamine as a cofactor. New data implicate a conformational change in ShlA during activation. In addition, ShlA not only forms pores in erythrocytes but also in fibroblasts and epithelial cells. The cytotoxic action of ShlA is mainly determined by lysis of infected cells in vitro. In sublytic doses, as will normally be the situation in vivo, ShlA exerts additional effects which are currently under investigation. The knowledge of the structure, activation, secretion and mode of action of S. marcescens hemolysin has implications for proteins, related in sequence or in mode of secretion and activation.

Hertle et al. 1999. Cytotoxic action of Serratia marcescens hemolysin on human epithelial cells. Infect. Immun. Vol. 67(2): 817-825. Incubation of human epithelial cells with nanomolar concentrations of chromatographically purified Serratia marcescens hemolysin (ShlA) caused irreversible vacuolation and subsequent lysis of the cells. Vacuolation differed from vacuole formation by Helicobacter pylori VacA. Sublytic doses of ShlA led to a reversible depletion of intracellular ATP. Restoration to the initial ATP level was presumably due to the repair of the toxin damage and was inhibited by cycloheximide. Pores formed in epithelial cells and fibroblasts without disruption of the plasma membrane, and the pores appeared to be considerably smaller than those observed in artificial lipid membranes and in erythrocytes and did not allow the influx of propidium iodide or trypan blue. All cytotoxic effects induced by isolated recombinant ShlA were also obtained with exponentially growing S. marcescens cells. The previously suggested role of the hemolysin in the pathogenicity of S. marcescens is supported by these data.


BACKGROUND: Serratia marcescens, a frequent agent of catheterization-associated bacteriuria, strongly adheres to human bladder epithelial cells in culture. The epithelium normally provides a barrier between lumal organisms and the interstitium; the tight
adhesion of bacteria to the epithelial cells can lead to internalization and subsequent lysis. However, internalisation was not shown yet for *S. marcescens* strains. METHODS: Elektronmicroscopy and the common gentamycin protection assay was used to assess intracellular bacteria. Via site directed mutagenesis, an hemolytic negative isogenic Serratia strain was generated to point out the importance of hemolysin production. RESULTS: We identified an important bacterial factor mediating the internalization of *S. marcescens*, and lysis of epithelial cells, as the secreted cytolysin ShlA. Microtubule filaments and actin filaments were shown to be involved in internalization. However, cytolysis of eukaryotic cells by ShlA was an interfering factor, and therefore hemolytic-negative mutants were used in subsequent experiments. Isogenic hemolysin-negative mutant strains were still adhesive, but were no longer cytotoxic, did not disrupt the cell culture monolayer, and were no longer internalized by HEp-2 and RT112 bladder epithelial cells under the conditions used for the wild-type strain. After wild-type *S. marcescens* became intracellular, the infected epithelial cells were lysed by extended vacuolation induced by ShlA. In late stages of vacuolation, highly motile *S. marcescens* cells were observed in the vacuoles. *S. marcescens* was also able to replicate in cultured HEp-2 cells, and replication was not dependent on hemolysin production. CONCLUSION: The results reported here showed that the pore-forming toxin ShlA triggers microtubule-dependent invasion and is the main factor inducing lysis of the epithelial cells to release the bacteria, and therefore plays a major role in the development of *S. marcescens* infections.


The efficacy and toxicity of ciprofloxacin, an orally administered fluoroquinolone, were evaluated in 24 infections in 23 patients with osteomyelitis caused by aerobic gram-negative bacilli. The diagnosis was confirmed by surgical findings and the results of bone biopsy and culture of bone or deep soft tissue. The aerobic gram-negative bacilli were *Pseudomonas aeruginosa* (15 isolates), *Serratia marcescens* (five isolates), *Escherichia coli* (three isolates), *Enterobacter* species (three isolates), *Proteus mirabilis* (one isolate), *Pseudomonas fluorescens* (one isolate), and *Klebsiella pneumoniae* (one isolate). Minimal bactericidal concentrations (MBCs) were 1.56 micrograms/ml or less for all but one isolate. Nine infections were polymicrobial, involving aerobic gram-positive cocci or anaerobes in addition to aerobic gram-negative bacilli. Additional antibiotics to which the aerobic gram-negative bacilli were resistant were given when the additional organisms were resistant to ciprofloxacin. Patients received 750 mg of ciprofloxacin twice daily for a mean of 62 days. Peak serum levels of ciprofloxacin were at least threefold higher than the MBCs in 20 of 24 patients. Twenty of 22 infections in which a full course of therapy was completed were without evidence of active disease at one to 17 months posttreatment. A sternotomy wound infection relapsed after eight weeks of therapy with a newly resistant *S. marcescens* strain, and an infection of a compound fracture relapsed two months posttreatment with a still sensitive *P. aeruginosa* strain. Toxicity was minimal in most patients: eosinophilia (six patients), nausea (eight patients), mild elevation in transaminase levels (three patients), pruritus (one patient), diarrhea (two patients), thrush (two patients), rash (two patients), and mild leukopenia (one patient). Two additional patients had severe side effects (vertigo in one and acute renal failure in another) that
required discontinuation of ciprofloxacin therapy. Overall, ciprofloxacin is a promising agent for the oral treatment of gram-negative bacillary osteomyelitis.


**Hirabayashi et al. 1983.** Fundamental and clinical studies on T-1982 (cefbuperazone) in the field of obstetrics and gynecology. *Jpn. J. Antibiot.* Vol. 36(5): 1041-1053. Fundamental and clinical studies on T-1982 (cefbuperazone), a new cephamycin antibiotic, were carried out, and the following results were obtained. When T-1982 was administered at a dose of 1 g by intravenous drip infusion for 30 minutes or 1 hour, the concentration in serum showed as high as 23.0 micrograms/ml or 25.0 micrograms/ml even 2 hours after administration. The concentrations in the genital tissues about 5 hours after administration ranged 1.2-45.6 micrograms/g for 30 minutes drip infusion and 0.9-26.8 micrograms/g for 1 hour drip infusion. From these results, T-1982 was supposed to maintain the in vivo concentration to inhibit 80-100% the growth of bacteria such as S. aureus, E. coli, Klebsiella, Proteus, *S. marcescens* and Gram-negative anaerobic bacteria, B. fragilis which were often isolated clinically in the field of obstetrics and gynecology. When T-1982 was administered at a dose of 1-2 g twice a day to 14 patients with female genital infection; 2 intrauterine infection, 2 pyometra, 7 pelveoperitonitis, 1 adnexitis, 1 adnexitis abscess and 1 vaginal cuff abscess, the clinical results were excellent in 9, effective in 4 and poor in 1. The efficacy rate was 92.9%. No side effects nor abnormalities in laboratory findings were observed in any of the 14 cases. These results suggest that T-1982 has efficacy for the treatment of obstetrical and gynecological infections.

**Hirakata. 2002.** Serratia. *Nippon Rinsho.* Vol. 60(11): 2156-2160. Serratia species, in particular, *Serratia marcescens* frequently causes bloodstream infections. Recently, several outbreaks of nosocomial bloodstream infections due to *S. marcescens* have been reported in Japan. Although Serratia is an opportunistic pathogen, the organism can develop endotoxin shock and multiple organ failure because of being gram-negative rod when a number of bacteria invade the bloodstream. Serratia in the intestinal tract can invade bloodstream endogenously in compromised hosts. However, the possible causes of an outbreak are contamination of antiseptics, and consequent contamination of transfusion. To prevent outbreaks of *S. marcescens* bloodstream infection, management of antiseptics and transfusion in addition to contact precaution should be taken.

**Hohenhaus et al. 1997.** Serratia marcescens contamination of feline whole blood in a hospital blood bank. *J. Am. Vet. Med. Assoc.* Vol. 210(6): 794-798. During a 7-month period, 29 units of feline whole blood in a hospital blood bank were confirmed, and 2 units were suspected, to be contaminated with Serratia marcescens. An
The investigation of the outbreak identified S. marcescens in a jar of alcohol-soaked cotton balls and in a bag of saline solution used during venipuncture. Fifteen of the contaminated units were administered to 14 cats, and 6 of the 14 developed clinical signs of a transfusion reaction. The most common sign was vomiting; 4 cats died. The report underscores the importance of using aseptic techniques during collection of blood for transfusion and of thoroughly investigating any transfusion reaction.

PURPOSE: Twelve volunteers participated in a study designed to measure the overnight corneal edema response with a variety of hydrogel contact lenses. During the study four subjects (5 eyes) experienced a contact lens related acute red eye (CLARE) reaction, which manifested as severe ocular pain, photophobia, corneal infiltration, and conjunctival hyperemia. An additional five subjects (7 eyes) developed corneal infiltrates only. Twelve eyes (of 9 subjects) showed no response. METHODS AND RESULTS: Upon microbiological examination of the contact lenses and storage solutions, gram-negative bacteria were isolated in large amounts. The bacteria were identified as Serratia marcescens, Pseudomonas putida, and Pseudomonas aeruginosa. Significantly greater numbers of bacteria were isolated from contact lenses of subjects who experienced CLARE than from the other subjects (P = 0.005) and from the contact lenses of subjects who experienced an adverse reaction (CLARE or infiltrates) than from the other subjects (P < 0.001). The contaminating bacteria are thought to have been introduced to the lens storage vials as a result of lens handling and subsequent failure to disinfect lenses.

CONCLUSIONS: This study draws attention to the possible contribution of contaminated lenses and storage cases in contact lens related acute inflammation and specifically implicates gram-negative bacteria, in particular Pseudomonas spp. and Serratia spp., in the induction of acute inflammatory reactions such as CLARE.

The carbapenem-induced endotoxin release was evaluated using experimental models of gram-negative bacterial sepsis in Wistar rats. Infections with Escherichia coli, Serratia marcescens, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus vulgaris and Proteus mirabilis resulted in an increase of the plasma endotoxin concentration after treatment with ceftazidime and carbapenems including imipenem, panipenem, meropenem and biapenem. Except for P. aeruginosa, the plasma endotoxin concentrations after carbapenem treatment were significantly lower than those after ceftazidime treatment. It is noteworthy that treatment of P. aeruginosa sepsis with meropenem or biapenem induced significantly more endotoxin release than other carbapenems and the endotoxin concentrations induced by these carbapenems reached those of ceftazidime treatment. The plasma endotoxin concentrations appeared to correlate with the reduction of platelet counts and the elevation of both glutamic oxaloacetic transaminase and glutamic pyruvic transaminase values.

Twenty-four pediatric patients with infections were treated with ceftazidime (CAZ) by one-shot intravenous injection in the doses of 39 approximately 149 mg/kg/day in 4 divided doses as a rule. These patients' ages ranged from 2 months to 13 years 4 months. The duration of the administration ranged from 4 to 19 days, and total doses ranged from 1.38 to 57 g. Infections consisted of respiratory tract infections in 19 cases (acute tonsillitis in 3, acute bronchitis in 7, and pneumonia in 9), urinary tract infection in 1 case, acute peritonitis in 1 case, and suspected sepsis in 3 cases. Clinical efficacy was excellent in 18, good in 1, fair in 1, and poor in 4 cases, and the efficacy rate (excellent + good) was 79.2%. Bacteriological response was evaluated on 14 strains of bacteria isolated from lesions, assumed as the causative organisms (7 strains of S. aureus, 3 of P. aeruginosa, 1 of H. influenzae, 1 of K. pneumoniae, 1 of E. coli, and 1 of S. marcescens). Out of these strains, 10 were eradicated, and 1 (P. aeruginosa) decreased, but 2 strains (both S. aureus) persisted. (One strain of S. aureus was not examined.) No adverse effect suspected to be related to the drug was observed either in subjective symptom or in objective findings.


Tay-Sachs or Sandhoff disease results from a deficiency of either the alpha- or the beta-subunits of beta-hexosaminidase A, respectively. These evolutionarily related subunits have been grouped with the “Family 20”; glycosidases. Molecular modeling of human hexosaminidase has been carried out on the basis of the three-dimensional structure of a bacterial member of Family 20, Serratia marcescens chitobiase. The primary sequence identity between the two enzymes is only 26% and restricted to their active site regions; therefore, the validity of this model must be determined experimentally. Because human hexosaminidase cannot be functionally expressed in bacteria, characterization of mutagenized hexosaminidase must be carried out using eukaryotic cell expression systems that all produce endogenous hexosaminidase activity. Even small amounts of endogenous enzyme can interfere with accurate K(m) or V(max) determinations. We report the expression, purification, and characterization of a C-terminal His(6)-tag precursor form of hexosaminidase B that is 99.99% free of endogenous enzyme from the host cells. Control experiments are reported confirming that the kinetic parameters of the His(6)-tag precursor are the same as the untagged precursor, which in turn are identical to the mature isoenzyme. Using highly purified wild-type and Arg(211)Lys-substituted hexosaminidase B, we reexamine the role of Arg(211) in the active site. As we previously reported, this very conservative substitution nevertheless reduces k(cat) by 500-fold. However, the removal of all endogenous activity has now allowed us to detect a 10-fold increase in K(m) that was not apparent in our previous study. That this increase in K(m) reflects a decrease in the strength of substrate binding was confirmed by the inability of the mutant isozyme to efficiently bind an immobilized substrate analogue, i.e., a hexosaminidase affinity column. Thus, Arg(211) is involved in substrate binding, as predicted by the chitobiase model, as well as catalysis.

Huang et al. 2001. Protean infectious types and frequent association with neurosurgical
Serratia marcescens is a rare pathogen of adult central nervous system (CNS) infection. We report on the clinical features and therapeutic outcomes of two adult patients with such infections. The clinical characteristics of 13 other reported adult cases are also included for analysis. The 15 cases were nine males and six females, aged 19-83 years, in whom, underlying post-neurosurgical states and ear operation were noted in 93% (14/15). Fever and conscious disturbance were the most common clinical manifestations of these 15 cases, followed by hydrocephalus, seizures, and wound infections. The manifestation types were protean, including meningitis and focal suppurations such as brain abscess, cranial and spinal epidural abscess, cranial subdural abscess, and infected lumbar pseudomeningocele. One case of S. marcescens CNS infection was diagnosed postmortem; the other 14 were diagnosed by the positive culture from CSF or pus. Antibiotic therapy with or without neurosurgical intervention was the management strategy in 14/15 cases. The therapeutic results showed a high mortality rate.

Necrotizing fasciitis (NF), a devastating soft tissue infection, is rarely attributed to Serratia marcescens. We here report two patients with *S. marcescens* NF, both of whom had underlying renal disease and had been receiving corticosteroid therapy. The first patient, a 40-year-old man with systemic lupus erythematosus and uremia on prednisolone therapy, developed fulminant cellulitis and septic shock 1 month after a skin biopsy for cutaneous vasculitis of the left foot. The cellulitis evolved to NF, and blood and necrotic tissue cultures both grew *S. marcescens*. The patient completely recovered after debridement and ceftazidime therapy. The second patient, a 73-year-old man receiving prednisolone therapy for nephrotic syndrome, developed right leg cellulitis that evolved to NF. Blood and necrotic tissue cultures both grew *S. marcescens*. After aggressive debridement and ciprofloxacin therapy, the NF improved. However, the patient died of aspiration pneumonia and massive gastrointestinal bleeding 1 month later. These findings illustrate that *S. marcescens* should be considered as a potential pathogen causing NF in susceptible hosts.

Alopecia (hair loss) is among the most distressing side effects of cancer chemotherapy. Little progress has been made, however, in its prevention or treatment, partly because of the lack of suitable experimental model. In recent work on the treatment of myelogenous leukemia in the rat, the following observations were made: (i) treatment of 8-day-old rats with cytosine arabinoside consistently produced alopecia, and (ii) ImuVert, a biologic response modifier derived from the bacterium Serratia marcescens, uniformly produced complete protection against the alopecia. In subsequent experiments, both cyclophosphamide and doxorubicin also produced alopecia in this model, and the
doxorubicin-induced alopecia was prevented by treatment with ImuVert. The potential relevance of these observations to chemotherapy-induced alopecia in the clinical setting should be examined.


Persistent diabetes was induced in male Scl:ddY mice by a single intraperitoneal injection of 200 mg/kg streptozotocin (STZ). In these mice, the numbers of aerobic gram-negative bacilli, staphylococci (including micrococci), and streptococci increased, while those of other bacteria were almost unchanged in both oral and caecal floras. The mice were vulnerable to oral infection of Salmonella enteritidis, intranasal infection of Klebsiella pneumoniae and Serratia marcescens, and contact infection with mice infected with *S. enteritidis* and *K. pneumoniae*. These findings suggest that STZ-treated mice might be a useful model for investigating opportunistic infection.


We present a case of a 78-year-old man suffering from a chronic psoriasiform eruption, with rapid deterioration over the previous 8 weeks. Langerhans' cell histiocytosis with skin and bone involvement was diagnosed, and there was evidence of liver and lung dysfunction. The patient was treated with prednisolone and etoposide, and initially experienced a partial improvement. Three weeks later, haemophagocytic lymphohistiocytosis and subsequently a large pulmonary abscess with sepsis attributed to opportunistic gram-negative enterobacteriaceae Serratia marcescens developed, and the patient died. The present case of Langerhans' cell histiocytosis is of particular interest because of the previously unreported development of haemophagocytic lymphohistiocytosis in the elderly population.


Clinical mastitis with infection of Serratia marcescens occurred in a tied-up dairy herd in Sweden on a scale widely exceeding what has hitherto been reported in veterinary literature. The herd contained 37 milking cows before the disease period but only 14 at slaughter 21 months later in spite of some recruitment. A very large number of mastitis cases, usually rather mild and of short duration, had then occurred--during one single month not less than 47 cases. Hardly any cow escaped the disease. Instead, the single cows fell ill at short intervals with mastitis in the same quarter as previously or in another
quarter. Antibiotic therapy in clinical cases, dry cow therapy and teat dipping had no obvious effect. Serratia marcescens was isolated in all 14 slaughtered cows in one or more quarters. The morphological changes were remarkably mild. Isolated Serratia strains revealed no distinctive marks compared with ordinary saprophytic strains in laboratory tests. Serratia-contaminated sawdust used as litter was possibly the source of infection and the milking machine possibly the tool for the transmission of bacteria to the udder, in the latter case by the aspiration of contaminated sawdust when the claw was attached or detached, or it fell off during milking. The pathogenicity of the bacteria and the susceptibility of the cows to udder infection may have been increased.

**Ito et al. 1985.** Clinical evaluation of amikacin by intravenous drip infusion for infections in the field of internal medicine. *Jpn.J.Antibiot.* Vol. 38(8): 2108-2118. Amikacin (AMK) by intravenous drip infusion was given to patients with infections in the field of internal medicine and the results were followings: AMK was administered to 19 patients. Diagnosis included sepsis or suspected sepsis (11 cases), pneumonia (2 cases), chronic respiratory tract infections (3 cases) and urinary tract infections (3 cases). Underlying disease included hematologic disease (13 cases), lung fibrosis (1 case), chronic respiratory insufficiency (1 case), diabetes mellitus (1 case), hepatic coma and bronchial asthma (1 case) and prostatic hypertrophy (1 case). Nineteen episodes responded to single therapy (2 cases) or combined therapy with other antibiotics (17 cases). AMK by intravenous drip infusion (dissolved in not less than 100 ml of saline or glucose) was administered at the dose of 200 mg/day to 600 mg/day divided into 2 or 3 times, over 1 hour to 2 hours. The mean duration of therapy was 10 days and the mean total dose was 4.3 g. Clinical effects: Excellent in 7 cases, good in 7 cases, fair in 3 cases and poor in 2 cases, and efficacy rate was 74%. Bacteriological effects: Disappeared in 3 cases, partly disappeared and unchanged in 3 cases, superinfection in 1 case and newly appeared in 1 case. Four strains out of 7 cases of which were detected the causative bacteria were disappeared. GM resistant bacteria (S. marcescens in 2 strains and C. diversus in 1 strain) were disappeared by the administration of AMK, also some clinical symptoms and signs were improved. No side effects and no abnormalities in laboratory findings were noted in any cases attributed to AMK. In conclusion, high efficacy rate was obtained without any side effects, intravenous drip infusion of AMK seemed to be useful for infections in patients with bleeding tendency (e.g. leukemia) or malignant disease.

**Jabrane et al. 2002.** Characterization of serracin P, a phage-tail-like bacteriocin, and its activity against Erwinia amylovora, the fire blight pathogen. *Appl.Environ.Microbiol.* Vol. 68(11): 5704-5710. Serratia plymuthicum J7 culture supernatant displayed activity against many pathogenic strains of *Erwinia amylovora*, the causal agent of the most serious bacterial disease of apple and pear trees, fire blight, and against *Klebsiella pneumoniae*, Serratia liquefaciens, Serratia marcescens, and Pseudomonas fluorescens. This activity increased significantly upon induction with mitomycin C. A phage-tail-like bacteriocin, named serracin P, was purified from an induced culture supernatant of *S. plymuthicum J7*. It was found to be the only compound involved in the antibacterial activity against sensitive strains. The N-terminal amino acid sequence analysis of the two major subunits (23 and 43 kDa) of serracin P revealed high homology with the Fels-2 prophage of Salmonella enterica, the
coliphages P2 and 168, the phiCTX prophage of Pseudomonas aeruginosa, and a prophage of Yersinia pestis. This strongly suggests a common ancestry for serracin P and these bacteriophages.


An analysis of hospital-acquired bacteraemia among ICU patients was carried out over a two-year period in order to determine the incidence, associated mortality rate and susceptibility pattern of causative pathogens. There was a high incidence of bacteraemia, occurring in 127 (18.4%) of 692 patients. Mortality attributable to nosocomial bacteraemia was 52% of the total 79 deaths from all causes. The highest mortality rate (58.5%) occurred in patients with fungal infections, whilst death from Gram-negative bacteraemia was only 17%. Over 98% of patients had underlying disease. Nearly half (46.8%) of 267 organisms isolated were Gram-positive. In comparison, Gram-negative bacteria accounted for 36.6% and the rest (17.6%) were fungi (mainly Candida albicans). The majority of the bactereamic episodes were monomicrobial (90.2%). Coagulase-negative staphylococci (CNS) were the commonest pathogens isolated, representing 32.6% of all organisms. Inducible beta-lactamase producing organism (Enterobacter spp. 9.7%, Serratia marcescens 6.7%, Klebsiella pneumoniae 6% and Pseudomonas aeruginosa 6%) formed the bulk of Gram-negative bacteria. In contrast, Escherichia coli (7.5%) and K. pneumoniae (4%) were the commonest Gram-negative bacteria from hospital-acquired bacteraemia in the general hospital population. The majority (80%) of CNS were resistant to methicillin (MRSE) but susceptible to vancomycin; they were relatively resistant to erythromycin, clindamycin and beta-lactams antibiotics. Whilst Gram-negative organisms were relatively susceptible to imipenem (85%), ciprofloxacin (88%) and amikacin (87%), they had unacceptably low levels of susceptibility to cefuroxime (59.3%), cefotaxime (71%), ceftazidime (60.9%), and piperacillin (51.1%). This study shows that hospital-acquired bacteraemia in ICU patients carries a poor prognosis. Information regarding the infective agents and their susceptibility in the ICU setting is valuable for the selection of empirical therapy before culture and susceptibility results are known.


Serratia marcescens is a well-recognized hospital-acquired pathogen, which has been associated with a number of specific outbreaks, particularly in critically ill neonates. We used pulsed-field gel electrophoresis (PEGE) typing to analyse an outbreak in a neonatal intensive care unit (NICU). We included samples from nine patients, three handwashes and ten environmental isolates from an outbreak (February to August 1999) in addition to four patient isolates from different wards of our hospital during the same time period. The clinical presentations of the outbreak included bacteraemia (four cases), pneumonia (three cases), umbilical wound infection (one case) and conjunctivitis (one case). Nine outbreak isolates exhibited an identical PFGE fingerprint, while the epidemiologically unrelated strains demonstrated distinct patterns. Epidemiological investigation failed to reveal a common source of the outbreak, although the epidemic *S. marcescens* strain was
isolated from hand-washes and doors of incubators. We concluded that cross-transmission via transient contamination of hands was the major route for this outbreak. Strict handwashing practices, the cohorting and isolation of colonized and infected patients, and the regular dis-infection of incubators are crucial steps for preventing the transmission of *S. marcescens* in an NICU. This PFGE method is highly discriminatory for the thorough epidemiological investigation of an outbreak of *S. marcescens*.

Serratia marcescens is commonly isolated from the urine of patients with an indwelling urinary catheter and in the absence of symptoms is often regarded as a contaminant. A case of fatal Serratia marcescens septicaemia with meningitis, brain abscesses, and myocarditis discovered at necropsy is described. The patient was an 83 year old man with an indwelling urinary catheter who suffered from several chronic medical conditions and from whose urine Serratia marcescens was isolated at the time of catheterisation. Serratia marcescens can be a virulent pathogen in particular groups of patients and when assessing its significance in catheter urine specimens, consideration should be given to recognised risk factors such as old age, previous antibiotic treatment, and underlying chronic or debilitating disease, even in the absence of clinical symptoms.


Several examples of antagonistic combinations between cefoxitin and other beta-lactam antibiotics have been reported in the literature. This phenomenon may occur especially with Enterobacter spp, Pseudomonas aeruginosa, Citrobacter spp, and Serratia marcescens. In these species, induction of chromosomally mediated beta-lactamases by certain potent inducers, such as cefoxitin, has been suggested as the main mechanism of antagonism. These in vitro interactions may have clinical relevance; however, although studies in animal models have shown a few examples of in vivo antagonism, the actual clinical significance of interactions between beta-lactam antibiotics requires further thorough and controlled clinical studies.

Outbreaks of infection in neonatal intensive care units (NICUs) due to Serratia marcescens are well recognized. In some outbreaks no point source has been found, whereas in others cross-infection has been associated with contaminated ventilator equipment, disinfectants, hands and breast pumps. We report an outbreak due to *S. marcescens* that involved two geographically distinct NICUs. The outbreak occurred over a six week period; 17 babies were colonized, 12 at Glasgow Royal Maternity Hospital (GRMH) and five at the Queen Mothers Hospital (QMH). At GRMH three babies developed septicaemia, of whom two died. The outbreak isolates were of the same serotype and phage type and were indistinguishable on the basis of restriction fragment
length polymorphism analysis. During the outbreak, two babies shown consistently to be negative on screening, were transferred between the two units. In addition, two members of medical staff attended both units. In QMH no means of cross infection was identified. However, in GRMH the outbreak strain of \textit{S. marcescens} was isolated from a laryngoscope blade and a sample of expressed breast milk.


The incidence of endocarditis produced by the so-called “;opportunists”; as a complication of prosthetic valve surgery is progressively increasing in frequency and gradually transforming the clinical picture habitually associated with this disease. We report six cases of endocarditis produced by opportunistic microorganisms (two cases by Candida, and the remaining by Serratia, Actinobacillus, Acinetobacter calcoaceticus, and Bacteroides fragilis, and by Corynebacterium diphtheriae) in four male and two female patients, making special comment on our findings, diagnostic criteria, and treatment. The patients' ages ranged from 9 to 54 years, and all six patients had long-term complications, with symptoms appearing between 45 days and four years after prosthetic valve surgery. The progressive increase of this new type of prosthesis infection is favored by the indiscriminate use of certain drugs and especially by the prophylactic use of antibiotics.

Via special media, Serratia marcescens isolates were found in 3 bedding pack samples and in 2 milking parlor floor samples, and in milk samples from 19 cows during an episode of mastitis in a dairy cow herd. Chromosomal digest patterns of isolated S marcescens were indistinguishable for 18 of the milk samples and all bedding pack samples. Our findings provide strong evidence that the bedding pack was the reservoir of S marcescens associated with the outbreak of intramammary infections. Additionally, our ability to match digest patterns of isolates in the bedding pack and milk confirms the theory that S marcescens is an environmental pathogen capable of causing mastitis.

A possible cause and the difference in clinical severity of serratial keratitis were investigated. Two strains of Serratia marcescens were isolated: one from a patient with severe liquefactive keratitis, who had diabetes mellitus, and one from a patient with mild superficial keratitis, but who had no underlying disease. When the same numbers of bacteria were injected separately into corneas of the same rabbits or guinea pigs, the strain from the first patient elicited severe corneal destruction, remarkable intracorneal edema; and liquefactive necrosis, but the strain from the second caused mild keratitis with erosion or intracorneal abscess. The keratitis induced by the former strain required a longer time to heal, and the prognosis was poorer than that for the other keratitis. Therefore, the difference in severity between the two cases of experimentally induced keratitis paralleled that of the clinical cases. Thus, the severity of the serratial keratitis
might be attributed more to the virulence of the bacteria than the condition of the host. The virulence factor seemed to be a heat-labile metabolic product (or products) of the bacteria. To clarify this virulence factor, the major secretory protease (56K protease) produced by these two strains of bacteria was compared by using in vitro and in vivo systems. The virulent strain produced about ten times more protease during culture than the less virulent strain. When injected into the corneas of experimental animals, the 56K protease from the virulent strain induced severe lesions similar to those caused by the living virulent strain of bacteria. These results indicated that one of the major factors causing the virulence was correlated with the tissue destructive 56K protease produced by *S. marcescens*.


Recently, in many institutions, *Serratia marcescens* has been isolated more frequently. Therefore, we made a statistical analysis of *S. marcescens* infections. *S. marcescens* was isolated from the urine of 327 of the 1,773 patients admitted to our Department between 1975 and 1981. *S. marcescens* was the most frequently isolated organism in the urine of both inpatients and outpatients all of the 7 years. *S. marcescens* was often isolated in patients with some underlying disease, elderly patients or postoperative patients, in which case the individual defense mechanism protecting the patient from infections is often low. Because 276 of the patients who had *S. marcescens* infection had urethral indwelling catheters, *S. marcescens* infection may be nosocomial. The most effective antibiotic against *S. marcescens* was chloramphenicol followed by amikacin, sulfamethoxazole-trimethoprim, and fosfomycin. The effectiveness of gentamycin, dibekacin and kanamycin was not as high as expected.


**OBJECTIVE:** To investigate the contamination of a vitrectomy apparatus with *Serratia marcescens*. **DESIGN:** Descriptive microbiological and molecular environmental study. **SETTING:** An 1,800-bed university hospital. **RESULTS:** *S. marcescens* was found inside the vitrectomy apparatus at the pressure transducer. Molecular typing by randomly amplified polymorphic DNA-automated laser fluorescence analysis and pulsed-field gel electrophoresis identified a single pattern for all strains isolated from the apparatus. Surprisingly, the contaminating strain was identical to two strains of *S. marcescens* isolated nearly 2 years earlier from two patients who were involved in a small outbreak of acute postoperative endophthalmitis following cataract surgery at another hospital. The emergency vitrectomies in these patients were performed at our hospital with the same apparatus that was found to be contaminated 2 years later. **CONCLUSION:** Performing a systematic environmental search for the assumed bacterial reservoir within the system of the vitrectomy apparatus finally made it possible to find and eliminate the nidus for the gram-negative rod. Molecular typing demonstrated that all isolates belonged to a single genotype, and revealed unexpectedly a link to two vitrectomies performed 2 years earlier. The data support the hypothesis that the source of the contamination was one of these patients, and thus contamination of the apparatus was present for almost 2 years.
Gram-negative bacillary pneumonia has become an increasingly important disease in immunosuppressed, elderly, and hospitalized patients. The clinical features, etiologic agents, population at risk, treatment, and outcome in patients with well-documented gram-negative pneumonia were compared in two groups of patients: those with bacteremic pneumonia and those with nonbacteremic pneumonia documented by transtracheal aspiration. Clinical features were frequently subtle in both groups. A wide range of gram-negative bacilli were implicated as pathogens and pneumonias documented by transtracheal aspiration were frequently mixed infections. Pseudomonas aeruginosa and Serratia marcescens were the most common pathogens causing bacteremic pneumonias, whereas Escherichia coli and Klebsiella were more common in the nonbacteremic group. Gram-negative bacillary pneumonia was frequently a lethal disease despite two-drug therapy, particularly in bacteremic patients.


Patients who develop bacterial pneumonia in the community often require admission to acute-care hospitals. Knowledge of the incidence of pneumonia due to different pathogens that are brought into an institution from the community may play a role in determining the patterns of infecting organisms responsible for hospital-acquired pneumonia. For 1 year, we prospectively reviewed the records of patients admitted to our 1000-bed community hospital with community-acquired bacterial pneumonia (CABP). Patients had clinical signs and symptoms, positive radiologic findings, and pure cultures of potential pathogens from sputum, blood, pleural fluid, lung aspirate, lung biopsy, or transtracheal aspirate. Pneumonia due to Legionella pneumophila was diagnosed by serum indirect fluorescent antibody (IFA) titer greater than or equal to 1:256 and clinical signs and symptoms along with response to erythromycin. Of 204 patients with bacterial pneumonia, the following pathogens were implicated: Streptococcus pneumoniae, Haemophilus species, L. pneumophila, Staphylococcus aureus, Klebsiella pneumoniae, Escherichia coli, oral anaerobic bacteria, Psuedomonas aeruginosa, Serratia marcescens, and others. Most patients were more than 50 years of age and many had evidence of underlying pulmonary disease. The etiology of CABP may not be as predictable as in the past. Empiric antimicrobial therapy for CABP should include agents with activity against the pathogens prevalent in the community.

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Health Effects of *Serratia marcescens*
Knowles et al. 2000. An outbreak of multiply resistant Serratia marcescens: the importance of persistent carriage. Bone Marrow Transplant. Vol. 25(8): 873-877. An outbreak of multi-resistant Serratia marcescens involving 24 patients occurred in a bone marrow transplant and oncology unit, from September 1998 to June 1999, of whom 14 developed serious infection. This is the first such outbreak described in a BMT unit. All isolates demonstrated the same antimicrobial susceptibility pattern and were the same unusual serotype O21:K14. The antimicrobial susceptibility profile showed reduced susceptibility to ciprofloxacin, gentamicin and piperacillin-tazobactam. As the latter two antimicrobials are part of our empiric therapy for febrile neutropenia, they were substituted with meropenem and amikacin during the outbreak. Investigation revealed breaches in infection control practices. Subsequently, the outbreak was contained following implementation of strict infection control measures. A prominent feature of the outbreak was prolonged carriage in some patients. These patients may have acted as reservoirs for cross-infection. This report also indicates that patients who become colonised with Serratia marcescens may subsequently develop invasive infection during neutropenic periods.


Kondrat'eva et al. 1990. Nonspecific non-reactivity in mice induced by joint administration of Newcastle disease virus and cyclophosphamide. Vopr.Virusol. Vol. 35(6): 494-497. The immunomodulating effect of Newcastle disease virus (NDV) was investigated in vitro and in vivo in mice. NDV was shown to induce a mitogenic effect in splenocytes in vitro. Combined injections of NDV and CP resulted in nonspecific suppression of immunoreactivity in mice. The antibody production and development of delayed type hypersensitivity to sheep erythrocytes were markedly reduced. Injections of NDV alone slightly increased the reactions. The NDV + CP injections led also to a reduction of immune response to thymus-independent antigen, LPS. Thus, the combined injections of NDV and CP led to nonspecific suppression of T and B cell immunity in mice. The mechanisms of this form of anergy require further study.


Kraus et al. 1976. Interference by Neisseria gonorrhoeae growth by other bacterial species. J.Clin.Microbiol. Vol. 4(3): 288-295. Growth of Neisseria gonorrhoeae from clinical specimens has been enhanced by the use of selective media that inhibit the simultaneous growth of other microorganisms. One explanation for this enhancement could be that certain other bacteria inhibit gonococcal growth. This hypothesis was examined by testing 167 bacterial isolates for in vitro gonococcal inhibition: 34.1% of the isolates failed to inhibit the gonococcus, but 12.0% produced weak inhibition and 53.9% strongly inhibited N. gonorrhoeae. The pattern of in
in vitro gonococcal inhibition was consistently the same for all the individual isolates within some species, but individual isolates within other bacterial species varied in their ability to inhibit the gonococcus. Consistently strong in vitro N. gonorrhoeae inhibitors were Citrobacter diversus, Enterobacter cloacae, Serratia marcescens, and Pseudomonas. The in vivo significance of gonococcal interference was demonstrated in the subcutaneous chamber model of N. gonorrhoeae infection.


Amplification of DNA fragments surrounding rare restriction sites (ADSSRS-fingerprinting) is a novel assay based on suppression of polymerase chain reaction (PCR). This phenomenon allows the amplification of only a limited subset of DNA fragments, since only those with two different oligonucleotides ligated at the ends of complementary DNA strands are amplified in the PCR. The DNA fragments can be easily analyzed on polyacrylamide gels, stained with ethidium bromide. We have implemented this method using a set of clinical Serratia marcescens isolates from three outbreaks ongoing in the Public Hospital in Gdansk (Poland). Clustering of ADSRRS-fingerprinting data matched epidemiological, microbiological, random amplification of polymorphic DNA (RAPD) and pulsed-field gel electrophoresis (PFGE) data. Based on this study, we found that there is at least a similar power of discrimination between the present 'gold-standard' PFGE and the novel method, ADSRRS-fingerprinting. Although the ADSRRS-fingerprinting method may appear to be more complex than the RAPD technique, we found it fast and reproducible.


Serratia marcescens is an important pathogen in hospitalized urologic patients. We herein describe an epidemic of 134 urinary tract infections caused by a multipe antibiotic-resistant Serratia marcescens. A common source in the cystoscopy area was responsible for 105 infections Cross-contamination on patient floors amplified the magnitude of the epidemic. There was significant patient morbidity, although no deaths could be attributed directly to the outbreak. Particular attention is directed to patient risk factors and the clinical significance of nosocomial Serratia marcescens infections. The clinical approach to epidemic antibiotic-resistant Serratia urinary tract infection should not rely primarily on antibiotic therapy. Stress is placed on the importance of an interdisciplinary approach to hospital-acquired infections in general and Serratia marcescens urinary tract infections in particular.


Twenty-three isolates of Serratia marcescens were isolated over a 10-month period from the blood and arteriovenous shunt sites of patients undergoing haemodialysis in an artificial kidney unit. Surveillance measures performed on the equipment, sterile materials, environment and personnel of this unit yielded Serratia from the air conditioner.
and one of the dialysis units. The isolates from the patients and dialyser unit were pigmented and had an identical biochemical profile, antibiograms, phage typing pattern and O serotype. The isolate from the air conditioner, though of the same biotype, had a different phage and serotype. It was concluded that the dialyser was the ‘common source’ and that the organism was persisting in the machine in spite of recommended sterilization procedures being implemented.


A total of 416 samples comprising faecal samples from diarrhoeic cases of man, calves, sheep and goats, and urine samples from patients with urinary tract infections, were examined for the presence of enterobacteria of emerging pathogenic significance. Citrobacter freundii from 20, C. intermedicius biotype-a from four, Serratia marcescens (serotype 05:H13, bactericin type 16) from one and Erwinia herbicola from two human stool samples were isolated. Only two urine samples yielded C. freundii. Citrobacter freundii was isolated from 10 and C. intermedicius biotype-a from two calves. From sheep and goats, two isolates of C. freundii and three of C. intermedicius biotype-a were obtained. None of these samples yielded Edwardsiella tarda or Yersinia enterocolitica. The examination of 99 toads and 145 wall lizards revealed that toads were reservoirs for C. freundii, C. intermedicius biotype-a and Salmonella brijbhum, whereas wall lizards were reservoirs for C. freundii, C. intermedicius biotype-a, E. herbicola, Enterobacter cloacae and Salmonella spp. These bacteria were present in the range of 2.0 x 10(6) to 6.0 x 10(11) organisms per gram of intestinal contents. In addition, toads were carriers for Edwardsiella tarda (new serotypes 04167:H1 and 05159: non-motile). None of the toads and wall lizards proved positive for C. intermedicius biotype-b (C. kosleri), S. marcescens and Y. enterocolitica. C. freundii, C. intermedicius biotype-a, E. herbicola and S. marcescens were resistant to penicillin and erythromycin whereas E. tarda isolates were also resistant to gentamycin, neomycin, colistin and sulfamethaxazole.


PURPOSE: To present the microbial spectrum and susceptibilities of isolates in endophthalmitis following penetrating keratoplasty. DESIGN: Interventional case series. METHODS: The 1,074 consecutive cases of endophthalmitis presenting to Wills Eye Hospital between 1989 and 2000 were reviewed. Fourteen patients with endophthalmitis after penetrating keratoplasty were identified, and vitreous biopsy isolates from these patients were examined. RESULTS: Eleven (78.6%) of 14 vitreous samples were culture-positive, and two others (14.3%) had organisms viewed on pathology specimen, for a total of 13 (92.9%) organism-proven cases of endophthalmitis. Isolates included 10 (76.9%) gram-positive cocci (six Streptococcus sp., three Staphylococcus sp., one
identified on pathology specimen only) and three (23.1%) gram-negative organisms (Proteus mirabilis, Serratia marcescens, one identified on pathology specimen only). Susceptibilities to organism-appropriate antibiotic testing are reported, including cefazolin (six of eight, 75.0%), ciprofloxacin (four of seven, 57.1%), nafcillin (four of six, 66.7%), and vancomycin (seven of seven, 100.0%). CONCLUSION: This is the largest series on microbial susceptibilities in postpenetrating keratoplasty endophthalmitis. We report a high percentage of culture-positivity, and a high incidence of gram-positive species, and in particular Streptococcus species, with all tested gram-positive organisms susceptible to vancomycin.


Serratia marcescens can become a formidable nosocomial (hospital acquired) pathogen, and is reported increasingly in the world literature. However, it is only a recently recognized problem in Australia. Serratia can carry an antibiotic-resistance plasmid, and, after entry of the organism into very sick patients, it may be hard or impossible to eliminate. Initial experience of Serratia in 34 consecutive cases isolated in a three-months period is presented. Rapid increase in the number of Serratia infections occurred after the appearance of a resistant strain. Urinary infection was the commonest presentation (91% of cases). The presence of an indwelling urinary catheter in a debilitated patient was the major predisposing factor. Significant bacteraemia followed in four cases with one death. Contamination of burns (surfaces) and surgical wounds was found in four cases. Serratia strains were found to be highly resistant to most antimicrobial agents in routine sensitivity testing, 20% being fully resistant to all tested agents, and nalidixic acid being the most effective inhibitor in the remainder. With bacteriocin typing of Serratia, two types were found to be dominant. These two bacteriocin types were not identified among strains isolated from other sources such as soil, water and local hospitals. Pharyngeal carriage was found in only one case, but faecal excretion of Serratia was found in 11 cases and may be a significant portal of dissemination. Cross-infection from a hospital reservoir of resistant organisms is postulated. A model of cross-infection is also proposed, and methods of control are discussed. In view of the established danger of Serratia in the hospital setting, its isolation can no longer be ignored.


The penetration, pharmacokinetics and therapeutic efficacy of fleroxacin and pefloxacin were investigated in a rat abscess model. Abscesses were induced by implanting a dialysis tube unit contaminated with Serratia marcescens in the subcutaneous tissue. Simultaneous serum, interstitial fluid (IF) and abscess fluid concentrations of the investigated antibiotics were measured 24 and 96 h after implantation. The concentrations were determined at various time intervals after the last intramuscular administration of each drug (20 mg/kg). Peak fleroxacin and pefloxacin concentrations in the serum of the...
infected animals were 14.6 +/- 4.7 mg/l and 13 +/- 2.9 mg/l respectively, peak fleroxacin and pefloxacin abscess fluid concentrations after 24 h were 12.3 +/- 2.5 mg/l and 8.9 +/- 2.2 mg/l, respectively (85% and 68% of peak serum concentrations). Abscess fluid concentrations at 96 h were: fleroxacin 4.7 +/- 2.6 mg/l and pefloxacin 4.5 +/- 1.7 mg/l. Both antimicrobials persisted significantly longer in the abscess fluid than in serum. Both drugs failed to sterilize the abscesses following a single administration; however after four consecutive administrations all abscesses became sterile. We conclude that fleroxacin and pefloxacin may be suitable for the therapy of closed space infections caused by susceptible micro-organisms.


We report two cases of severe endophthalmitis, which were caused by Serratia marcescens, and developed in the immediate postoperative period in two recipients of corneal grafts from the same donor. The cause of the donor's death was massive CVA. He had been on mechanical ventilation for 12 days before he died, and had shown no sign of infectious disease while in the hospital. Vitrectomies were performed in the recipients' eyes on the third day after corneal transplantation. On the same day, and again 1 day later, the transplanted eyes were injected intravitreally with vancomycin and ceftazidime. Two months after surgery, both eyes developed phthisis. These cases are similar to other rare reported cases describing the virulence of *S. marcescens*.


We report an outbreak of serious infections with *Serratia marcescens* in patients on a neurosurgery ward. The epidemiological investigations undertaken are described. Features of outbreaks of infection with *serratia* and control measures are discussed.


An outbreak of colonisation and infection with a netilmicin resistant strain of *Serratia marcescens* occurred in a special care baby unit. *S. marcescens* was isolated from a total of 13 babies; significant infection occurred in five, of whom two died. Epidemiological investigation failed to detect a common source but gastrointestinal colonisation of babies formed a prolonged and possibly important reservoir for infection. Containment proved difficult until the unit was closed to new admissions, and even then spread to a temporary unit ensued. O Serotyping and bacteriophage typing disclosed a single epidemic strain. This produced an aminoglycoside acetylating enzyme (AAC(6')) conferring resistance to netilmicin and tobramycin and moderate resistance to amikacin. Use of gentamicin resulted in the isolation of *serratia* with increased resistance to all aminoglycosides, and, similarly, increased resistance to third generation cephalosporins emerged with their use.


A method to characterize strains of *Serratia marcescens* based on the PCR amplification of enterobacterial repetitive intergenic consensus sequences has been developed. The PCR fingerprints were generated from boiled supernatants prepared directly from bacterial colonies without the need for DNA extraction. The technique was applied to isolates obtained during an outbreak of pneumonia from seven mechanically ventilated patients, and its result indicated that the outbreak was due to the spread of two epidemic strains. This technique was validated by comparison with rRNA gene restriction analysis. There was complete concordance between these two techniques in discriminating the outbreak-related strains from epidemiologically unrelated isolates. Typing with both biochemical profile and antibiogram profile, though simple, was found to be less reliable than genotyping. The results show that this enterobacterial repetitive intergenic consensus PCR provides a rapid and simple means of typing *S. marcescens* isolates for epidemiologic studies.


This report deals with the results of a study that was made on the passage of fosfomycin into the CSF in 22 children with meningitis (11 parotideal meningitis and 11 meningococcal meningitis). The plasma and liquor levels of fosfomycin were determined in the acute phase of the illness and after the normalization of the CSF, with the object of studying the passage of the antibiotic through the blood-brain barrier in the presence and absence of meningeal inflammation. A greater permeability of the meninges was found to exist when they were in an inflammatory state and there seems to be a certain accumulative effect in the CSF when the fosfomycin is administered by intravenous perfusion. The concentrations that were obtained in the CSF were not high enough to justify the exclusive use of fosfomycin in the treatment of meningitis. Nevertheless, considering its wide antibacterial spectrum, its MIC against different microbial species and its lack of toxicity, we believe that fosfomycin can be of use when associated with other antibiotics in the treatment of meningitis caused by *S. aureus*, *D. pneumoniae*, *H. influenzae*, *E. coli*, *P. mirabilis* and *S. marcescens*.

BACKGROUND: To assess the clinical features and therapeutic outcomes of gram-negative bacillary meningitis (GNBM) in adult postneurosurgical patients. METHODS: Thirty adult patients with GNBM were included in this study. Their clinical features, laboratory data, prognostic factors, and therapeutic outcome were analyzed. The patients were 22 males and 8 females, aged 17-72 years. Seven had community-acquired
infections and 23 had nosocomial infections. Two patients were associated with brain abscess. RESULTS: The pathogens found in the 30 GNBM patients were Pseudomonas aeruginosa, Klebsiella species, Escherichia coli, Acinetobacter baumannii, and some rare pathogens including Citrobacter freundii, Serratia marcescens, Enterobacter cloacae, and Proteus mirabilis. Among these 30 patients, 8 patients with third-generation cephalosporin-resistant GNBM were identified since 1994; all infections were nosocomially acquired. Appropriate antibiotics were given to 22 patients. Eight patients did not receive appropriate antibiotic therapy. All eight died. The mortality rate in those treated with appropriate antibiotics was 14%. CONCLUSIONS: There has been an increase of GNBM in postneurosurgical patients in recent years. In addition, the emergence of strains resistant to third-generation cephalosporins in this specific group of patients has also been noted in recent years, and has become a great therapeutic challenge. We noted many prognostic factors in postneurosurgical patients in this study; however, appropriate antibiotic therapy and initial consciousness level are the most significant ones. Therefore, in cases of postneurosurgical patients with nosocomially acquired GNBM, the possibility of third-generation cephalosporin resistance should be strongly suspected. Early initiation of appropriate antibiotic therapy is needed in this potentially fatal disease.


Patients with chronic tracheostomy are subject to significant bacterial colonization of the airways, a risk factor for respiratory infections. The aim of our study was to verify whether bacterial colonization and humoral immune response in the airways can be influenced by the disease which led to chronic respiratory failure and tracheostomy. Thirty-nine clinically stable outpatients with chronic tracheostomy were considered: 24 were affected by chronic obstructive pulmonary disease (COPD) (mean age 66 years, range 54-78, M/F 19/3; months since tracheostomy 23, range 3-62), 15 by restrictive lung disease (RLD) (12 thoracic wall deformities, three neuromuscular disease; age 57 years, range 41-72; M/F 3/12, months since tracheostomy 22, range 2-68). Recent antibiotic or corticosteroid treatments (< 1 month) were among exclusion criteria. Bacterial counts were assessed in tracheobronchial secretions with the method of serial dilutions. Identification of bacterial strains was performed by routine methods. Albumin, IgG, A, and M were measured in airways secretions with an immunoturbidimetric method. No significant differences were found between the two groups as regards either the quantitative bacterial cultures (RLD 81.4, 2.6-4200 x 10(4); COPD 75.9, 1.0-1530 x 10(4) colony forming units (cfu)/ml, geometric mean, range) or the prevalence of the main bacterial strains, (Pseudomonas species: 38 and 37%, Serratia marcescens: 31 and 23%, Staphylococcus aureus: 14 and 6%, Proteus species: 3 and 8%, for RLD and COPD respectively) as a percentage of total strains isolated (RLD = 26, COPD = 48). Immunoglobulin levels did not show significant differences, apart from being higher in underweight subjects. We conclude that in our series of stable outpatients with chronic tracheostomy, bacteria-host interaction in the airways was not influenced by the clinical history.

An outbreak of Serratia marcescens involving 42 patients admitted to the general intensive care unit of the Hospital of Varese, Italy, occurred from March 1994 to August 1995. The causative strains were resistant to oxyimino-cephalosporins and monobactams due to their production of an extended-spectrum beta-lactamase. Another outbreak caused by Serratia marcescens strains had occurred in the same unit a few months earlier, from February to October 1993, with the strains involved producing a novel TEM-derived extended-spectrum beta-lactamase. In order to verify whether there were any relationships between isolates from the two epidemics, the strains and their enzymes were characterized. Biochemical data and gene amplification experiments showed that the isolates of the second outbreak harbored a non-conjugative plasmid of approximately 48 kb, codifying for the production of an SHV-derived extended-spectrum beta-lactamase with pl 8.2. Restriction fragment length polymorphism analysis of total genomic DNA by pulsed-field gel electrophoresis of Serratia marcescens isolates unambiguously identified two different bacterial clones responsible for the two epidemics. Epidemiological and microbiological investigations demonstrated the long persistence of Serratia marcescens strains and their circulation in other hospital wards, thus suggesting their possible role as a long-term reservoir for further epidemic spread.


Body substance isolation (BSI) is a system of infection precautions intended to reduce nosocomial transmission of infectious agents among patients and to reduce the risk of transmission of hepatitis B virus, human immunodeficiency virus, and other infectious agents to health care personnel. Harborview Medical Center in Seattle, Wash., was the first facility in the United States to implement the BSI system. Between 1984 and 1988 a systematic evaluation of the implementation process was conducted and the effects of BSI on appropriate glove use by hospital personnel and on the incidence of nosocomial colonization and infection by sentinel organisms was measured. Results of the evaluation showed (1) significant increments in knowledge of infection control procedures and practices as measured by comparing written examination responses before and after training sessions, (2) significant increases in appropriate glove use as determined by direct observation of hospital employees for 18 months, and (3) significant reductions in nosocomial colonization and infection caused by sentinel microorganisms during the period from 1984 to 1988.


The hospital records of 48 patients with infections due to Serratia marcescens were reviewed. Isolates from these patients had been cultured during the period from August 1973 through July 1975, at which time an increase in frequency of infections due to Serratia had been noted. Most of these patients were elderly males with chronic debilitating diseases. All patients had received antimicrobial therapy prior to the time Serratia was first isolated. The majority had had indwelling urinary catheters inserted.
during some period of their hospitalization. Isolates were obtained predominantly from
the urinary tract. In six of the 11 patients who died, Serratia appeared to play a role in the
outcome, and all three patients with Serratia septicemia died. Serratia marcescens can be
a virulent pathogen with a high degree of resistance to antibacterial agents. Attention
must be given to the use of a sterile technique for insertion of urinary catheters, frequent
care and cleansing of the catheter-meatal junction and use of a closed drainage system.

Macias et al. 2000. Parenteral infusions as culture media from a viewpoint of nosocomial
OBJECTIVE: To assess the growth patterns of selected organisms in common parenteral
solutions, in order to ascertain implications for nosocomial bacteremia. DESIGN: A
microbial suspension of approximately 300 CFU/mL was sequentially inoculated into
common parenteral infusions from three different manufacturers and incubated at room
temperature. Initially, 11 bacterial isolates and one Candida species from clinical
specimens were studied. Eight gram-negative rods (GNR) were tested at varying pH's.
Species variability was examined by testing an additional 39 isolates. RESULTS: The
eight GNR grew in Ringer's lactate (RL) from two manufacturers and only two grew in
dextrose 5% in water (D5/W) (Klebsiella pneumoniae and Serratia marcescens). No
organism grew in saline or dextrose 5% in saline. The gram-positive cocci and Candida
did not grow in any solution. No significant changes in growth were found after
modifying the pH of solutions. Significant inter- and intra-species growth variability was
noted. CONCLUSIONS: RL is a good culture media for GNR and D5/W is a poor culture
media with the exception of some bacteria of the Tribe Klebsielleae. We recommend to
follow high standards of nursing practice for administering intravenous infusions and to
avoid nutrient-containing solutions for prolonged parenteral use, when possible.

Mad'iarov. 1969. On the use of prodigiosan in combination with antibiotics for the
treatment of acute and chronic inflammatory diseases of the cerebral membranes.


Mamraeva. 1972. Some immunological criteria of the effectiveness of prodigiosan in the

Mandell. 1980. Cefamandole treatment of pulmonary infection caused by gram-negative
The increasing incidence of pneumonia caused by H. influenza and the problem of beta
lactamase production (18% of strains in recent reports) are important considerations in

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the therapy of pneumonia. An antibiotic that is effective for these strains and other
common respiratory pathogens will be useful for the therapy of pneumonia. Cefamandole
nafate is a new cephalosporin antibiotic with an antimicrobial spectrum similar to
cephalothin with increased activity against Escherichia coli, Proteus spp., Enterobacter
spp., and Haemophilus influenzae. Seventeen patients with pneumonia presumed to be
due to susceptible gram-negative organisms isolated from transtracheal aspirate or
sputum were treated with 6 to 8 g/day of parenteral cefamandole nafate. Organisms
isolated were Haemophilus influenzae in 6, E. coli in 3, Proteus mirabilis in 2, Klebsiella
pneumoniae in 1, Serratia marcescens in 1 and mixed gram-negative rods in 4. The
Serratia were resistant (MIC greater than 100 microgram/ml and 50 microgram/ml); other
MIC’s ranged from 0.2 to 6.2 microgram/ml; median 1.6 microgram/ml. Satisfactory
clinical response (improvement in pulmonary function; resolution of infiltrate; decrease
in temperature, sputum production and white count) was noted in 13 of 17 patients. Two
patients died from their underlying disease. Adverse clinical reactions questionably
related to cefamandole included SGOT rises in 3 and rash in one. Serum antibiotic levels
were 22.0 to 88.0 microgram/ml (peak) and 1.1 to 12.5 microgram/ml (trough). Sputum
levels were 0.27 to 2.5 microgram/ml. Cefamandole appears to be an effective antibiotic
for treatment of gram-negative pneumonia caused by susceptible organisms.

**Mandell et al. 1969.** Leukocyte function in chronic granulomatous disease of childhood.

**Manfredi et al. 2000.** Clinical and microbiological survey of Serratia marcescens
Clinical charts of 2,398 consecutive HIV-infected patients hospitalized over an 8-year
period were reviewed retrospectively to identify all cases of Serratia infection and to
evaluate the occurrence and outcome of these cases according to several epidemiological.
clinical, and laboratory parameters. Seventeen of 2,398 (0.71%) patients developed
Serratia marcescens infections: nine had septicaemia, six had pneumonia, one had a
lymph node abscess, and one had cellulitis. All patients were severely
immunocompromised, as evidenced by a mean CD4+ lymphocyte count of <; 70
cells/microl and a frequent diagnosis of AIDS (13 patients). When compared with other
disease localizations, septicaemia was related to a significantly lower CD4+ cell count
and a more frequent occurrence of neutropaenia. Antibiotic, corticosteroid, or
cotrimoxazole treatment was frequently carried out during the month preceding disease
onset. Hospital-acquired Serratia spp. infection was more frequent than community-
acquired infection and was significantly related to AIDS, neutropaenia, and sepsis.
Antimicrobial sensitivity testing showed complete resistance to ampicillin and
cephalothin but elevated susceptibility to ureidopenicillins, second- and third-generation
cephalosporins, aminoglycosides, quinolones, and cotrimoxazole. An appropriate
antimicrobial treatment attained clinical and microbiological cure in all cases, in absence
of related mortality or relapses. Since only 13 episodes of HIV-associated Serratia spp.
infection have been described until now in nine different reports (7 patients with
pneumonia, 3 with sepsis, 1 with endophthalmitis, 1 with perifoliculitis, and 1 with
cholecystitis), our series represents the largest one dealing with Serratia marcescens
infection during HIV disease. Serratia marcescens may be responsible for appreciable morbidity among patients with HIV disease, especially when a low CD4 + cell count, neutropaenia, and hospitalization are present. The clinician and the microbiologist facing a severely immunocompromised HIV-infected patient with a suspected bacterial disease should consider the Serratia spp. organisms. In fact, a rapid diagnosis and an adequate and timely treatment can avoid disease relapses and mortality.


BACKGROUND: Fourteen patients in the pediatric cardiac intensive care unit (CICU) had >; or =1 positive culture for a single strain of Serratia marcescens from April through December 1995 (study period). OBJECTIVES: To identify risk factors for S marcescens infection or colonization in a pediatric CICU. METHODS: Retrospective case-control study. Assessment of CICU infection control practices and patient exposure to CICU health care workers (HCWs). Epidemiologic-directed cultures of the environment and HCWs' hands were obtained. SETTING: Pediatric CICU. PATIENTS: Fourteen patients in the pediatric CICU had >; or =1 positive culture for a single strain of S marcescens from April through December 1995 (study period). CICU patients who did not have S marcescens infection or colonization during the study period were randomly selected as controls. RESULTS: A case patient was more likely than a noncase patient to have exposure to a single HCW (odds ratio [OR], 19.5; 95% CI, 2.6-416; P<;.003); however, this association was not adequately explained by epidemiologic or microbiologic studies. Interviews suggested that during the outbreak period, handwashing frequency among HCWs might have been reduced because of severe hand dermatitis. CONCLUSIONS: A combination of factors, including breaks in aseptic technique, reduced frequency of handwashing among HCWs before and between caring for patients, decreased attention to infection control practices, and environmental contamination may have indirectly contributed to this S marcescens infections outbreak.


Patients with bacteriuria are at risk for local and distant infectious complications at the time of urologic procedures. The American Heart Association recommends that penicillin and streptomycin be given prophylactically to patients with rheumatic or congenital heart disease without reference to the presence or absence of bacteriuria. A patient with unrecognized calcification of the mitral annulus who underwent cystoscopy for evaluation of urinary retention is reported. Although bacteriuria was present preoperatively antibiotics were not given. Subsequently, Serratia marcescens and possibly Proteus morgani mitral valve infection developed and the patient died. Calcification of the mitral valve annulus and an extensive urinary tract infection were identified at autopsy. This case suggests that calcification of the mitral annulus may be an endocarditis risk factor. The spectrum of prophylactic antibiotic coverage given at the
time of urologic procedures to patients with congenital or acquired heart disease, including calcification of the mitral annulus, should include whatever organisms are present in the urine.


Endogenous or metastatic bacterial endophthalmitis is a severe, sight-threatening infection of the vitreous humor that is only rarely due to *Serratia marcescens*. We report the case of a hemodialysis-dependent diabetic patient who had endogenous endophthalmitis of the right eye due to *S marcescens*, presumably from an infected dialysis catheter. The patient had total visual loss in the affected eye, which required enucleation.


An infection control program was instituted at The Victoria General Hospital, an 800-bed acute care hospital, in July 1977. *Serratia marcescens* had infected or colonized (I/c) 225 to 232 patients yearly for each of the three previous years. Since this organism is usually acquired nosocomially, we decided to use *Serratia I/C* as a marker for our infection control program. During the years 1977 to 1980, we identified and eliminated several reservoirs of *Serratia* (contaminated urine measuring containers, urometers, diabetic urine testing equipment and in-use contamination of 2% H intentane). Readmission of previously I/C patients proved to be an increasingly important reservoir. During 1980, only 120 patients were I/C, and gentamicin-resistant isolates of *S. marcescens* had dropped from 44% in 1977 to 4.4% in 1980. Use of *Serratia* as a marker enabled us to monitor the efficacy of our infection control program and allowed us to prove to our health care workers the usefulness of many of the measures we introduced.


One hundred fifty-six isolates of *Serratia marcescens* from patient specimens in Showa University Fujigaoka Hospital between April 1999 and March 2002 were investigated in this study. Forty-two isolates with serotype O2, detected mainly from patient respiratory specimens, were susceptible to the antimicrobial agents tested, whereas 30 isolates with serotype O14, detected mainly from patient urine, were resistant. Moreover, 19 isolates with serotype O14 susceptible to imipenem were intermediate or resistant to meropenem, while they did not produce metallo beta-lactamase. Both serotypes were significantly distributed in the ICU and surgical wards, compared with other wards. Ten isolates with O2/B (bacteriocin type) 16 and 14 isolates with O14/B76J, showing identical or closely-related clones by pulsed-field gel electrophoresis (PFGE) analysis of Spe I-restricted chromosome, were detected from different inpatients' specimens during approximately 2 and a half years. The existence of such long-lasting microorganisms suggested the
possibility of hospital-acquired infection caused by inadequate use of antimicrobial agents and disinfection procedures for medical tools such as bite blocks and catheters.

An 86-year-old woman presented with a chronic granulomatous skin lesion on the dorsal aspect of her left hand. Histologic examination showed pseudoepitheliomatous hyperplasia and a dense dermal infiltrate largely composed of lymphocytes and histiocytes. Abscess formation and fibroblastic proliferation were also present. Use of Fite, Giemsa, and periodic acid-Schiff stains did not show specific organisms. The gram-negative bacillus Serratia marcescens was the only microorganism isolated from all cultures performed. Trimethoprim-sulfamethoxazole, 960 mg every 12 hours for 20 days (orally), was given and resulted in complete disappearance of the lesion and negative culture findings. Cutaneous infection by S marcescens may represent a distinctive entity, whose clinical and possible pathogenic features are presented here.

**Matsumoto et al. 1995.** Preventive effect of ulinastatin on renal scarring in rat model of pyelonephritis induced by direct or ascending infection with Serratia marcescens or Escherichia coli. *Nephron.* Vol. 69(1): 65-70.
Renal scarring is considered to be a characteristic of reflux nephropathy. The effects of ulinastatin, a strong inhibitor of polymorphonuclear leukocyte elastase, on renal scarring following direct parenchymal or intravesical ascending infection by Serratia marcescens or Escherichia coli were determined. Four days of treatment with ulinastatin initiated 2 or 5 days after infection prevented renal scarring. Doses of 1,000-4,000 units/kg inhibited renal scar formation, but 8,000 units/kg did not. These results suggest that it may be possible to limit renal scar formation in pyelonephritis by the use of an appropriate pharmacologic agent.

Renal scars have been considered to occur in later stages of chronic pyelonephritis. In our experimental pyelonephritis model, bacteria which possessed mannose-sensitive (MS) pili on the surface promoted renal scarring following inoculation to the renal parenchyma. Polyethylene glycol-modified superoxide dismutase (PEG-SOD) and 2-O-octadecylascorbic acid (CV3611) significantly suppressed scarring when administered orally or parenterally during the early stage of kidney infection with MS-piliated bacteria. These findings suggest that the superoxide and other active oxygens play an important role in renal scarring following infection and that PEG-SOD and CV3611 may be agents capable of preventing renal scarring following bacterial pyelonephritis.


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Epidemic aminoglycoside resistance may be caused by the spread of a species with distinctive chromosomal genes (e.g., Pseudomonas aeruginosa), or it may be due to the dissemination of plasmids or transposons between genera. Although strains of P. aeruginosa resistant to aminoglycosides because of impermeability may cause nosocomial outbreaks, most of the acute increases in aminoglycoside resistance are due to the spread of inactivating enzymes by plasmids. The index species for intergeneric outbreaks is usually Klebsiella pneumoniae carrying the ANT(2”;) or AAC(3) gene; however, the distribution of resistance varies greatly by location and species. The AAC(6’)-I gene is most common in Serratia marcescens and in East Asian isolates of other species, whereas the AAC(3) gene is common in Chile. In the United States, the ANT(2”;) and AAC(3) genes are particularly common among Enterobacteriaceae, except for Proteus and Providencia, which often carry the AAC(2’) gene. The most common patterns of epidemic resistance lead to the inactivation of gentamicin and, less frequently, tobramycin, but only rarely affect amikacin.


Over an 18-month period we encountered 12 episodes of Serratia marcescens bacteraemia in 10 patients in a paediatric oncology unit. These were associated with long-term indwelling Hickman intravenous catheters (right atrial) and caused three deaths. Seven of the patients had only mild pyrexial illnesses and made a complete recovery. The source was traced to contaminated aqueous chlorhexidine in a bedside container in which plastic clamps were stored. When this was rectified the outbreak ceased. The identity of the causal Serratia strains was confirmed by plasmid analysis and they showed multiple antibiotic resistance, including the aminoglycosides. The study illustrates the emergence of S. marcescens as an opportunistic pathogen and emphasises the dangers of Hickman-associated bacteraemia.


In a comparative study of significant bacteriuria in an African population, 1.7% of 697 healthy subjects (10 females and 2 males) were found to have positive urine cultures. Of these, 5 subjects grew E. coli, 4 Klebsiella strains, 2 Staphylococcus aureus and 1 Serratia marcescens. Among 116 patients with glomerular disease, 15.5% (7 males and 11 females) yielded positive cultures. E. coli, Staph. aureus and Proteus species were commonly isolated organisms. There was a nine fold increase in prevalence of bacteriuria in patients with glomerular disease and in females, this correlated with the amount of protein lost per 24 hours. It is postulated that the presence of protein in urine per se favours bacterial growth and because of the high prevalence of bacteriuria in patients with glomerular disease, it is recommended that all such patients should be screened and treated appropriately.

Five children with the acquired immunodeficiency syndrome (AIDS) and unusual gastrointestinal disease are described. Two children presented with malnutrition, abdominal distention, and diarrhea. One was found to have moderately severe villus atrophy on jejunal biopsy and was initially thought to have celiac disease. Jejunal biopsy from the second child revealed infiltration of the mucosa with acid-fast bacilli-laden macrophages. A third child suffered recurrent abdominal pain, progressive weight loss, diarrhea, and severe gastrointestinal hemorrhage secondary to infection with cytomegalovirus. Pseudomembranous necrotizing jejunitis associated with overgrowth of Klebsiella pneumoniae in the duodenal fluid occurred in one patient. The fifth child presented in the newborn period with Serratia marcescens cholecystitis. Gastrointestinal disease in children with AIDS may be due to idiopathic villus atrophy and bacterial or opportunistic infection.


pH-Dependent bactericidal activity on four gram-negative bacilli that are mainly responsible for gastric to airway colonisation has been investigated. Organisms studied were Escherichia coli, Enterobacter cloacae, Klebsiella pneumoniae and Serratia marcescens. At pH of the medium adjusted to 2.7 or lower all four organisms were killed in 1.5 h. At pH 3.1 or greater, no reduction in viable bacterial number was noted over 2 h. Even when pH of the medium was adjusted to 6.8, no increase in bacterial count was observed in 4 h. Relevance of these findings in relation to airway colonisation and prophylaxis of acid aspiration and stress ulcer syndromes is discussed. It is suggested to maintain pH of the gastric contents above 4.0 by H2 antagonists and prevent growth of gram-negative organisms in the stomach by keeping it empty.


A 36-year-old man, with a history of recurrent respiratory infection, dermatomycosis, arthralgia and abnormal stools for 12 years, developed a febrile illness (up to 40 degrees C). A Serratia marcescens septicaemia responded to antibiotics. Four months later cervical and abdominal lymph-adenopathies were noticed. Cervical lymph node biopsy revealed lymphadenitis with epithelioid cell nests. Duodenoscopy with biopsy demonstrated Whipple's disease associated with lambliasis. Electron-microscopy showed rod-shaped bacteria typical of Whipple's disease, and Giardia lamblia. Using the polymerase chain reaction, Whipple-specific DNA fragments of 284 base pairs from the genome of the Whipple bacterium (*Tropheryma whippelii*) were demonstrated. Antibiotic treatment with Ampicillin (2 g three times daily) and ceftriaxone (2 g once daily) i.v. for 21 days, followed by oral ofloxacin (200 mg daily) and co-trimoxazole (three times daily 800 mg sulfamethoxazole and 160 mg trimethoprim), brought about remission of Whipple's disease. Long-term antibiotic treatment was continued with co-trimoxazole.
Lambliasis recurred after 3 and 5 months, despite treatment with metronidazole, 250 mg three times daily for 7 days.


215 water samples were taken from 49 dental treatment units and investigated for the existence of free-living amoebae. In all water-carrying systems of the dental treatment units it was possible to verify the incidence of one or more amoeba species. In 8.2 per cent of the units Naegleria species was found and in 12.2 per cent Acanthamoeba species was present. Seven Naegleria and six Acanthamoeba strains (2 A. castellanii and 4 A. polyphaga) were isolated. From samples originating from 12 dental treatment units (DTU) another 42 amoeba strains were isolated which consisted of 14 different species within 9 classes. Among them Vannella mira (in 19 per cent of samples) and Hartmannella vermiformis (10.6 per cent) were found to be the most frequent species, followed by H. cantabrigensis (9.5 per cent), V. platypodia, Platyamoeba stenopodia and V. simplex (7.1 per cent each). In 10 per cent of samples monotrichous and bitrichious flagellates such as the Bodo species were found, whereas two samples contained ova, larvae and adult free-living nematodes. Among the isolated Naegleria strains no thermophilic strain was present. Consequently they belong to the N. gruberi complex. Among the Acanthamoebae five of the six strains were thermophilic. All strains were investigated for pathogenic properties by means of the mice inoculation test. Two strains proved pathogenic - it was possible to isolate them from the brain and lung of dead mice. Another two strains proved to have invasive properties because they were isolated from the brain of infected animals; however, they did not give rise to disease or death of the respective animals. Supplementary microbiological tests demonstrated the existence of bacteria and fungi in 84 per cent of dental treatment units. Pseudomonas spec. were detected in 75% of dental units, Serratia marcescens in 2% and fungi in nearly 3%. 58.3% of all water samples contained total germ counts of more than 100/ml.


Mixed infection of the mosquitoes' larvae of the first age group by densonucleasis virus and entomopathogenic strains of Pseudomonas fluorescens and Serratia marcescens enhanced viral infection in the presence of toxicosis induced by exogenic entomotoxic bacterial metabolites. Possibility of interaction between bacterial cells and the mosquito densonucleasis virus, producing an adverse effect on the duration of the disease, was demonstrated. Duration of the disease provoked by bacterioviral infection of the larvae was of a specific character: nontypical degeneration and untimely replacement of
intestinal epithelium at the fourth larval stage were observed along with acute viral lesions of all the tissues.


We studied 385 episodes of nosocomial bloodstream infections occurring over 45 months to ascertain if the etiologic organisms were independent predictors of death and morbidity. Independent predictors of death included respiratory failure, oliguria, metabolic acidosis, hypotension, increased age, antibiotic therapy in cases where susceptibility data were unknown, and infection with *Pseudomonas aeruginosa*. If parameters associated with septic shock were excluded, increased age, severity of disease, and infection with *Candida* spp. or *P. aeruginosa* predicted death. Infection with *P. aeruginosa*, *Enterococcus*, and *Klebsiella pneumoniae* predicted hypotension; severity of disease, polymicrobial infection, and infection with *Candida* spp., *Enterococcus*, *Enterobacter*, or *Serratia marcescens* predicted oliguria; infection with *Candida* spp. or *P. aeruginosa*, increased age, severity of disease, and inability to meet hospital financial obligations without assistance predicted respiratory failure. Inability to meet hospital financial obligations without assistance and severity of disease predicted hypothermia; infection with *Candida* spp. or *P. aeruginosa* and sex (male) predicted metabolic acidosis.


An extensive survey of patients and the environment in a newly refurbished intensive care unit showed that the principle species on patients in sites other than the rectum were *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Serratia marcescens*, *Acinetobacter anitratus* and *Enterobacter cloacae*. Multiple episodes of cross-infection were occurring with 10 different strains of these organisms. Three oral solutions (mouthwashes, 'Clinifeeds' and residual water from nasogastric aspiration apparatus) were heavily contaminated with coliforms including some epidemic strains and this corresponded with the finding that colonization with the above species usually occurred first in the mouth or respiratory tract. Attempts to eliminate contamination of the solutions reduced colonization and cross-infection by over 50%, but did not eradicate it. Two sinks without heat-traps on the drains possibly provided a long term reservoir of epidemic strains.


Serine proteases are thought to be involved in the initial attack on sheep skin by *Dermatophilus congolensis* and are obvious antigens for inclusion in a vaccine to prevent lumpy wool disease (dermatophilosis). Degenerate primers were designed after alignment of seven bacterial serine proteases. Inosine was incorporated into the primers at positions of three- and four-base redundancy, and this reduced the complexity of the primer mixtures from several thousand to sixteen different sequences for each primer. The primers were validated by production and sequencing of amplicons from serine protease genes in *Bacillus subtilis* and *Serratia marcescens*. The primers were used with heat-soaked polymerase chain reaction (PCR) to produce amplicons from two *D. congolensis*
strains, AG and MB. In the amplicon codons for arginine, rather than the expected serine, were found where inosine was used for both the first and third positions for a codon in the primer. A search with the deduced amino acid sequences of the amplicons showed significant similarity to a keratinase and other serine proteases from various organisms. Similarity was most apparent around the active site residues and other essential secondary structural elements.


Serratia marcescens is a well-known cause of nosocomial infections and outbreaks, particularly in critically ill neonates and immunocompromised patients. Numerous methods have been proposed for typing. We used pulsed-field gel electrophoresis (PFGE) typing to analyze an outbreak in a neonatal intensive care unit (NICU). We included 23 patient isolates from an outbreak (March to July 1995), and 10 patient isolates from different wards during the same time period. PFGE of whole-cell DNA digested by *SpeI* was used as a marker of strain identity. The most common presentation of the infection was sepsis in 18 of 23 (78%) neonates. Only four different biotypes were identified; biotype A8d accounted for 84% of the strains. PFGE typing revealed two clones responsible for two different clonal strain dissemination outbreaks from March to July, with 24 patient isolates being pattern A and 4 patient isolates being pattern E. PFGE typing suggests cross transmission between patients in the NICU and other wards. The isolates from 5 other patients showed distinct PFGE patterns. Extensive investigation and cultures failed to identify any environmental or staff reservoir of *S. marcescens*. This is one of the first reports applying PFGE to the study of *S. marcescens*, and this method was a useful marker of strain identity. PFGE typing distinguished strains which appeared to be the same by biotyping.


OBJECTIVE: To analyze an outbreak of Serratia marcescens in a neonatal intensive care unit and identify the risk factors associated to the development of infection. MATERIAL AND METHODS: It was a case-control study from March to July 1995. Factors included were age, sex, intravascular devices, nebulizers, mechanical ventilation, use of total parenteral nutrition (TPN), underlying diseases, surgical interventions, tubes, previous antimicrobial treatment and days of exposure. The associations were explored using the odds ratio. RESULTS: 24 cases and 30 controls were included. In the univariate analysis the significant risk factors (OR,IC) were use of central venous catheter (4.57, 1.01-23.5), days of use of TPN (4.38, 1.03-16.5), days of previous antimicrobial treatment (4.87, 1.60-22) and days of exposure (2.7, 2.65-27.6). In the multivariate analysis the significant risk factors were previous antimicrobial treatment (3.98, 2.36-18.2), days of previous antimicrobial treatment (6.76, 3.02-24.6) and days of use of TPN (4.87, 1.67-15.6). CONCLUSIONS: The significant risk factors in our study were previous antimicrobial treatment, days of antimicrobial and days of use of TPN.
Though Serratia marcescens is widely known to be the cause of serious infections in immunocompromised hosts, a lung abscess caused by *S. marcescens* is very rare. A 5 year old boy who had previously been diagnosed with autoimmune neutropenia was admitted because of fever and cough. In spite of treatment with some antibiotics, he developed a lung abscess. Aspiration of the pleural fluid revealed that *S. marcescens* was the pathogen of the disease. In the present case, there were feasible risk factors for the development of Serratia lung abscess namely neutropenia, chronic gingivitis at the time, and treatment with cyclosporin A. There are no reported cases of autoimmune neutropenia which developed into *S. marcescens* lung abscess in the literature as far as we can determine.

In an investigation of the source of an outbreak of Serratia marcescens infection in a special care baby unit, several breast pumps used in the hospital and community were examined. The epidemic strain was isolated from two pumps and other Gram-negative organisms, Staphylococcus aureus and Streptococcus faecalis were isolated from seven. The findings indicate that breast pumps may be a potential source of contamination of the user, her breast milk, infant and environment. Our recommendations regarding the use of breast pumps are presented.

An epidemic caused by Serratia marcescens that involved 26 infants admitted to the Neonatal Intensive Care Unit (NICU) and 82 infants admitted to the Nursery of the 2nd Medical School of Naples is reported. Two different biotypes of *S. marcescens* with two completely different epidemiological patterns were identified. The prevalent biotype (A8b trigonelline-) was isolated in the delivery room, in the operating room, in the Nursery and in the NICU from items, healthy infant excreters and affected infants; the second biotype (A3a) was isolated only in the NICU from staff, two healthy infant excreters and two affected infants. Colonization of the throat and the gastrointestinal tract was frequent. Infected and colonized infants were the most important reservoir for serratia in the Nursery and in the NICU particularly for the type strain A3a. A mucus aspiration apparatus contaminated in the delivery room and the contamination of several instruments and items probably had a major role in the initiation and maintenance of the spread of the A8b strain. Mass contamination of the nursery has been related to overcrowding and a lack of the control measures; the transfer of high-risk colonized infants caused spread in the NICU. In the NICU the attack rate 26%; 69% of infants became ill; the case fatality ratio was 19%. Epidemiological investigation of the infants at risk showed some factors predisposing to infection with serratia. The hygienic measures failed to control the spread of serratia and it was necessary to refuse new admissions to pregnant women in order to decontaminate and re-organize the wards.
PURPOSE: The purpose of this study was to determine the effectiveness of mupirocin and polymyxin B, alone and in combination, in vitro and in vivo using rabbit models of, and keratitis. METHODS: Rabbit eyes were intrastromally injected with 1,000 colony-forming units (CFUs) of or or 100 CFUs of Rabbits were then treated with 2.7 mg/mL mupirocin, 10,000 U/mL polymyxin B, a mupirocin:polymyxin B combination, or 0.3% ciprofloxacin. Vehicle and untreated controls were also included. Treatment schedules depended on the strain injected. The number of CFUs was determined for all eyes after treatment. RESULTS: The mupirocin:polymyxin B combination was effective for all three genera both in vitro and in vivo. For keratitis, the mupirocin:polymyxin B combination was more effective than either drug alone and significantly reduced the log number of bacteria in the cornea by more than 3 logs compared with the vehicle or untreated controls (p <;or= 0.0016). For, the mupirocin:polymyxin B combination treatment significantly reduced the number of CFUs per cornea relative to the individual drugs, vehicle, or untreated controls (p <;or= 0.016). For, the mupirocin:polymyxin B combination therapy significantly reduced the number of bacteria in rabbit corneas relative to the individual drugs, vehicle, or untreated groups (p <;or= 0.0001). Therapy with the mupirocin:polymyxin B combination was equivalent to ciprofloxacin therapy (p = 0.80). CONCLUSION: The mupirocin:polymyxin B combination was effective in treating experimental, and keratitis.

Forty patients with chronic osteomyelitis were treated with hyperbaric oxygen as an adjunct to surgical therapy and antibiotics and followed for an average of 2 years with a recurrence rate of 15%. The mechanism of action of hyperbaric oxygen in osteomyelitis is probably an indirect one of improving local vascularity and potentiating phagocytosis. Many of these patients represent a refractory group with poor prognosis due to the etiology of the infection, site of involvement, and duration of infection prior to treatment. The recurrence rate following this mode of treatment seems to be primarily related to inadequate surgical management. There was no definite correlation between the site of the infection of pathologic organism and recurrence. Although this is a preliminary report, the results are encouraging. Hyperbaric oxygen may be indicated as an adjunct to good surgical and medical management, particularly in patients with refractory chronic osteomyelitis and in whom ablative surgery is under consideration as the only other means of controlling the infection.

Two fatal cases of Serratia marcescens sepsis and meningitis are reported here. The first case, a 1,420-g male infant born after 35 weeks of gestation, developed abdominal distension, hypotension and acidosis on the 3rd day after birth. Cerebrospinal fluid (CSF) was cloudy; blood and CSF cultures were positive for S. marcescens. He died within 24 hours after the appearance of symptoms, and purulent meningitis was found at autopsy.
The second case, a 1,100-g boy born after 29 weeks of gestation, developed Escherichia coli sepsis at 14 days of age, from which he recovered. At 26 days of age he developed convulsions. Blood and CSF cultures grew *S. marcescens*. He was given gentamicin, chloramphenicol and supportive treatment, but expired 48 hours after the onset of symptoms. Both cases appeared within a 2-day period.


We report 2 cases of severe corneal infections caused by *Serratia marcescens* after laser in situ keratomileusis (LASIK). Twenty-four hours after LASIK, 2 patients developed infectious keratitis, 1 bilaterally. In each eye, the corneal flap was edematous, ulcerated, and detached from the stromal bed. Treatment included removal of the necrotic flap and aggressive antibiotic therapy. Cultures from corneal exudates were positive for *S. marcescens*. After 1 year, both patients had a loss of best corrected visual acuity (BCVA) ranging from 20/40 to 20/22 because of irregular astigmatism. Overrefraction with a hard contact lens resulted in a BCVA of 20/20 in the 3 affected eyes. Slitlamp examination showed trace subepithelial haze without severe corneal scarring. Videokeratography disclosed areas of paracentral inferior steepening resembling keratoconus. Refraction and videokeratography remained stable after 6 months of follow-up. Ulcerative keratitis caused by *S marcescens* is a potential complication of LASIK. Bilateral involvement may occur if bilateral simultaneous surgery is performed.


During a 10-week period, 11 patients were involved in an outbreak of cross-infection with a non-pigmented strain of *Serratia marcescens* resistant to sulphonamides, trimethoprim, ampicillin, tetracycline, chloramphenicol, cephalaxin, gentamicin, tobramycin, colistin, ticarcillin and kanamycin. The problem was confined to the intensive therapy areas of the hospital. The organism was apparently spread by a nursing sister who harboured it in a paronychial lesion. Prolonged carriage of *S. marcescens* was demonstrated. Methods of investigation of the outbreak and the measures adopted to terminate it are described.


We evaluated pneumococcal bacteremia retrospectively for 3.5 yr. Sixty-three episodes occurred in 62 patients; 37 were nosocomial in origin; 26 were community-acquired. Pneumococcal bacteremia was most common between January and June. Patients with nosocomial disease had significantly more ultimately fatal disease and sustained more manipulation of the respiratory tract than patients with community-acquired bacteremia. The mortality of nosocomial pneumococcal bacteremia (75.8%) or nosocomial pneumococcal pneumonia with bacteremia (66.7%) was significantly greater than community-acquired bacteremia (26.9%; p less than 0.01) or pneumonia with bacteremia.
All 62 patients were eligible for pneumococcal vaccine, and 57 could have received immunoprophylaxis. A vaccine trial is indicated in the hospital setting.

We have established 950 and 430 oligoclonal B-lymphoblastoid cell lines (LCL) from two normal persons and eight autoimmune disease patients, respectively by using Epstein-Barr virus (EBV)-induced transformation. To re-evaluate the EBV technique for production of human monoclonal antibodies (mAb) related to infectious disease, we screened these oligoclonal LCLs for antibodies against 31 bacterial strains systematically. A total of 74 cultures out of 1380 were reactive to a total of 18 strains out of 31. Among these, eight cultures showed 10(-3) antibody (Ab) titers to Pseudomonas aeruginosa serotypes C, E, F and I, Staphylococcus aureus, Serratia marcescens and Bacillus cereus. Ten cultures showed 10(-2) Ab titers to Ps. aeruginosa serotypes D, E, F and I, Ps. maltophilia, Staph. epidermidis, Klebsiella ozaenae, Ser. marcescens and B. subtilis. The results reveal the further possibilities for the EBV technique to produce various infectious disease-related human mAbs.

Simultaneous outbreaks of *S. marcescens* infection going on in the Neonatal Intensive Care Unit and the Surgical Department of the same hospital were investigated by pyrolysis mass spectrometry (PyMS). The PyMS analysis of the strains clearly demonstrated that the two outbreaks were caused by different strains. The 14 *S. marcescens* isolates from the first outbreak were closely related, with the exception of one environmental isolate, which did not harbour the ESBL plasmid, which was present in all other isolates. However, the phage type of all 14 isolates was the same. Among the 9 *S. marcescens* isolates from the second outbreak, PyMS clearly distinguished 3 that exhibited gentamicin resistance from the remaining 6 gentamicin-susceptible isolates. Phage typing was unhelpful in this case, as none of the isolates were typable. The PyMS typing of nosocomial outbreak strains can reach the level of discrimination approaching that achieved by molecular genetic analysis.

Cefminox sodium (CMNX, MT-141), a new semisynthetic cephemycin, having marked resistance to beta-lactamase, and a broad spectrum of antibacterial activity against various bacterial species, including Haemophilus influenzae, Serratia marcescens and Citrobacter freundii, CMNX has higher activity in vivo than in vitro. For therapeutic purpose, CMNX was given in a daily dose of 0.5 g (0.5 g X 1) to 2 g (1 X 2) by intravenous drip infusion for 4 to 8 days to 24 cases with acute peritonitis (17 cases with acute appendicitis, 1 with localized peritonitis after gastrectomy, 1 with diffuse peritonitis due to perforative duodenal ulcer and 5 with panperitonitis due to intestinal obstruction).
The clinical response was rated excellent in 9 cases, good in 14 cases and fair in 1 case and poor in none. No adverse effect was observed. There were 29 strains isolated organisms included 12 Escherichia coli, some Enterococcus faecalis and Pseudomonas aeruginosa. These isolated organisms were eradicated after CMNX treatment, except a strain of E. faecalis was decreased. In 19 cases of them, 16 cases with acute peritonitis due to acute appendicitis and 3 cases with acute panperitonitis due to intestinal obstruction, CMNX was administered intravenously in a dose of 1 g (1 case was 0.5 g) before or during the operation, and tissue specimens and body fluids samples were taken during the operation. CMNX concentration was determined to a bioassay with Escherichia coli NIHJ or Vibrio vercolans ATCC 8461 as the test organisms. CMNX concentrations in purulent ascites were 47.2 +/- 38.5 micrograms/ml (n = 23), those in infected appendix wall were 32.2 +/- 21.7 micrograms/g (n = 16), that in pus in appendix were 22.1 +/- 24.3 micrograms/ml (n = 8) and that in other non infected tissues were 24.3 +/- 22.0 micrograms/g (n = 8). CMNX concentrations in infected tissues were higher than the non infected tissues. In the 3 cases with empyemic appendicitis, CMNX levels in pus in appendix were more higher than that in appendix wall itself. Therefore, CMNX sodium appears to be a very useful drug when used for chemotherapy on acute peritonitis.


In an epidemic of septic arthritis due to Serratia marcescens, the intra-articular injection of contaminated methylprednisolone may have played a key role. The epidemic strain was found in used multiple-dose vials of methylprednisolone and in a canister of cotton balls soaked in benzalkonium chloride. The cotton balls had been used for antisepsis and disinfection. Growth characteristics of the epidemic strain of S. marcescens were compared with those of control strains of S. marcescens which had been obtained from unrelated nosocomial outbreaks. The epidemic strain was able to survive in 1:100 dilutions of benzalkonium chloride and was able to grow to greater than 10(5) CFU/ml in multiple-dose vials of methylprednisolone; control strains could not be recovered after 24 h in the same solutions. The preservative in methylprednisolone is gamma-myristyl picolinium chloride, a compound chemically related to benzalkonium chloride. We speculate that the epidemic strain of S. marcescens, which was resistant to benzalkonium chloride, had cross-resistance to gamma-myristyl picolinium chloride. If the cotton balls were used to disinfect the tops of the multiple-dose vials of methylprednisolone, small numbers of organisms subsequently introduced into the solution could have grown to high concentrations.


During a 6-week period, 10 patients were admitted to a hospital for treatment of knee or shoulder joint infections due to Serratia species. Isolates from eight patients were identified as Serratia marcescens with identical biochemical characteristics and antibiotic susceptibility patterns. Before the onset of infections, all patients had been treated by two orthopedic surgeons who shared an office. Studies revealed that infections were
associated with previous joint injections \( (P = 4.44 \times 10^{-5}) \) of methylprednisolone and lidocaine. Environmental cultures revealed that a canister of cotton balls soaked in aqueous benzalkonium chloride and two multiple-dose vials of methylprednisolone previously used by office personnel were contaminated with the epidemic strain of \( S.\) \textit{marcescens}. The canister may have served as a potential reservoir for contamination of sterile solutions and equipment used for joint injections, of skin at the injection site, and of hands of personnel. No further cases occurred after the use of aqueous benzalkonium chloride was discontinued.


\( S.\) \textit{marcescens} (SM) produced a prolonged outbreak in a neonatal intensive care unit of high level gastrointestinal colonization \( (10^9\) SM/g feces) which in the early part of the outbreak predisposed to respiratory infection. The early outbreak featured a strain of SM carrying a \( 54 \times 10^6\) dalton conjugative plasmid which mediated resistance to gentamicin, tobramycin and beta-lactam agents. The second part of the outbreak involved primarily gastrointestinal colonization with SM strains that were plasmid-free. Acquisition of SM was related to very low birth weight (less than 1500 g). Among very low birth weight neonates, SM colonization was associated with pneumonia, patent ductus arteriosus, congestive heart failure and septicemia. Among neonates greater than 1500 g, SM colonization was associated with bronchopulmonary dysplasia, use of a respirator, patent ductus arteriosus and congestive heart failure. Respirator contamination, respiratory tract colonization and consequent pneumonia were reduced by more frequent changing of respirator tubing. Colonized sinks remained chronically colonized with multiresistant SM.


The authors have carried out the clinical and laboratory evaluation of aspoxicillin (ASPC, TA-058). The results were as follows: Antibacterial activities The susceptibility to ASPC was estimated by plate dilution method on 26 strains each of \( S.\) \textit{aureus}, \( E.\) \textit{coli}, \( S.\) \textit{Salmonella} and \( P.\) \textit{aeruginosa} and 19 strains of \( S.\) \textit{marcescens} isolated from clinical specimens. Minimum inhibitory concentration (MIC) of ASPC against \( E.\) \textit{coli} and \( S.\) \textit{Salmonella} was about twice active to compare with ampicillin (ABPC), but MIC of ASPC against \( S.\) \textit{aureus} was two-fold less active than that of ABPC. Antimicrobial activities of ASPC against \( S.\) \textit{marcescens} were similar to that of ABPC, while against \( P.\) \textit{aeruginosa} its activities were two-fold higher than that of carbenicillin. Serum levels and urinary excretions When ASPC was administered at 20 mg/kg by one shot intravenous injection, serum concentration was 75 micrograms/ml after 15 minutes and half-life (T \( 1/2 \) beta) was 1.65 hours. Urinary excretion within 6 hours after ASPC injection reached to 245.6 mg (26.1%). The reason of this law urinary excretion rate was due to the
underlying disease (hydronephrosis). In case of 20 mg/kg administration of ASPC by intravenous drip infusion, peak serum level reached to 88 micrograms/ml at the end of injection, and half-life (T 1/2 beta) was 0.77 hour. Since ASPC degradation by beta-lactamase was proceeded, urinary excretion of this case was not measured by microbiological method. Penicillonic acid and its epimer were detected by HPLC method. It was found that beta-lactamase producing strain was S. marcescens which was isolated by urine culture. (ABSTRACT TRUNCATED AT 250 WORDS)


Six species of bacteria (family Enterobacteriaceae) not commonly reported as associated with disease in American alligators (Alligator mississippiensis) were documented, suggesting that Aeromonas is not the only bacterium responsible for septicemia in crocodilians. These included Citrobacter freundii, Enterobacter agglomerans, Proteus sp., Morganella morganii, Serratia marcescens, and Klebsiella oxytoca. Clinical signs of disease included intensive basking, anorexia, lethargy, flaccid limb paralysis, stomatitis, and dermatitis. Our data indicated that early treatment with broad-spectrum antibiotics was preferable to waiting for sensitivity results.

We prepared solutions of human IgM and IgG to various lipopolysaccharide (LPS) species. These were then tested, along with solutions of non-LPS specific human IgG or IgM, for their ability to confer passive immunity against experimental endotoxemia in two animal models. The immunoglobulins were first tested for an effect on the lethality induced by seven different LPSs in actinomycin-D sensitized mice, or by three different bacteria in normal mice. When the immunoglobulins were administered 1 h before challenge, a small protective effect was observed. This protection was dependent upon both the anti-LPS agent, the chemical composition of the LPS, or the strain of gram-negative bacteria used for injection. The anti-LPS IgM and IgG preparations reduced the mortality induced by Escherichia coli but not by Serratia marcescens or Klebsiella pneumoniae, indicating protection by strain-specific antibodies. When the antibodies were preincubated with LPS or bacteria for 30 min before administration, almost complete protection was seen. The influence of these immunoglobulin preparations or of human albumin (as a control) on the hypotensive and vascular-permeabilizing effects of LPS in rats was then studied. A dose-dependent inhibitory effect was observed with IgG preparations and albumin. At 200 mg/kg, anti-LPS IgG reduced the effects of LPS, while at 400 mg/kg, both anti-LPS and normal IgG preparations showed protection, as did
human albumin used at the same dose. The IgM-enriched preparation worsened the initial hypotensive phase after LPS, whereas the anti-LPS IgM significantly reduced the second phase of the hypotension, but only at the largest dose of 400 mg/kg. In this second model using the rat, a clear difference between the activity of IgG and IgM was thus observed. We conclude that pretreatment with human immunoglobulins from large plasma pools modestly, but significantly, attenuated the effects of murine and rat Gram-negative sepsis, but that protection was incomplete. Our results suggest that single regimen intervention strategies may not be sufficient to influence the course of the disease.

Results of susceptibility tests of Enterobacteriaceae isolated at 14 different centers demonstrate synergy between trimethoprim (TMP) and sulfamethoxazole (SMZ) against sulfonamide-susceptible isolates, which account for between less than 50% and greater than 75% of the isolates at different centers. Only 1%-4% of the isolates of Escherichia coli or Proteus mirabilis from the five centers in the United States were found to be resistant when tested with a disk containing both TMP and SMZ, but greater than 8% of such isolates from five of the other centers were resistant to the combination disk. A larger percentage of isolates of Klebsiella pneumoniae or Serratia marcescens were resistant, but the number varied from center to center. In the United States, resistance of human and animal isolates of Salmonella to the TMP-SMZ combination was almost completely absent, although greater than 50% of the animal isolates were resistant to sulfonamides. At a center that tested TMP and SMZ resistance with separate disks, resistance to TMP was found to be 30 times more common in sulfonamide-resistant than in sulfonamide-susceptible E. coli. This ratio may be useful as a monitor as treatment with TMP alone increases.

The susceptibility of opportunistic pathogens associated with chronic granulomatous disease (CGD) to the non-oxidative killing mechanisms of neutrophils has been assessed by incubation in human neutrophil primary granule lysate. The dose and pH-dependency of killing of Aspergillus fumigatus, Candida albicans, Escherichia coli, Nocardia asteroides, Serratia marcescens and Staphylococcus aureus differed markedly and may partly explain their virulence in CGD, in which oxygen-dependent killing mechanisms are defective. At the acid pH in CGD neutrophil phagosomes S. aureus, Ser. marcescens, N. asteroides and A. fumigatus spores were highly resistant but C. albicans, a less frequent pathogen in patients with CGD, was much more susceptible.

Serratia appears as a pathogen of increasing frequency and clinical significance in bone and joint infections in heroin users. This is the fifth case report of septic arthritis due to Serratia marcescens in intravenous heroin users. The clinical and laboratory features were not different from other acute pyogenic arthritides. Signs of infection were obscure even
in the presence of debilitating disease. Although Pseudomonas and Staphylococcus are more common organism in bone and joint infections of heroin users, Serratia should be considered as a possible pathogen in such patients. In the present case, immediate open drainage followed by systemic Gentamicin treatment gave rapid relief of pain and restoration of full range of motion of the joint.


A prolonged outbreak (December 1980 to July 1982) of nosocomial urinary tract infections appeared to be due to strains of Serratia marcescens that were resistant to currently available antibiotics. The serotyping and antibiotic susceptibility patterns suggested a few endemic strains of serotypes O13, O2/3, O12/14, and nontypable strains. These strains were isolated from the urine samples of inpatients with urinary tract infections in the urology ward and in other wards. The strains of O12/14 (gentamicin susceptible) were replaced with those of O2/3 (gentamicin resistant) between June and September 1981, whereas the other serotypes were isolated continuously. They were resistant to sulbenicillin, cefmetazole, gentamicin, and amikacin, and susceptible to micronomicin and ofloxacin, a new quinolone antibiotic. Most of them were also resistant to the disinfectant chlorhexidine, which had been used widely for hand washing in the hospital.


Ofloxacin is an established fluoroquinolone agent which achieves good concentrations in genitourinary tract tissues and fluids. It has good in vitro activity against most Enterobacteriaceae, Staphylococcus saprophyticus, methicillin-susceptible S. aureus, Neisseria gonorrhoea, Chlamydia trachomatis and Haemophilus ducreyi, intermediate activity against Ureaplasma urealyticum and most enterococci, but limited or no in vitro activity against enterococci, Serratia marcescens, Pseudomonas aeruginosa and many anaerobes. However, high concentrations achieved in the urine ensure its activity against most urinary tract pathogens. Ofloxacin demonstrates consistent efficacy in a broad range of urinary tract infections, achieving bacteriological response rates in excess of 80% in uncomplicated and 70% in complicated infections. The efficacy of ofloxacin was similar to that of all comparators tested including other fluoroquinolones, cephalosporins and cotrimoxazole (trimethoprim/sulfamethoxazole). Ofloxacin is also effective as a single-dose regimen in the treatment of uncomplicated gonorrhoea, as a 7-day regimen in uncomplicated C. trachomatis infections, and as monotherapy in uncomplicated pelvic inflammatory disease (PID). Again, ofloxacin demonstrated similar efficacy to alternative treatments in each type of infection. The availability of an intravenous formulation and near-complete oral bioavailability allow ofloxacin to be administered as a sequential regimen without loss of activity. The tolerability and drug interaction profile of ofloxacin is consistent with that of other fluoroquinolones. The most commonly reported adverse events with ofloxacin are gastrointestinal, neurological and dermatological. It was associated with a lower incidence of photosensitivity and tendinitis and higher incidence of some neurological events than some other fluoroquinolones. Ofloxacin seems to have a lower propensity to interact with xanthines than other fluoroquinolones. Conclusion:
ofloxacin has established efficacy in the treatment of a wide variety of urinary tract infections, although, like other fluoroquinolones, it should be used rationally to preserve its activity. Currently, ofloxacin also holds an important place among fluoroquinolones in the treatment of C. trachomatis infections and uncomplicated PID, although its acceptance as monotherapy in PID is likely to depend on clarification of the causative role of anaerobic pathogens in this infection.


During a 14-year period, 42 cases of microbial keratitis were associated with contact lens (CL) wear. Pseudomonas aeruginosa was isolated in 40% of the cases and Staphylococcus in 31%; Streptococcus pneumoniae, alpha-hemolytic Streptococcus, and Serratia marcescens were the next most commonly isolated pathogens. There was a single fungal corneal ulcer. Bandage CL use was associated with a high prevalence of infection with quasi-commensal organisms and with polymicrobial keratitis, a pattern of disease quite distinct from that induced by other types of CLs. Marked visual loss frequently occurred. There was a disturbing increase in the number of infections associated with extended-wear CLs (worn for either aphakia or myopia) over the last 18 months of the study.


**BACKGROUND:** From June 30, 1998, through March 21, 1999, several patients in the surgical intensive care unit of a hospital acquired Serratia marcescens bacteremia. We investigated this outbreak. **METHODS:** A case was defined as the occurrence of *S. marcescens* bacteremia in any patient in the surgical intensive care unit during the period of the epidemic. To identify risk factors, we compared patients with *S. marcescens* bacteremia with randomly selected controls. Isolates from patients and from medications were evaluated by pulsed-field gel electrophoresis. The hair of one employee was tested for fentanyl. **RESULTS:** Twenty-six patients with *S. marcescens* bacteremia were identified; eight (31 percent) had polymicrobial bacteremia, and seven of these had Enterobacter cloacae and *S. marcescens* in the same culture. According to univariate analysis, patients with *S. marcescens* bacteremia stayed in the surgical intensive care unit longer than controls (13.5 vs. 4.0 days, P<;0.001), were more likely to have received fentanyl in the surgical intensive care unit (odds ratio, 31; P<;0.001), and were more likely to have been exposed to two particular respiratory therapists (odds ratios, 13.1 and 5.1; P<;0.001 for both comparisons). In a multivariate analysis, receipt of fentanyl and exposure to the two respiratory therapists (adjusted odds ratio for one therapist, 6.7; P=0.002; adjusted odds ratio for the other therapist, 9.5; P=0.02) remained significant. One respiratory therapist had been reported for tampering with fentanyl; his hair sample tested positive for fentanyl. Cultures of fentanyl infusions from two case patients yielded *S. marcescens* and *E. cloacae*. The isolates from the case patients and from the fentanyl infusions had similar patterns on pulsed-field gel electrophoresis. After removal of the implicated respiratory therapist, no further cases occurred. **CONCLUSIONS:** An outbreak of *S. marcescens* and *E. cloacae* bacteremia in a surgical intensive care unit was traced to extrinsic contamination of the parenteral narcotic fentanyl by a health care
worker. Our findings underscore the risk of complications in patients that is associated with illicit narcotic use by health care workers.


The toxic effects of endotoxin-free human recombinant tumor necrosis factor (rH-TNF), shown to contain less than 50 pg endotoxin/mg rH-TNF, were investigated and compared with those of rH-TNF and endotoxin coadministered at 4-400 ng endotoxin/mg rH-TNF in female Sprague-Dawley rats. The mean lethal dose of 5.9 mg/kg rH-TNF found for the endotoxin-free rH-TNF was far higher than that attributed to rH-TNF by other investigators. Coadministration with endotoxin derived from E. Coli. Salmonella abortus equi, or Serratia marcescens reduced the apparent mean lethal dose of rH-TNF in correspondence to the endotoxin concentration, with a value of 0.7 mg/kg rH-TNF observed at 1600 ng, 757 ng, and 5260 ng endotoxin/mg rH-TNF, respectively. Coadministration also resulted in more severe histopathologic and physicochemical effects than rH-TNF alone. Histopathologic abnormalities observed only in coadministration included interlobular edema and hemorrhage of the pancreas and, most remarkably, splenomegaly, which was not observed with rH-TNF alone even at lethal doses. The results indicate that particular care in determining endotoxin contamination is essential in any consideration of TNF toxicity.


The result documenting the disappearance of obligate anaerobic bacteria as the predominant intestinal organisms with the onset of septicemia from *S. marcescens* calls for exploration into the clinical significance of anaerobic bacteria in the intestine in relationships between gut flora and host. The finding that no significant difference could be seen between the rates of sepsis under protective isolation and in uncontrolled environments is indicative of the fact that the disease most likely originated as an infection of endogenous nature. In the five cases of leukemia in children with bone marrow transplantation cited in this presentation, not one case of bacterial or fungal infection was recorded. The establishment of endogenous infections surrounding the results presented herein is discussed in terms of the biological phenomena of the interaction between intestinal flora and host, and between the intestinal bacterial flora.


Serratia marcescens has recently been identified as an important etiological agent in nosocomial infections, and is considered to be an opportunistic pathogen agent in immunosuppressed patients undergoing long periods of intensive care. Research carried out in 1991 and 1992 showed that it was of epidemiological relevance in only 1-2% of clinical isolates at the Ospedale di Circolo, Varese, Italy. However, between 7 February
and 11 October 1993, the incidence of cases attributable to *S. marcescens* had increased to 5%; 157 strains of *Serratia marcescens* were isolated from clinical specimens of 43 patients admitted to an intensive care unit; these strains, characterized by epidemic spread, showed the same pattern of multiresistance to antibiotics including monobactams and oxyimino-cephalosporins. During the same period 23 isolates were also recovered from 18 patients admitted to wards other than the intensive care unit; these strains, characterized by a wide range of antibiotic susceptibility, were also sensitive to beta-lactam antibiotics with the exception of first generation cephalosporins. The production of extended-spectrum beta-lactamases (ES beta Ls) and their genetic determinism were studied. All the epidemic strains of *S. marcescens* resistant to ceftazidime, cefotaxime, ceftriaxone and aztreonam produced three different beta-lactamases with pI 5.4, 5.5 and 8.4 respectively. In contrast, non-epidemic strains produced only a beta-lactamase with pI 8.4. The beta-lactamase with pI 5.5 was plasmid-mediated, hydrolizing ceftazidime and aztreonam, showing it to be an ES beta L; while the beta-lactamase with pI 5.4, although plasmid-mediated, did not hydrolize monobactams or oxyimino-cephalosporins.

**Pair et al. 2004.** Overwintering squash bugs harbor and transmit the causal agent of cucurbit yellow vine disease. *J. Econ. Entomol.* Vol. 97(1): 74-78.

Since 1988, cucurbit crops, particularly watermelon, cantaloupe, and squash, grown in Oklahoma and Texas have experienced devastating losses from cucurbit yellow vine disease (CYVD), caused by the phloem-limited bacterium *Serratia marcescens* Bizio. Squash bug, *Anasa tristis* (De Geer), is a putative vector of the pathogen. In 2000-2001, overwintering populations of squash bug collected from DeLeon, TX, were tested for their ability to harbor and transmit the bacterium. Individual squash bugs (n = 73) were caged serially for periods of up to 7 d on at least four squash seedlings. Two studies were conducted, one with insects collected in November 2000 placed on first true leaf-stage seedlings and the second with insects from an April 2001 collection, placed on 3-5 true leaf-stage squash. Controls consisted of squash seedlings caged without insects. Squash bug transmission rates of the pathogen in studies I and II were 20 and 7.5%, respectively. Overall, 11.0% of the squash bugs harbored and successfully transmitted the bacterium to squash seedlings. All control plants tested negative for *S. marcescens* and did not exhibit CYVD. Female squash bugs killed a significantly greater proportion of young first leaf-stage seedlings than males. Feeding on 3-5 leaf-stage squash resulted in no plant mortality regardless of squash bug gender. This study demonstrated that the squash bug harbors *S. marcescens* in its overwintering state. The squash bug-*S. marcescens* overwintering relationship reported herein greatly elevates the pest status of squash bug and places more importance on development of integrated strategies for reducing potential overwintering and emerging squash bug populations.


OBJECTIVES: To determine whether aerosolized antibiotics can be delivered efficiently to the lower respiratory tract in mechanically ventilated patients and to define possible clinical responses to these agents. DESIGN: Prospective serial study with cases as their own control. SETTING: A 10-bed respiratory care unit for patients with chronic


Serratia marcescens is a Gram negative rod which for a century and a half was considered a harmless saprophyte. However, medical technology and the use of antibacterial agents have created ecological niches for this bacterium, which is now a medical problem. The bacterium is encountered in connection with contact lens keratitis, often associated with contaminated contact lens solutions. The concentrations of
chlorhexidin and thiomersal required in contact lens solution to suppress the bacterium have been proved toxic to the eye. Modern contact lens solutions with biguanids have rapid killing kinetics, while in solutions with polyquaternium *S. marcescens* can survive in reduced numbers for up to 72 hours. The adherence of a specific isolate of *Serratia* to hydrogel lenses increased with decreased water content of the lenses. However, there has been no correlation between hydrophobicity markers or hemagglutinins and adherence to contact lenses or urinary tract epithelium. When handling medical plastic devices, such as contact lenses, strictly enforced hygiene remains the most important method to combat environmental bacteria such as *Serratia marcescens*.


A new genotyping method for *Serratia marcescens* is described. This method uses the flagellin gene as target for polymerase chain reaction amplification and Alu I restriction fragment length polymorphism. The strains tested belonged to 13 different hospital clusters of *S. marcescens* isolated between 1983 and 1988, concerning outbreaks and/or patient environments in different hospital units in Lyon and the Rhone-Alpes region of France. Initially, the classification had been performed by marcescinotyping. These strains were then tested by ribotyping and genotyping of the flagellin gene. Genotyping showed similar classification to ribotyping. The genotyping method is the easiest technique, as reproducible as ribotyping, and with almost the same ability to discriminate different strains. It does not need expensive equipment, is more rapid, and is less labor intensive than ribotyping. With this method, all strains of *S. marcescens* including sporadic isolates could be amplified and typed. Antibiotic sensitivity determination was found to be a useful complementary and confirmation test for all these typing methods.


We describe a fatal case of spontaneous necrotizing myositis due to a highly resistant strain of *Serratia marcescens* in a renal transplant recipient. Though *Staphylococcus aureus* and *Clostridium* are the usual agents which cause either pyomyositis or necrotizing myositis, gram-negative bacteria are a dangerous and rarely suspected possibility. Such an aggressive disease should be promptly recognized because immunosuppression in susceptible hosts makes conservative management unsuccessful. The prognosis for myositis in immunodepressed hosts is poor and wide excision of all the necrotic muscles, leaving the wound open, and intensive antibiotic therapy are required.


Populations of the shallow-water Caribbean elkhorn coral, *Acropora palmata*, are being decimated by white pox disease, with losses of living cover in the Florida Keys typically in excess of 70%. The rate of tissue loss is rapid, averaging 2.5 cm2 x day(-1), and is
greatest during periods of seasonally elevated temperature. In Florida, the spread of white pox fits the contagion model, with nearest neighbors most susceptible to infection. In this report, we identify a common fecal enterobacterium, Serratia marcescens, as the causal agent of white pox. This is the first time, to our knowledge, that a bacterial species associated with the human gut has been shown to be a marine invertebrate pathogen.


Resistance emerging after ceftazidime or cefepime therapy was investigated in a peritonitis model. Mice were given a peritoneal challenge (10(8) cfu plus talcum) and treated by either antibiotic (50 mg/kg/dose, which produced similar antibiotic concentrations in peritoneal fluid in both cases). After one or three doses, resistance never developed in Serratia marcescens or Citrobacter freundii infections. After Enterobacter cloacae and Pseudomonas aeruginosa challenge, ceftazidime selected more resistance (21/36 cases) than did cefepime (1/36 cases). In mice challenged with resistant strains selected by ceftazidime therapy, cefepime (six doses) successfully treated 7/18 E. cloacae infections but 0/18 P. aeruginosa infections; ceftazidime was never effective.

Neither cefepime nor ceftazidime cured mice infected with the resistant strain selected by cefepime. MICs were poor predictors of further emergence of resistance in mice inoculated with strains classified as susceptible, but antibiotic-containing agar gradients plated with a high inoculum (10(8) cfu) allowed better prediction. In selected clinical situations, cefepime may be preferable because it may be associated with less frequent emergence of resistance.


BACKGROUND: Nosocomial bloodstream infection is an important cause of morbidity and mortality among neonates. From September 1 through December 5, 1990 (epidemic period), gram-negative bacteremia developed in 26 neonates after their admission to the neonatal intensive care unit (NICU) of Hospital General, a 1000-bed public teaching hospital in Guatemala with a 16-bed NICU. Twenty-three of the 26 patients (88%) died.

METHODS: To determine risk factors for and modes of transmission of gram-negative bacteremia in the NICU, we conducted a cohort study of NICU patients who had at least one blood culture drawn at least 24 hours after admission to the NICU and performed a microbiologic investigation in the NICU. RESULTS: The rate of gram-negative bacteremia was significantly higher among patients born at Hospital General, delivered by cesarian section, and exposed to selected intravenous medications and invasive procedures in the NICU during the 3 days before the referent blood culture was obtained. During the epidemic period, the hospital's chlorinated well-water system malfunctioned; chlorine levels were undetectable and tap water samples contained elevated microbial levels, including total and fecal coliform bacteria. Serratia marcescens was identified in 81% of case-patient blood cultures (13/16) available for testing and from 57% of NICU personnel handwashings (4/7). Most *S. marcescens* blood isolates were serotype O3:H12 (46%) or O14:H12 (31%) and were resistant to ampicillin (100%) and gentamicin (77%), the antimicrobials used routinely in the NICU. CONCLUSIONS: We hypothesize that gram-negative bacteremia occurred after invasive procedures were performed on
neonates whose skin became colonized through bathing or from hands of NICU personnel.


We report an outbreak of Serratia marcescens infection in the neonatal intensive care unit of a community hospital. The outbreak involved eight neonates, (five infected and three colonized), one of whom died. Pulsed-field gel electrophoresis confirmed that all isolates were identical strains. Cohorting and isolation of the infected neonates helped to control the outbreak. No environmental source of infection was found.

http://deploymentlink.osd.mil/current_issues/shad/shad_glossary.shtml [As of September 1, 2004]


JRS4(HE), a highly encapsulated, mouse-passaged variant of group A streptococcal strain JRS4, was characterized. The mucoid phenotype of JRS4(HE) was preserved after
extensive passage in vitro. The level and size of csrRS transcript in JRS4(HE) was similar to that of JRS4, yet JRS4(HE) expressed high levels of has and sagA and exhibited an increased activity of streptolysin S. These findings indicate that the CsrRS repressor system was inactive in JRS4(HE). JRS4(HE) adhered to HEP-2 cells at the stationary phase but did not internalize these cells. At midlogarithmic phase, JRS4(HE) neither adhered to nor internalized cells, because of an increased amount of hyaluronic acid. Mice injected subcutaneously with JRS4(HE) developed large, deep necrotic lesions. In contrast, mice challenged with JRS4 developed small, superficial lesions. Despite the use of a high inoculum, mice challenged with JRS4(HE) did not develop a lethal bacteremic infection. It is concluded that inactivation of CsrRS in vivo is insufficient to cause a spreading necrotic disease.


As long as the illicit use of heroin and other drugs continues in our society, infective endocarditis will remain a significant medical problem in the drug-using population. The majority of infections are produced by S. aureus, and the tricuspid valve is most commonly involved. Addicts, unlike the general population, may also develop endocarditis with a variety of gram-negative bacilli and have a higher incidence of fungal infection. The outcome of each individual infection is dependent on the prompt recognition of the underlying valvular infection and the institution of antimicrobial therapy. Infection of the tricuspid valve has a much more favorable prognosis than does infection of the aortic or mitral valves. Fungal endocarditis, and frequently gram-negative bacillary endocarditis, require valvular surgery to effect a cure.


An outbreak of infections with pigmented Serratia marcescens involving 3 patients in a cardiothoracic surgical intensive care unit is reported. A respirator is thought to have been the source of pneumonia in 2 patients, and fomite spread from 1 of these is considered responsible for the induction of fatal endocarditis in the third patient. This outbreak demonstrates the rapid dissemination of a bacterial strain within the unit, several methods of dissemination, the wide variation in apparent virulence of the organism, the alterations of antibacterial host defense which made bacterial disease possible and which determined the site of infection, and the difficulties of adequate therapy. The third patient is the seventh reported with serratia infection of a prosthetic heart valve.

We retrospectively reviewed the cases of 23 adults and six children who had been given a presumed diagnosis of acute supraglottitis between 1987 and 1997. The most common symptoms in these patients were odynophagia, dysphagia, hoarseness, and fever. Stridor and drooling were also observed, primarily in the children. Fiberoptic laryngoscopy confirmed the presence of edema and erythema of the supraglottic structures in all patients. Blood cultures were positive for Hemophilus influenzae type b in three children and for Serratia marcescens in one adult. All other blood cultures were negative. All patients were treated with intravenous broad-spectrum antibiotics and humidified oxygen, and two-thirds received intravenous corticosteroids. Patients were monitored with pulse oximetry and serial fiberoptic laryngoscopy. Two patients required intubation; one had an epiglottic abscess, and the other had laryngeal edema so severe that vocal fold mobility could not be assessed. The length of stay in the intensive care unit ranged from 1 to 7 days (mean: 1.9). All patients recovered and were discharged free of symptoms after 2 to 11 days of overall hospitalization (mean: 4.4).

An unusual presentation of calcaneal osteomyelitis is described, where-by the infection remained undiagnosed for 25 years. The 36-year-old patient recently sought medical treatment for a reported ankle sprain, but the pain was recalcitrant to conservative care. Further investigation yielded a history significant for stepping on a chicken bone as a child, which entered the inferior lateral heel. Magnetic resonance imaging revealed what plain radiographs did not: a well demarcated lytic lesion in the body of the calcaneus. Intraoperative findings were consistent with an abscess of chronic osteomyelitis. The treatment included incision and drainage, antibiotic beads, and a tricortical bone graft.

An epidemic caused by Serratia marcescens occurred in intensive care unit of the Children's clinic in Essen, with three deaths. Although there was good sensitivity of the strain to gentamicin in vitro, there was no noticeable clinical improvement when it was administered. But cotrimoxazole, given systemically and locally, and colistin locally cured the disease.


Health Effects of *Serratia marcescens*
At the Vanderbilt University Medical Center, Nashville, Tennessee, resistance to gentamicin was encountered with increasing frequency among several species of gram-negative bacilli between 1973 and 1977. Representative strains were screened for plasmid DNA content using agarose gel electrophoresis. In strains of Pseudomonas aeruginosa and Serratia marcescens isolated early in the outbreak, gentamicin resistance was mediated by a common 9.8-megadalton nonconjugative plasmid. Either an 80- or a 100-megadalton transferable plasmid coexisted with the nonconjugative plasmid in the isolates of Serratia. Transposition between the 100- and 9.8-megadalton plasmids in this species resulted in the formation of a 105-megadalton conjugative plasmid that mediated gentamicin resistance; this was observed in strains of Serratia and Klebsiella isolated in 1976-1977. Thus, during this five-year investigation separate outbreaks of nosocomial infections that were caused by different bacterial species were shown to be related by the presence of plasmids that contained a common transposable DNA sequence.

The API (Analytab Products, Inc., New York, N.Y.) biotypes of 117 clinical isolates of Serratia marcescens were determined and fell into 13 different patterns. The O and H antigens were determined by tube agglutination, and 27 serotypes were identified. The biotype and serotype appeared to vary independently. Serotyping and biotyping combined divided these isolates into 56 different types. There was a problem interpreting the endpoints for inositol fermentation and urease production, which could affect reproducibility of API biotypes. Biotyping is a simple way of screening for possible nosocomial outbreaks of S. marcescens.

OBJECTIVE: To determine the cause(s) of an outbreak of gram-negative bacteremia (GBA) in open-heart-surgery (OHS) patients at hospital A. DESIGN: Case-control and cohort studies and an environmental survey. RESULTS: Nine patients developed GNB with Enterobacter cloacae (6), Pseudomonas aeruginosa (5), Klebsiella pneumoniae (3), Serratia marcescens (2), or Klebsiella oxytoca (1) following OHS; five of nine patients had polymicrobial bacteremia. When the GNB patients were compared with randomly selected OHS patients, having had the first procedure of the day (8 of 9 versus 12 of 27, P = .02), longer cardiopulmonary bypass (median, 122 versus 83 minutes, P = .01) or cross-clamp times (median, 75 versus 42 minutes, P = .008), intraoperative dopamine infusion (9 of 9 versus 15 of 27, P = .01), or exposure to scrub nurse 6 (6 of 9 versus 4 of 27, P = .001) were identified as risk factors. When stratified by length of the procedure, only being the first procedure of the day and exposure to scrub nurse 6 remained significant. First procedures used pressure-monitoring equipment that was assembled before surgery and left open and uncovered overnight in the operating room, whereas other procedures used pressure-monitoring equipment assembled immediately before the procedure. At night, operating rooms were cleaned by maintenance personnel who used a disinfectant-water solution sprayed through a hose connected to an automatic diluting system.
Observation of the use of this hose documented that this solution could have contacted and entered uncovered pressure-monitoring equipment left in the operating room. Water samples from the hose revealed no disinfectant, but grew P aeruginosa. The outbreak was terminated by setting up pressure-monitoring equipment immediately before the procedure and discontinuing use of the hose-disinfectant system. CONCLUSIONS: This outbreak most likely resulted from contamination of uncovered preassembled pressure-monitoring equipment by water from a malfunctioning spray disinfectant device. Pressure-monitoring equipment should be assembled immediately before use and protected from possible environmental contamination.

Ruegg et al. 1992. Microbiologic investigation of an epizootic of mastitis caused by Serratia marcescens in a dairy herd. J.Am.Vet.Med.Assoc. Vol. 200(2): 184-189. An epizootic of subclinical and clinical mastitis caused by Serratia marcescens was investigated in a 1,000-cow dairy farm in California. Serratia marcescens was isolated from 13 to 18% of composite milk samples obtained from lactating dairy cows. During monthly milk sampling performed during a 4-month period, S marcescens was isolated from 38.8 to 62.3% of composite milk samples obtained from cows from which S marcescens was previously isolated. Few cows infected with S marcescens had evidence of clinical mastitis. Somatic cell count value was associated with isolation of S marcescens. Cows with somatic cell counts greater than 500,000 were 5.48 times as likely to have intramammary infections with S marcescens, compared with cows with somatic cell count less than or equal to 500,000. Lactation number also was associated with S marcescens intramammary infection. After adjusting for the effect of lactation number, cows with high somatic cell count values were 2.98 times as likely to have intramammary infection with S marcescens, compared with cows with low somatic cell counts. Infection with S marcescens was independent of days in lactation, production string, and daily milk production. Eleven months after the beginning of the epizootic, S marcescens was isolated from organic bedding samples obtained from the dairy. Despite numerous attempts, other sources of S marcescens could not be identified on this dairy.

Russell et al. 1999. Respiratory pathogen colonization of the dental plaque of institutionalized elders. Spec.Care Dentist. Vol. 19(3): 128-134. Although it has been established that aspiration of pharyngeal bacteria is the major route of infection in the development of nosocomial pneumonia, colonization of the pharyngeal mucosa by respiratory pathogens has been shown to be a transient phenomenon. It has been suggested that the dental plaque may constitute an additional, possibly more stable, reservoir of respiratory pathogens. The purpose of this study was to assess the prevalence of oral colonization by potential respiratory pathogens in a group of elderly (mean age = 75.9 yrs) chronic-care-facility residents (n = 28) and a group of age-, gender-, and race-matched outpatient control subjects (n = 30), with specific attention to plaque present on tooth, denture, and oral mucosal surfaces. Plaque scores on teeth and dentures were significantly higher in the chronic-care-facility (CCF) subjects than in the dental outpatient control (DOC) subjects (PII 2.3 vs. 1.2 and denture plaque 1.4 vs. 0.3). While no subjects in the DOC group were found to be colonized with respiratory pathogens (>; 1.0% of the cultivable aerobic flora), 14.3% (4/28) of the CCF subjects were found to be colonized. Oral colonization with respiratory pathogens in CCF subjects was associated
with the presence of chronic obstructive pulmonary disease (COPD) and higher plaque scores. These results suggest that deficient dental plaque control and the presence of COPD may be related to respiratory pathogen colonization of dental plaque in chronic-care-facility residents.


An outbreak of nosocomial infections of the urinary tract due to a multiply drug-resistant strain of Serratia marcescens occurred at a community hospital. Acquisition of the epidemic strain was associated with the following factors: (1) exposure to the intensive care unit, (2) presence of an indwelling bladder catheter, (3) treatment with antibiotics, and (4) exposure to devices used from measurements of specific gravity and urine volume. An extensive microbiologic evaluation of the hospital environment failed to reveal the epidemic strain of *S. marcescens* from any site other than urinometers and urine volume measuring containers. Four of four urinometers and three of seven urine measuring containers tested revealed the epidemic organism. Notably, six of these seven positive cultures were obtained in hospital areas in which no patients infected with *S. marcescens* were located at the time of sampling. The resistant organism was also recovered from one of three pooled handwashings taken from nursing personnel. Thus, the urinometer and urine measuring container may have served as inanimate reservoirs for the resistant *S. marcescens* which was subsequently inoculated onto the hands of medical personnel or directly to a catheterized patient. Disinfection procedures were identified which eliminated these items as reservoirs. No additional cases of multiply drug-resistant *S. marcescens* urinary tract infections have been observed since institution of routine disinfection of the inanimate reservoir.


Arabidopsis thaliana ecotype Columbia plants (Col-0) treated with plant growth-promoting rhizobacteria (PGPR) Serattia marcescens strain 90-166 and Bacillus pumilus strain SE34 had significantly reduced symptom severity by Cucumber mosaic virus (CMV). In some cases, CMV accumulation was also significantly reduced in systemically infected leaves. The signal transduction pathway(s) associated with induced resistance against CMV by strain 90-166 was determined using mutant strains and transgenic and mutant Arabidopsis lines. NahG plants treated with strains 90-166 and SE34 had reduced symptom severity indicating that the resistance did not require salicylic acid (SA). Strain 90-166 naturally produces SA under iron-limited conditions. Col-0 and NahG plants treated with the SA-deficient mutant, 90-166-1441, had significantly reduced CMV symptom severity with reduced virus accumulation in Col-0 plants. Another PGPR mutant, 90-166-2882, caused reduced disease severity in Col-0 and NahG plants. In a time course study, strain 90-166 reduced virus accumulation at 7 but not at 14 and 21 days post-inoculation (dpi) on the non-inoculated leaves of Col-0 plants. NahG and npr1-1 plants treated with strain 90-166 had reduced amounts of virus at 7 and 14 dpi but not at 21 dpi. In contrast, no decrease in CMV accumulation occurred.
in strain 90-166-treated fad3-2 fad7-2 fad8 plants. These data indicate that the protection of Arabidopsis against CMV by strain 90-166 follows a signaling pathway for virus protection that is independent of SA and NPR1, but dependent on jasmonic acid.

The clinical distinction between bacterial colonization of the tracheobronchial tree and nosocomial pneumonia is difficult, especially in intubated patients. We studied 51 intubated, intensive care unit patients prospectively by serial examinations of tracheal aspirates for elastin fibers, graded Gram's stains, and quantitative bacterial cultures in conjunction with clinical and radiologic observations in an attempt to develop criteria for the early detection of pulmonary infection. Patients with infection had new or progressive pulmonary infiltrates plus 1 of the following: positive blood culture results, radiographic evidence of cavitation, or histologic evidence of pneumonia, or 2 or more of the following: new fever, new leukocytosis, or grossly purulent tracheal aspirates. Twenty-one patients developed infection, 22 remained colonized, and 8 had an uncertain status. Infiltrates developed in 34 patients (21 infected, 8 colonized, 5 uncertain status). Gram-negative bacilli were most commonly isolated and were more frequent in infected patients (81 versus 47%, p less than 0.05); Pseudomonas aeruginosa and Serratia marcescens were most often associated with infection. No differences were observed between infected and colonized patients in demographic features, smoking history, underlying disease, previous antibiotic therapy, days in hospital before intubation, preexisting pneumonia upon intubation, or highest temperature or leukocyte count during course. By univariate analysis, infected patients had a longer duration of intubation (p less than 0.05), higher Gram's stain grading for neutrophils (p less than 0.05) or bacteria (p less than 0.005), higher bacterial colony counts (p less than 0.05), and more frequent detection of elastin fibers in tracheal aspirates (p less than 0.02). (ABSTRACT TRUNCATED AT 250 WORDS)

OBJECTIVE: To determine the role of nonmedicated soap as a source of Serratia marcescens nosocomial infections (NIs) in hospital units with endemic S marcescens NI and to examine the mechanisms of soap colonization. SETTING: University-affiliated tertiary-care hospitals. METHODS: A prospective case-control study and an environmental investigation were performed to assess the relationship between S marcescens NIs in hospital units and S marcescens-contaminated soap. Soap-bottle use and handwashing practices were reviewed. Cultures of healthcare workers' (HCWs) hands were obtained before and after hand washing with soap. RESULTS: 5 of 7 hospital units with S marcescens NIs had soap bottles contaminated with S marcescens, compared to 1 of 14 other units (P=.006). After hand washing with an S marcescens-contaminated soap pump, HCWs' hands were 54 times more likely to be contaminated with S marcescens (Pc<.001). CONCLUSIONS: Extrinsic contamination of a non-medicated liquid soap by S marcescens resulted in handborne transmission of S marcescens NIs by
HCWs in our setting. This finding led to the application of strict guidelines for nonmedicated soap use and to the reinforcement of alcoholic hand disinfection.


Serratia marcescens is recognized as an important and potentially hazardous nosocomial pathogen. The organism has been implicated here as the first reported case of *S. marcescens* meningitis associated with skin disinfection. A quaternary ammonium compound (QAC--Benzalkonium Chloride), was used to sterilize the skin prior to injection in a physician's office. Epidemiological studies were initiated. Six spray bottles containing disinfectant, the opened stock bottle of QAC, and an unopened bottle of disinfectant were all cultured. *S. marcescens* was noted growing in the spray bottles as well as in the opened stock bottle. Antibiograms of the patient and epidemiological isolates are essentially the same. It is our contention as well as that of the Centers for Disease Control that an appropriate skin disinfectant such as Tincture of Chlorhexidine, Iodophors, or Tincture of Iodine should be used, and that physicians performing surgical techniques in the office be aware of the potential hazard of contamination. The consequences of nosocomial infection with resistant organisms warrant every precaution by health care professionals.


Interhospital spread appeared to be responsible for a large epidemic of infections due to a strain of *Serratia marcescens* that was resistant to all currently available parenteral antibiotics. Between April 1, 1973 and January 1, 1975, 210 patients in four geographically separate hospitals in Nashville, Tennessee, were infected with the epidemic strain; 21 patients were bacteremic and eight died. Catheter-associated urinary tract infection accounted for the majority of isolates, and broad-spectrum antibiotic exposure appeared to promote the acquisition of the epidemic strain. The serotype (O1:H7) and phage type (186) of the organism were identical in all four hospitals, but background, sensitive strains of *S. marcescens* yielded a variety of other serotypes. Carriage on the hands of hospital personnel was implicated as the mode of spread within the hospital and apparently was the mode of transmission between the hospitals. Antibiotic resistance was largely episomally mediated, but resistance to gentamicin, cephalothin, and colistin was not transferable.


The development of antimicrobial resistance by bacteria has had profound effects of the clinical use of antibiotics, especially in hospital-acquired infections. In 1973, a large outbreak of nosocomial infections due to *Serratia marcescens* began at the Vanderbilt University medical complex, a major characteristic of which was high-level resistance to gentamicin and carbenicillin. Investigation of the outbreak and subsequent in vitro studies have shown that the evolution and epidemiology of this high-level resistance operated at three levels of organizations: (1) dissemination of individual strains, (2) dissemination of a plasmid among different strains and (3) movement of a discrete genetic element, or
transposon, between plasmids. The investigations of this outbreak and other studies reviewed support the concept that resistant strains can evoke as a result of R-plasmid exchange within the hospital environment, providing an opportunity for control of this exchange can be interrupted.


Agarose gel electrophoresis of the plasmid deoxyribonucleic acids from 60 gram-negative bacilli recovered during investigations of nosocomial epidemics was used to fingerprint the strains. This method was as specific at differentiating bacterial strains as more conventional phenotyping methods. In all cases, plasmid band fingerprints of epidemic strains isolates were identical whereas coisolate plasmid deoxyribonucleic acid patterns were different. Agarose gel electrophoresis of plasmid deoxyribonucleic acid is proposed as a method which can be used in conventional microbiology laboratories as an adjunct to or, possibly, replacement for other methods of identifying bacterial strains.


AIM: To define the clinical and microbiological profile of bacterial keratitis at the Jules Gonin Eye Hospital and to test the in vitro bacterial resistance. METHODS: Patients presenting with bacterial keratitis were prospectively followed; clinical features (age, risk factors, visual acuity) and response to therapy were analysed. Bacteriological profile was determined and the sensitivity/resistance of isolated strains were tested towards 12 ocular antibiotics (NCCLS disc diffusion test). RESULTS: 85 consecutive patients (mean age 44.3 (SD 20.7) years) were prospectively enrolled from 1 March 1997 to 30 November 1998. The following risk factors were identified: contact lens wear, 36%; blepharitis, 21%; trauma, 20%; xerophthalmia, 15%; keratopathies, 8%; and eyelid abnormalities, 6%. The most commonly isolated bacteria were Staphylococcus epidermidis, 40%; Staphylococcus aureus, 22%; Streptococcus pneumoniae, 8%; others Streptococcus species, 5%; Pseudomonas, 9%; Moraxella and Serratia marcescens, 5% each; Bacillus, Corynebacterium, Alcaligenes xylooxidans, Morganella morganii, and Haemophilus influenza, 1% each. 1-15% of strains were resistant to fluoroquinolones, 13-22% to aminoglycosides, 37% to cefazolin, 18% to chloramphenicol, 54% to polymyxin B, 51% to fusidic acid, and 45% to bacitracin. Five of the 85 patients (5.8%) had a poor clinical outcome with a visual loss of one or more lines of visual acuity. CONCLUSION: Fluoroquinolones appear to be the therapy of choice for bacterial keratitis, but, based upon these in vitro studies, some strains may be resistant.


Until the 1950's Serratia marcescens was generally considered as non-pathogenic for humans. Since then the organism has been reported repeatedly as a cause of nosocomial infections. Contract No. IOM-2794-04-001

Health Effects of *Serratia marcescens*
infections. The major clinical concern about Serratia marcescens is its implication in epidemic infections and its resistance to usual antibiotics causing therapy to be difficult. We report the occurrence of Serratia marcescens as the cause of severe septicemia in three premature infants. Two infants showed a severe course of sepsis, the third infant suffered from additional meningitis and a brain abscess. All infants survived, but only one had no sequela.


Of 125 patients treated with ciprofloxacin at the Columbia-Presbyterian Medical Center, New York, 34 had infections due to bacteria other than Pseudomonas aeruginosa. The mean age of the patients was 50 years (19-88 years) and most had significant underlying disease. There were nine lower respiratory infections, eight urinary tract infections, eight soft tissue infections, three osteomyelitis, and three intra-abdominal infections. The pathogens were: Escherichia coli, 7 (mean MIC 0.07 mg/l); Serratia marcescens, 6 (0.2 mg/l); Enterobacter spp., 5 (0.1 mg/l); Klebsiella pneumoniae, 3 (0.1 mg/l); Proteus mirabilis, 3 (0.06 mg/l); Crotobacter freundii, 2 (0.06 mg/l), Staphylococcus aureus, 3 (0.5 mg/l); and one each of Acinetobacter anitratus. Haemophilus, influenzae, Salmonella enteritidis, Flavobacterium meningosepticum, and Streptococcus faecalis. Of these organisms 81% were resistant to ampicillin, 70% to carbenicillin, 22% to gentamicin, 49% to cefazolin and cephalaxin, and 25% to cotrimoxazole. Ten patients had concomitant Ps. aeruginosa infections. Patients were treated orally with 500 mg or 750 mg ciprofloxacin every 12 h. The overall clinical response rate was 88%, and the bacteriological response 76%, and 65% if Ps. aeruginosa is included. Resistance to ciprofloxacin developed in one Staph. aureus and one Ser. marcescens (MIC greater than 2 mg/l). Toxicity was minor. Ciprofloxacin was effective and safe therapy of infections due to Gram-negative bacteria resistant to many of the currently available oral and parenteral agents.


OBJECTIVE: To investigate an outbreak of Serratia marcescens bacteremia among patients after general anesthesia. DESIGN: A case-control study. SETTING: A 304-bed, pediatric teaching hospital. PATIENTS: Twenty-three pediatric patients who developed S. marcescens bacteremia within 2 weeks after general anesthesia between June 15 and September 22, 1999, were compared with 46 age-matched control-patients who had undergone procedures on the same clinical services of the hospital during the same period. RESULTS: Cases were distributed over a wide range of surgical services and were not correlated with exposure to any of the surgical, anesthesia, or nursing staff. Case-patients were significantly more likely than control-patients to have received cefazolin (odds ratio [OR], 11.1; 90% confidence interval [CI90], 1.9 to 24.3) or to have had perioperative placement of a central vascular catheter (OR, 4.2; CI90, 1.2 to 18.8). The timing of the procedures of patients who subsequently developed S. marcescens bacteremia was significantly associated with the shifts of one or more of five operating room technicians (OR, 2.9 to 6.8) who were responsible for preparing intravenous fluids.
used both to reconstitute perioperatively administered antibiotics and to prime central vascular catheter assemblies. CONCLUSIONS: Our findings are consistent with a pattern of intermittent contamination due to periodic breaches in sterile technique, rather than a point-source of contamination. The unique challenges that such a procedural breakdown presents to an epidemiologic investigation are discussed. This outbreak stresses the importance of providing comprehensive training in antisepsis when multifunctional personnel are incorporated into an operating room work environment.


BACKGROUND: The oral cavity is a reservoir for colonization and infection of systemic organs by pathogenic bacteria. It is understood that aging, tooth eruption, hormonal changes, active disease, oral hygiene, and other factors have an influence on biofilm formation and bacterial accumulation in the oral cavity. OBJECTIVE: To understand the influence of systemic health care on microfloral changes, we conducted epidemiological studies of nursing home residents in an attempt to elucidate the relationship between underlying systemic diseases and the isolation frequency of oral opportunistic pathogens. METHODS: The prevalence of bacteria and fungi causing pneumonia in association with oral biofilm bacteria were determined using detection culture plates. The influences of gender, age, denture-wearing status, number of teeth, and bedridden status in the patients residing in nursing homes were then analyzed. RESULTS: The isolation frequency rates of *Candida albicans*, *Pseudomonadaceae*, *Staphylococcus* spp., and some strains of *Enterobacteriaceae* in plaque samples, as well as *C. albicans* and *Xanthomonas maltophilia* in samples from the pharynx, were significantly higher in those requiring systemic care (mean age 83.9 years) than in those who did not require such care (mean 71.0 years). In particular, the frequencies of *Pseudomonas* spp., *C. albicans*, and *Serratia marcescens* in plaque were significantly higher in those who were bedridden. Furthermore, the isolation of *Pseudomonas* spp. and *Klebsiella pneumoniae*, and/or *C. albicans* in plaque was significantly associated with heart disease. CONCLUSION: The coexistence of *Pseudomonas* spp. and *C. albicans* in elderly with 10-19 teeth is a potential indicator of high risk for pneumonia and heart disease. Therefore, attention to oral hygiene and professional care for removing the indicators may diminish the occurrence of systemic disease in the elderly requiring systemic care.

**Severino et al. 1999.** The discriminatory power of ribo-PCR compared to conventional ribotyping for epidemiological purposes. *APMIS.* Vol. 107(12): 1079-1084.

Molecular typing techniques have become increasingly important for confirmation of epidemiological relationships and delimitation of nosocomial outbreaks. The discriminatory power of the two DNA-based typing methods, conventional ribotyping
and ribo-PCR, was assessed to distinguish between selected strains of Acinetobacter calcoaceticus, Enterobacter cloacae, Serratia marcescens and Pseudomonas aeruginosa. Overall, conventional ribotyping was more discriminatory than ribo-PCR.


Pulsed-field gel electrophoresis (PFGE) typing was applied to the epidemiological investigation of 20 Serratia marcescens isolates collected from urine specimens of 17 patients and three urinals over a 2-month period. Twenty-five epidemiologically unrelated strains were also tested to determine the discriminatory power of PFGE. The PFGE fingerprints of each isolate were consistent in three different tests. The 20 outbreak isolates had an identical PFGE fingerprint pattern, while the epidemiologically unrelated strains demonstrated unique PFGE fingerprint patterns. The source of the outbreak was inadequately disinfected urinals. We conclude that PFGE served as a highly discriminatory and reproducible method for the epidemiological investigation of the outbreak of *S. marcescens* infection addressed by this study.


Treatment of serious infections caused by gram-negative bacilli with beta-lactam antimicrobial agents can induce Class I beta-lactamase production. This phenomenon can result in resistant microorganisms, and has been postulated to be a cause of therapeutic failure. The charts of patients bacteremic with Pseudomonas aeruginosa, Serratia marcescens, Enterobacter cloacae, Citrobacter freundii, Proteus vulgaris, and Providencia species (*n* = 120) during a 3-year period were reviewed to determine how common the emergence of resistance was, and to determine if in vitro susceptibility testing was a reliable therapeutic guide. Emergence of resistance was believed to occur when a subsequent bacteremic isolate showed at least a fourfold increase in minimum inhibitory concentration accompanied by a change of interpretive susceptibility category. In the group of patients who survived at least 48 hours that received beta-lactam therapy (*n* = 76), one case of emergence of resistance was identified (1.3%). Emergence of resistance to beta-lactam antimicrobial agents did not commonly cause therapeutic failure at our institution, and susceptibility testing of gram-negative bacilli by usual methods was a reliable guide to antimicrobial therapy.


The recovery of multiple isolates of Serratia marcescens from bronchial lavage specimens was traced to contaminated fibreoptic bronchoscopes. Four patients were involved and none became infected. Awareness of a cluster of serratia cultures and immediate investigation and institution of control measures may have prevented the occurrence of true infections.

**OBJECTIVE:** To investigate an apparent outbreak involving simultaneous isolation of *Pseudomonas aeruginosa* and *Serratia marcescens* from bronchoalveolar lavage (BAL) samples. **DESIGN:** Retrospective and prospective cohort studies using chart review, environmental sampling, and ribotyping of all available isolates. Cleaning and disinfection procedures for the bronchoscopes were also evaluated. **SETTING:** A 380-bed private hospital in Sao Paulo, Brazil **PATIENTS:** Forty-one patients who underwent bronchoscopic procedures between December 1994 and October 1996 and from whom *P. aeruginosa* and *S. marcescens* were concomitantly isolated. Bronchoscopes and related items were microbiologically assessed. **RESULTS:** *P. aeruginosa* and *S. marcescens* were simultaneously isolated from BAL samples 12.6% of the time (41 of 324) during the epidemic period versus 1.8% of the time (1 of 54) in the pre-epidemic period (P = .035). Ribotyping revealed two strains of *P. aeruginosa* and one of *S. marcescens* that were isolated from BAL samples of patients with no signs of respiratory tract infection, suggesting a pseudo-outbreak. Evaluation of bronchoscope disinfection revealed that inappropriate methods were being used. Implementation of simple control measures resulted in a significant decrease in simultaneous isolation of these species. **CONCLUSION:** Prevention of pseudo-outbreaks requires meticulous use of preventive measures for infection-prone medical procedures.


Between March 1984 and February 1986, ten patients admitted to a spinal cord injury/stroke rehabilitation unit became bacteriuric with a strain of *Serratia marcescens* resistant to ampicillin, cephalothin, cefoxitin, ticarcillin, cotrimoxazole, gentamicin, and tobramycin. All the patients were catheterized, and in most, bacteriuria was asymptomatic. The organism was also recovered from their hospital environment (sinks, toilets, urine-collecting basins). Analysis of total plasmid content of multiresistant isolates revealed the presence of two plasmids (7 kilobase, 25.5 kilobase), not found in aminoglycoside susceptible strains of *Serratia marcescens*. Restriction endonuclease analysis and Southern hybridization (DNA probe: 25.5 kilobase plasmid) verified that these plasmids were identical. The 25.5 kilobase plasmid was purified, introduced by transformation into an Escherichia coli strain C recipient, and was found to mediate resistance to gentamicin and tobramycin. The emergence of multiresistant *Serratia marcescens* coincided with an increase in antibiotic usage on the ward. The reservoir
seemed to be the urinary tracts of asymptomatic catheterized patients and their contaminated hospital environment.


Over a 15-month period 732 babies were admitted to a neonatal unit, and Serratia marcescens was isolated from 153 (21%). In one-fifth (34) a clinical infection (9 major and 25 minor) developed. Major infection was associated with high mortality and morbidity and 2 cases presented after the neonatal period. No environmental reservoir was found. Colonised symptom-free neonates were considered to be the source, with transmission by staff-baby contact despite adequate hand-washing. Overcrowding was believed to be responsible for the difficulties experienced in eradicating this transmission.

Studies of total parenteral nutrition-related infection have incorrectly relied on positive results on culture of the cannula tip to confirm the source. We undertook a prospective study of total parenteral nutrition-related infections in adult patients by obtaining blood from all total parenteral nutrition lines for pour-plate culture twice weekly and culturing intravascular line segments by the technique of Maki. Twelve of 100 courses of total parenteral nutrition (12 percent) in 69 patients resulted in infections--five (5.0 percent) had sepsis, and seven (7.0 percent) had local infection. In five of these 12, pour-plate culture gave positive results (five of 38 pour plates) with counts of 8 colony-forming units per ml (cfu/ml) for Candida tropicalis, and 25 to more than 1,000 for bacterial isolates. In nine of 12, culture of the intravascular line segment gave positive results with more than 50 cfu/ml. Pathogens isolated from intravascular line segments included Staphylococcus epidermidis (three cases), Candida species (three cases), Staphylococcus aureus (two cases), Serratia marcescens (one case) and mixed bacterial pathogens (one case). In contrast, pour-plate culture gave positive results in only seven of 88 uninfected (control) courses (318 pour plates), and culture of intravascular line segments gave positive results in two of 65 uninfected courses (p less than 0.001). No differences existed among patients with and without infection with regard to age, underlying disease, surgery, systemic antibiotic usage, or the presence of other infections. The duration of total parenteral nutrition was longer in courses without infection than in courses with infection (14.7 +/- 9.4 days versus 11.0 +/- 4.0 days; p less than 0.02). In six of 12 courses with infection, the line had been violated compared with 22 of 88 courses without infection (p less than 0.001). T-connectors for the central administration of intralipid were associated with infection (p less than 0.02). The value of routine pour-plate culture was illustrated in three courses in which the positive pour-plate culture results antedated positive blood culture results or line removal.


Health Effects of *Serratia marcescens*

Two clusters of Serratia marcescens in 14 adult cardiac surgical patients occurred over 10 months in an 876-bed teaching hospital. The 14 infections that were studied were as follows: one sternal and five leg incisions, five pneumonias, one bacteremia, one urinary tract infection, and one infected internal defibrillator site. The first cluster included four pneumonias, one urinary tract infection, and one bacteremia. Corrective actions were taken based on outbreak data through no source was identified. No further infections occurred during the following 2 months. The second cluster included one sternal and five leg incisions, an infected internal defibrillator incision site, and one pneumonia. Serratia marcescens was isolated from six electrocardiogram rubber welsh bulbs with sensitivities identical to patient isolates that indicated a common source outbreak in at least the second cluster of infections. Disposable electrocardiogram leads were introduced and the problem was resolved. We conclude that reusable electrocardiogram welsh bulbs are a vector for postoperative infections.

Soloaga et al. 2001. Utility of prolonged incubation and terminal subcultures of blood cultures from immunocompromised patients. *Rev.Argent.Microbiol.* Vol. 33(3): 177-181. The value of blind terminal subcultures (7 and 30 days) and prolonged incubation (30 days) of blood cultures from immunosuppressed patients was analyzed in the Fundacion Favaloro, the Fundacion para la Lucha contra las Enfermedades Neurologicas de la Infancia and the Hospital de Ninos Ricardo Gutierrez. A total of 2707 blood cultures and 369 patients were included (transplantation of solid organs 154, oncohematologic disorders 106 and solid tumors 109). Bact-Alert bottles were incubated at 35 degrees C for 30 days in the Bact-Alert System. Bottles with positive signals were routinely removed, and aliquots of the broth were Gram stained and subcultured aerobically in chocolate agar and Sabouraud agar. A total of 136 bacteremic episodes were obtained. The positivization time of blood cultures was 81.6% at 24 h, 93.3% at 48 h, 94.5% at 72 h and 97.7% within 7 days. Only 3 (2.2%) episodes were positive by blind terminal subcultures and 1 (0.75%) by prolonged incubation (14 days). The median time and range of positivization in hours were 13.8 and 2.2-168, respectively. The microorganisms isolated were coagulase negative staphylococci (n = 24), Klebsiella pneumoniae (n = 22), Staphylococcus aureus (n = 21), Escherichia coli (n = 18), Acinetobacter spp (n = 9), Candida spp (n = 8), Pseudomonas aeruginosa (n = 6), Enterobacter cloacae (n = 5), Stenotrophomonas maltophilia (n = 5), Enterococcus faecalis, Salmonella spp and Capnocytophaga sputigena (n = 2), Enterobacter aerogenes, Enterococcus faecium, Citrobacter diversus, Candida albicans, Klebsiella oxytoca, Chryseomonas luteola, Serratia marcescens, Abiotrophia spp, Campylobacter jejuni, Moraxella catarrhalis, Moraxella urethralis, Neisseria sicca, beta hemolytic group G streptococci, Rhodococcus equi, Micrococcus spp, Cryptococcus neoformans and Streptococcus mitis (n = 1). In our experience, blind terminal subcultures and prolonged incubation of blood cultures from immunosuppressed patients are unnecessary and cost expensive.

In vitro lymphocyte responses to Pseudomonas aeruginosa have been found to be impaired in cystic fibrosis patients with advanced clinical disease. The responses to Klebsiella pneumoniae, Serratia marcescens, and Proteus mirabilis were studied in a similar group of cystic fibrosis patients and normal individuals. Cystic fibrosis patients found to be unresponsive to pseudomonas were also unresponsive to klebsiella, serratia, and proteus. Responsiveness to Staphylococcus aureus was not impaired in cystic fibrosis patients. We postulate that in vitro lymphocyte responses to several gram-negative bacteria require the function of a lymphocyte subpopulation which may be impaired in some cystic fibrosis patients.


Protracted hospital-based epidemics of urinary tract infection and bacteremia due to multiply resistant gram-negative bacilli have become an increasingly common and serious problem. Failure to control such outbreaks stems partly from inability to eradicate a key reservoir, the catheterized bladder. Since eradication of bacteriuria in noncatheterized patients can be achieved with single doses of antimicrobials and correlates with urinary rather than with serum antibiotic concentrations, drugs to which an organism appears resistant by disc-diffusion testing, if excreted in the urine in high concentrations, might also prove useful in eliminating catheter-associated bacteriuria. Alternatively, urinary antiseptics, for which antimicrobial sensitivity testing is not usually done, might be effective. To test this hypothesis we determined the minimum inhibitory concentrations (MICs) of 45 multiply resistant Proteus, Serratia, Klebsiella, and Pseudomonas strains isolated in 13 recent epidemics of nosocomial urinary tract infections against 10 selected antimicrobials and urinary antiseptics, and compared these MICs with expected urinary concentrations of each drug. For each genus tested, MICs for at least two antimicrobials or urinary antiseptics were well below easily achievable urinary drug concentrations. Zone size criteria often predicted which drugs had MICs below achievable urinary levels. Little difference was found between MICs determined in Mueller-Hinton broth and in urine. During an epidemic, simultaneous treatment of all patients with bacteriuria by administration of a urinary antiseptic or an antibiotic that achieves high concentrations in urine, in conjunction with brief catheter removal, might prove useful in controlling any further infection.

Serratia marcescens rarely causes infections in newborn infants. We recently studied an epidemic caused by a multiply-resistant, serotype 014:H12 Serratia marcescens that involved 42 infants. Cutaneous abscesses at previous intravenous infusion sites occurred nine times, usually required surgical drainage, and were the most striking infections during the outbreak. Six infants developed Serratia bacteremia and two died with Serratia meningitis; 34 patients were colonized with Serratia but remained uninfected. An epidemiologic investigation of the 83 infants at risk in the nursery assessed factors predisposing them to colonization or infection with the epidemic organism. Colonization of the throat, umbilicus, gastrointestinal tract, or skin was frequent among infants as was carriage of Serratia on nursery employees' hands. Infected and colonized infants were the most important reservoir for Serratia in the nursery and cross-infection between infants readily occurred. Scalp-vein needles appeared to provide a portal of entry of Serratia in colonized infants, predisposing them to abscess formation and bacteremia.


An outbreak of *S. marcescens* infection occurred among 17 obstetric patients during May-June 1990. Simultaneously 11 newborns were also affected. All the 28 strains were identical in their biochemical characteristics, serotype and phage type as well as antimicrobial susceptibility pattern. The source of infection was traced to a contaminated batch of cream, consisting of 0.5 per cent savlon in carboxy methyl cellulose base, used while doing pelvic examination. The affected patients were treated with appropriate antibiotics and there was no mortality. No further infection was reported after the removal of the contaminated cream.


BACKGROUND: We investigated an outbreak of Serratia marcescens in the neonatal intensive care unit (NICU) and the pediatric intensive care unit (ICU) of the University Children's Hospital Leipzig, Germany. PATIENTS AND METHODS: From September to November 1998 15 patients were infected or colonized by *S. marcescens*. During the outbreak swabs from eye, blood, throat and nose were taken from every patient hospitalized in the ICUs. RESULTS: In 15 cases (14 from the NICU and one from the pediatric ICU) the cultures yielded *S. marcescens*. All strains were investigated by pulsed field gel electrophoresis (PFGE) as well as by polymerase chain reaction (PCR) fingerprinting. Both molecular typing methods revealed corresponding fingerprint patterns in all of the 15 isolates. Typing results of the outbreak-related isolates demonstrated that two epidemic strains of distinct genotypes were associated with cross-infections of a group of five and a group of ten patients, respectively. The three invasive and seven of the colonizing isolates were related genotypically. CONCLUSION: This survey shows that PCR and PFGE are comparable in respect to the discrimination and reproducibility for epidemiological studies of *S. marcescens* strains in nosocomial outbreaks. Genotypic fingerprinting of bacterial isolates is useful and important to limit nosocomial infections. Fingerprinting sources of nosocomial infections can be traced...
both by PFGE and PCR. All patients infected recovered completely and the nosocomial outbreak could be stopped rapidly.

**STINEBRING et al. 1964.** PATTERNS OF INTERFERON APPEARANCE IN MICE INFECTED WITH BACTERIA OR BACTERIAL ENDOTOXIN. *Nature.* Vol. 204712.

During the past decade 44 patients with active endocarditis, defined as valvular infection requiring operative intervention before completion of a planned course of antibiotic therapy, have been treated at Stanford University Medical Center. Twenty-seven patients had infection of a native valve (primary endocarditis) and 17 had infection of a previously implanted intracardiac prosthesis. In 91 per cent of cases urgent valve replacement was dictated by rapid hemodynamic deterioration and in the remainder by recurrent macroemboli or persistent sepsis. Various species of Streptococcus were the most common organisms encountered, followed by Staphylococcus aureus. Unusual bacteria were mostly limited to patients with prosthetic infections; Candida was seen in both groups. Aortic valve replacement was required in 80 per cent of patients. Operative mortality rates were 30 per cent in the group with primary disease and 24 per cent in the group with disease of the prosthetic valve. Most deaths were attributable to multiple system complications generated preoperatively and were unrelated to duration of preoperative antibiotic administration. Five-year survival rates for operative survivors were 68 per cent (primary) and 54 per cent (prosthetic). This experience illustrates the potential therapeutic benefit of operative intervention during active infective endocarditis complicated by severe heart failure or other life-threatening events.

In recent years a significant increase in the incidence of *Serratia marcescens* infections was noted at the Chang Gung Memorial Hospital, Taoyuan, Taiwan. A review of laboratory (1991 to 2002) and infection control (1995 to 2002) records showed the possibility of an extended epidemic of nosocomial urinary tract infections (UTIs) caused by *S. marcescens.* Therefore, in 1998 and 1999, 87 isolates were collected from patients with such infections and examined and another 51 isolates were collected in 2001 and 2002. The patients were mostly elderly or the infections were associated with the use of several invasive devices. *S. marcescens* was usually the only pathogen found in urine cultures in our study. Neither prior infections nor disseminated infections with the organism were observed in these patients. Resistance to most antibiotics except imipenem was noted. Two genotyping methods, pulsed-field gel electrophoresis and infrequent-restriction-site PCR, were used to examine the isolates. A total of 12 genotypes were identified, and 2 predominant genotypes were found in 72 (82.8%) of the 87 isolates derived from all over the hospital. However, 63.9% of the isolates of the two genotypes were from neurology wards. A subsequent intervention by infection control personnel reduced the infection rate greatly. The number and proportion of the two predominant genotypes were significantly reduced among the 51 isolates collected in 2001 and 2002.
Thus, a chronic and long-lasting epidemic of nosocomial UTIs caused by *S. marcescens* was identified and a successful intervention was carried out. Both a cautious review of laboratory and infection control data and an efficient genotyping system are necessary to identify such a cryptic epidemic and further contribute to the quality of patient care.


In the treatment of one male patient with chronic pyelonephritis, complicated with renal stone, the pathological state of the renal inflammatory lesion was determined. The patient had been persistently infected by the same strain of *S. marcescens* for more than a year. When he was treated by several antimicrobial agents, the urinary bacteriological response was well correlated to the MICs of each agent. On the basis of the findings obtained, a new index of local antimicrobial activity was proposed. Analysis of such items as strains appearing after treatment, interval of relapse and the identification of the strains relapsed, were suggestive of the renal inflammatory, and pathological conditions. The clinical response also correlated well with the index. The lesion was considered to be mainly localized in the right lower calyx where a tiny stone existed. This disease is considered curable with effective chemotherapy after withdrawal of the stone. This index should be useful for evaluation of the effectiveness of antimicrobial agents.


Astromicin (ASTM) was administered by intravenous drip infusion (i.v.d.) to 22 patients with chronic complicated urinary tract infections and the clinical efficacy and safety of this drug were evaluated. The overall clinical efficacy rate obtained was 71.4% (excellent 6; moderate 9) of 21 evaluable cases by the UTI committee's criteria. Concerning the response on clinical isolates, the drug was highly effective especially against strains of *Escherichia coli*, indole positive *Proteus* and *Serratia marcescens*. It was not effective, however, against 2 strains of *Pseudomonas aeruginosa*. As for adverse reactions, there was one case which complained of headache on the 3rd day after starting treatment. In this case the drug administration was discontinued at the 5th day. The symptom disappeared within 24 hours without any treatment. No any other adverse reactions were noted. With regard to clinical test values for peripheral blood, liver and renal functions, no abnormality was observed in any of the cases treated with the drug. In conclusion, ASTM was found to be a highly effective and safe drug when administered by intravenous drip infusion in the treatment of chronic complicated urinary tract infections.


In recent decades, *Serratia marcescens* has been established as a cause of infections difficult to treat, and several outbreaks of nosocomial infections have been reported, mostly from the USA. However, *serratia* infections affecting bones and joints are very rare; only a few such cases have previously been reported from Europe. We report 7 patients with orthopaedic infections by *S. marcescens* chiefly of nosocomial origin where
previous antibiotic therapy apparently was a predisposing factor. The clinical course was generally protracted, often requiring repeated surgical interventions. Also, in some cases adequate therapy was considerably delayed as serratia was considered to be a nonpathogenic saprophyte. Multiresistance to antibiotics was a major clinical problem. However, the third generation cephalosporins are often effective against serratia and the aminoglycosides can thus be avoided. The increased use of prophylactic antibiotic therapy in orthopaedic surgery may bring about an increase in the incidence of infections by multiresistant microorganisms in orthopaedic wards.


OBJECTIVES: To investigate and control an outbreak of bloodstream infections (BSIs) caused by *Serratia marcescens* and to identify risk factors for respiratory colonization or infection with *S. marcescens*. DESIGN: Epidemiologic investigation, including review of medical and laboratory records, procedural investigations, pulsed-field gel electrophoresis (PFGE) typing of environmental and patient isolates, statistical study, and recommendation of control measures. PATIENTS AND SETTING: All patients admitted to a 380-bed, secondary-care hospital in Osaka Prefecture, Japan, from July 1999 through June 2000 (study period). RESULTS: Seventy-one patients were colonized or infected with *S. marcescens*; 3 patients who developed primary BSIs on the same ward within 5 days in June 2000 had isolates with indistinguishable PFGE patterns and indwelling intravenous catheters for more than 5 days. On multivariate analysis, among 36 case-patients with positive sputum specimens and 95 control-patients, being bedridden (odds ratio [OR], 15.91; 95% confidence interval [CI95], 4.17-60.77), receiving mechanical ventilation (OR, 7.86; CI95, 2.27-27.16), being older than 80 years (OR, 3.12; CI95, 1.05-9.27), and receiving oral cleaning care (OR, 3.10; CI95, 1-9.58) were significant risk factors. *S. marcescens* was isolated from the fluid tanks of three nebulizers and a liquid soap dispenser. The hospital did not have written infection control standards, and many infection control practices were found to be inadequate (eg, respiratory equipment was used without disinfection between patients). CONCLUSIONS: Poor hospital hygiene and the lack of standard infection control measures contributed to infections hospital-wide. Recommendations to the hospital included adoption of written infection control policies.


Throat secretions (TS) and bronchial secretions aspirated from tracheostomy (TSTA) were cultured at the same time in 9 subjects with long term tracheostomy every two weeks from January, 1990 to December, 1990. Total number of each examination in TS and TSTA were 200 times. Mean number of bacteria isolated by single culture were 2.9 strains in TS and 1.8 strains in TSTA. Isolated bacteria were mainly alpha-Streptococcus (84.8%) and Neisseria (69%) in TS, and *Pseudomonas aeruginosa* (53.5%) and *Serratia marcescens* (30%) in TSTA. Only 20% of *P. aeruginosa* or *S. marcescens* in TSTA were isolated from TS. In 8 cases of 9, *P. aeruginosa* in TSTA were isolated with every time or long term. There were 14 episodes of respiratory infections in 6 cases. *P. aeruginosa* were causative organisms in 7 episodes. It suggests that *P. aeruginosa* tended to colonize in
lower respiratory tracts of the patients with long term tracheostomy and to become causative organisms in respiratory infections.


**Tews et al. 1996.** Bacterial chitobiase structure provides insight into catalytic mechanism and the basis of Tay-Sachs disease. *Nat.Struct.Biol.* Vol. 3(7): 638-648. Chitin, the second most abundant polysaccharide on earth, is degraded by chitinases and chitobiases. The structure of Serratia marcescens chitobiase has been refined at 1.9 Å resolution. The mature protein is folded into four domains and its active site is situated at the C-terminal end of the central (beta alpha)8-barrel. Based on the structure of the complex with the substrate disaccharide chitobiose, we propose an acid-base reaction mechanism, in which only one protein carboxylate acts as catalytic acid, while the nucleophile is the polar acetamido group of the sugar in a substrate-assisted reaction. The structural data lead to the hypothesis that the reaction proceeds with retention of anomeric configuration. The structure allows us to model the catalytic domain of the homologous hexosaminidases to give a structural rationale to pathogenic mutations that underlie Tay-Sachs and Sandhoff disease.


**Theccanat et al. 1991.** Serratia marcescens meningitis. *J.Clin.Microbiol.* Vol. 29(4): 822-823. A case of Serratia marcescens meningitis in a 66-year-old man is reported. The infection occurred 4 weeks after apparently successful otic surgery, and a nidus of infection in the middle ear was established at autopsy. This is the second case of *S. marcescens* meningitis following ear surgery reported in the English-language literature.

**Thibodeaux et al. 2004.** Quantitative comparison of fluoroquinolone therapies of experimental gram-negative bacterial keratitis. *Curr.Eye Res.* Vol. 28(5): 337-342. PURPOSE: To determine the effectiveness of topically applied fluoroquinolones for experimental Pseudomonas or Serratia keratitis. METHODS: Bacteria were injected intrastromally (10(3) colony forming units [CFU]). From 16 to 22 hours post-infection (PI), a single topical drop of moxifloxacin (Vigamox, 0.545%), levofloxacin (Quixin, 0.5%), ofloxacin (Ocuflx, 0.3%) or ciprofloxacin (Ciloxan, 0.3%) was applied every 30 minutes. At 23 hours PI, corneas were cultured quantitatively. RESULTS: For Pseudomonas keratitis, untreated eyes contained 7 log CFU/cornea and antibiotic-treated eyes demonstrated a >; or = 5-log reduction in CFU/cornea (p <; or = 0.0001). Moxifloxacin, levofloxacin, or ciprofloxacin therapies were not significantly different.
from each other (p >; or = 0.67). For Serratia keratitis, untreated eyes contained 7 logCFU/cornea whereas treated eyes had a >; or = 2-log reduction (p <; or = 0.0001). Moxifloxacin therapy proved most effective (p <; or = 0.001). CONCLUSIONS: Overall, moxifloxacin was the most effective of the four fluoroquinolones in reducing CFU/cornea in the rabbit model of gram-negative keratitis.

Late in 1973 at the Nashville Veterans Administration Hospital, an intrusion of Serratia marcescens infections that were resistant to gentamicin sulfate and other antimicrobial agents occurred. This abated somewhat, only to be superseded by another wave of multiply-resistant infections due to Klebsiella pneumoniae beginning in the spring of 1974. Approximately 400 patients had substantial infections with these organisms during the 2 1/4 year period, imposing considerable morbidity and mortality. Due to the serious and lasting impact that these events imposed on patient care in our hospital, we sought explanations for the sequential infectious outbreaks. Both may have arisen because of the same persisting pressures favoring prevalence of multidrug-resistant bacteria. Indirect evidence including the sequential order of the outbreaks, similarity of antibiotograms, transferable multiple drug resistance from Serratia to Klebsiella, and possession of approximately equal molecular weight plasmids supported the notion that the two outbreaks were causally related.


The bacteria Proteus, Serratia, Escherichia and Pseudomonas possess sequences resembling the rheumatoid arthritis susceptibility sequence EQRRAA, but antibodies were elevated only to Proteus in 66 RA patients (P<;0.001) when compared to 61 active ankylosing spondylitis patients and 60 controls.


BACKGROUND: Over a period of 20 years, a total of 1,603 Serratia isolates were recovered from clinical specimens and examined for susceptibility to 29 antimicrobial drugs using the Bauer-Kirby agar disk diffusion test. Serratia marcescens was recovered most frequently (n = 1,409), followed by S. liquefaciens (n = 172); other Serratia species were scarce. During the 2-decade observation period there occurred 35 putative episodes/clusters of nosocomial cross-infection and 1 pseudo-outbreak due to *S. marcescens*, but none due to *S. liquefaciens*. METHODS: The antimicrobial
susceptibility data for *S. marcescens* and *S. liquefaciens* were subdivided into two observation periods: I = 1980-1993, and II = 1993-1999. The crude data (series A) obtained for *S. marcescens* were corrected in two ways: by the omission of repetitive patient isolates (series B) and the additional removal of outbreak isolates except for index case isolates (series C).

**RESULTS AND CONCLUSIONS:** Comparison of data obtained in series IC and IIC disclosed an increase in the susceptibility of *S. marcescens* to ampicillin + sulbactam, cefotaxime, chloramphenicol, doxycycline, fosfomycin, gentamicin, piperacillin, piperacillin + tazobactam, timentin and tobramycin during observation period II. Conversely, there was a decrease in susceptibility to ciprofloxacin, nalidixic acid and trovafloxacin, and slightly diminished susceptibility to norfloxacin and ofloxacin during observation period II as compared with the previous period. The crude data obtained for *S. liquefaciens* required no correction, as there were only a few repeat isolates. There was an increase in susceptibility to ampicillin, ampicillin + sulbactam, cefuroxime, doxycycline, fosfomycin, nitrofurantoin and polymyxin B (clear inhibition zones). However, there was an inexplicable decrease in susceptibility to piperacillin + tazobactam. Cocarde growth around polymyxin B disks was noted with 55.8% of the *S. marcescens* isolates as compared with 6.8% of the *S. liquefaciens* isolates. Slime around fluoroquinolone inhibition zones was produced by 83.4% of the *S. marcescens* isolates. Slime production around carbapenem inhibition zones was noted with 52% of the *S. liquefaciens* isolates, but with only a single isolate of *S. marcescens*.


The epidemiological efficacy of 0.02 per cent solution of prodigiosan, a bacterial polysaccharide was used for the treatment of children in an area with acute respiratory infections, such as influenza and parainfluenza. The drug was administered intranasally by means of a dosing sprayer in the amounts of 0.2 ml once in 4 days for 4 months. Among the children treated with prodigiosan the rate of the acute respiratory viral infections was 2 times lower and the average duration of the disease was 2.4 times lower as compared to the control group. After 4 months of the drug use the average value of the “skin autoflora”; test was much lower than that in the control group which testified to an increase in the non-specific immunobiological reactivity of the children under the effect of prodigiosan.


We report an outbreak of *Serratia marcescens* infection in a special-care baby unit Contract No. IOM-2794-04-001
(SCBU) of a university-affiliated community hospital in the United Arab Emirates. The outbreak involved 36 infants and lasted for 20 weeks. Seven of the colonized infants developed invasive illnesses in the form of bacteraemia (four cases), bacteraemic meningitis (two) and clinical sepsis (one). Three other term infants had purulent conjunctivitis. There were five deaths with an overall mortality of 14%. *S. marcescens* was cultured from airflow samples from the air conditioning (AC) which was the reservoir of infection in this outbreak. Elimination of the nosocomial source and outbreak containment were eventually achieved by specialized robotic cleaning of the entire AC duct system of the SCBU. Strict adherence to the infection control policies was reinforced to prevent transmission of cross-infection.


Electrocuting insect traps (EIT) are popular devices frequently used by homeowners and food handlers attempting to localize the control of flying insects, including the ubiquitous house fly (Musca domestica L.). The traps contain a visual attractant and a high-voltage metal grid. Upon contact with the grids, the insects are disintegrated by the high voltage. As part of a systematic evaluation of EITs and their role in infectious disease spread, we quantitated spread of bacteria and a bacterial virus during electrocution of house flies. We loaded flies with *Serratia marcescens* or with the Escherichia coli phage PhiX174 and placed sprayed or fed flies into a room containing an EIT. While flies were being electrocuted, liberated particles and bacteria were assayed via agar plates or via air filtration samplers. Sprayed flies released one of every 10,000 of the added bacteria or viruses, and fed flies released one of every 1,000,000 of the consumed bacteria or viruses. Results of our studies suggest EITs could play a role in the spread of infectious disease agents, but the potential is influenced by the insect's route of contamination.


Arbitrary primed polymerase chain reaction (AP PCR) assays are suited for the discrimination of isolates of all clinically relevant bacterial species. In a hospital setting, this type of DNA amplification test can be used for the timely detection of ongoing nosocomial outbreaks. For rapid screening of isolates of many medically important bacterial species, including *Acinetobacter baumannii*, *Staphylococcus aureus*, *Serratia marcescens*, *Xanthomonas maltophilia* and others, a single AP PCR assay can be used as a primary typing screen for genetic relatedness. In combination with epidemiological data, AP PCR testing is particularly useful for identifying true outbreaks caused by a single strain.

Between January 1996 and May 1997, a four-fold increased rate of isolation of Serratia marcescens was observed amongst patients admitted to the surgical Intensive Care Unit (SICU) of the Leiden University Medical Center compared to the preceding years. Random amplification of polymorphic DNA showed the involvement of genotypically distinct strains, implicating multiple different sources. After improvement of hygienic measures the frequency of isolation of *S. marcescens* returned to baseline. A case-control study was performed to assess patient-related risk factors for acquisition of *S. marcescens*. Nineteen cases and 38 controls were included. Hospital- and SICU-stay were significantly longer in case patients than in controls. By univariate analysis, statistically significant differences were found in body weight, the duration of mechanical ventilatory support, the cumulative use of antimicrobial agents, the use of aminoglycosides, parenteral nutrition and tube feeding. The sum of the number of days per invasive device (deep intravenous lines, arterial lines, wound drains and urinary catheters) was higher in cases than in controls (P = 0.08). Categorically, a cumulative number of device-days >; 25 was a statistically significant risk factor for acquisition of *S. marcescens*. Multivariable logistic regression analysis showed that body weight, parenteral feeding and mechanical ventilation were independent predictors of acquisition of *S. marcescens*. As transmission of *S. marcescens* appears to be by the hands of personnel, the identified risk factors may act by necessitating an increased frequency and intensity of direct contacts.


An outbreak of Serratia marcescens was seen on a pulmonary ward from September 1999 until September 2000. During this period, there were two distinct clusters of *S. marcescens* isolation. In the first episode, September-October 1999, *S. marcescens* isolates with the same resistance pattern were isolated in 10 patients. PFGE (pulsed-field gel electrophoresis) following digestion with SpeI confirmed that these isolates were identical. After an initial decline in the number of isolates, the incidence rose again in March 2000. The resistance pattern of these isolates differed from that in 1999. PFGE showed that most of the isolates in 2000 were identical and had replaced the previous strain (strain 1). In the second episode, January-August 2000, 26 patients were colonized with the subsequent strain (strain 2). Three of these patients had serious clinical problems due to *S. marcescens*, two had bacteraemia and one empyema. In September 2000, strain 2 was also detected in stock solutions for inhalation therapy. After discontinuation of the use of stock solutions and emphasizing hygienic measures, the outbreak resolved. The majority (68%) of the patients positive for *S. marcescens* suffered from COPD (chronic obstructive pulmonary disease). PFGE results suggest that several COPD patients were carriers of the same strain of *S. marcescens* for a prolonged time. Re-admission of these patients could have lead to re-introduction of the epidemic strains.

During a 9-month period when amikacin was the sole aminoglycoside used clinically in a hospital in Santiago, Chile, resistance to amikacin and other antibiotics was encountered in 42 strains of the family Enterobacteriaceae, including Escherichia coli, Klebsiella pneumoniae, Citrobacter freundii, Enterobacter cloacae, Serratia marcescens, and Serratia liquefaciens. Amikacin resistance was transferable by conjugation and carried by IncM plasmids ranging in size from ca. 48.4 to 58.1 kilobase pairs. The plasmids had ca. 70 to 80% of their structure in common, as judged after digestion with restriction endonucleases. The resistance was mediated by a 6′ aminoglycoside acetyltransferase.

We conclude that selective pressure has favored the dissemination of a wide-host-range amikacin resistance plasmid and its derivatives.

van Ogtrop et al. 1997. Serratia marcescens infections in neonatal departments: description of an outbreak and review of the literature. J.Hosp.Infect. Vol. 36(2): 95-103. An outbreak of colonization and infection with Serratia marcescens occurred in a neonatal intensive care unit (NICU). *S. marcescens* was isolated from five preterm infants (gestational age 25-30 weeks). Two infants developed septicaemia, which were both fatal, and one infant (the presumed index case) had conjunctivitis due to *S. marcescens*. Two infants were colonized without clinical signs of infection. All infants were treated with antibiotic regimens including ciprofloxacin and gentamicin. The DNA fingerprints of isolates were determined by enterobacterial repetitive intergenic consensus primers by the polymerase chain reaction. This showed that a single strain had spread in the NICU. An extensive investigation pointed to an infant born from a mother with an intra-uterine infection after prolonged rupture of foetal membranes as a presumed source of the outbreak. A reservoir, other than the infected or colonized infants and their immediate vicinity, was not found, with the sole exception of the waste jar of a Na+/K(+)—analysis apparatus. Containment of the outbreak was achieved by closure of the NICU for new admissions, strict hygienic measures and cohort nursing of the infected and colonized infants. It was considered especially important to handle the infants with gloves, since frequent hand carriage of staff with *S. marcescens* was found when gloves were not used.

Vandenbroucke-Grauls et al. 1993. An outbreak of Serratia marcescens traced to a contaminated bronchoscope. J.Hosp.Infect. Vol. 23(4): 263-270. An outbreak of colonization and infection with Serratia marcescens in a surgical Intensive Care Unit is described. A case-control study pointed to a bronchoscope as the source of the epidemic strain, and cultures of washing effluent of the incriminated bronchoscope yielded *S. marcescens*. Discontinuation of the use of the instrument and the implementation of recommendations for future use of bronchoscopes ended the outbreak.

Vergheese et al. 1983. Bacterial pneumonia in the elderly. Medicine (Baltimore). Vol. 62(5): 271-285. Bacterial pneumonia in the elderly is common, and causes more morbidity and mortality than in the younger adult. As patients live longer with more underlying disease and more iatrogenic disease, the incidence of nosocomial pneumonia will probably rise. Adequate sterilization of inhalation therapy equipment can reduce the risk of gram-negative nosocomial pneumonia. Methods to prevent colonization and microaspiration need to be investigated. The development of a gram-negative vaccine using Salmonella RE or E.
coli J5 mutant would augur well for the future. Most important, the elderly patient with pneumonia should be managed promptly and aggressively in an attempt to determine the specific etiology of the pneumonia. The practice of antibiotic “shotgunning”; of the elderly patient is to be avoided. Transtracheal aspiration or sheathed bronchoscopy can be performed if the patient is not able to produce sputum, or Gram stain is difficult to interpret. Morbidity and mortality can be reduced by early appropriate antibiotic therapy directed by Gram stain.


OBJECTIVE: To investigate and control a biphasic outbreak of Serratia marcescens in a neonatal intensive care unit (NICU). DESIGN: Epidemiological and laboratory investigation of the outbreak. SETTING: The NICU of the 1,470-bed teaching hospital of the University “Federico II,” Naples, Italy. PATIENTS: The outbreak involved 56 cases of colonization by S marcescens over a 15-month period, with two epidemic peaks of 6 and 3 months, respectively. Fourteen (25%) of the 56 colonized infants developed clinical infections, 50% of which were major (sepsis, meningitis, or pneumonia). METHODS: Epidemiological and microbiological investigations, analysis of macrorestriction pattern of genomic DNA through pulsed-field gel electrophoresis (PFGE) of clinical and environmental isolates, and institution of infection control measures. RESULTS: Analysis of macrorestriction patterns of genomic DNA by PFGE demonstrated that the vast majority of S marcescens isolates, including three environmental strains isolated from two handwashing disinfectants and the hands of a nurse, were of the same clonal type. The successful control of the outbreak was achieved through cohorting of noncolonized infants, isolation of S marcescens-infected and -colonized infants, and an intense educational program that emphasized the need for adherence to glove use and handwashing policies. The NICU remained open to new admissions. CONCLUSIONS: Outbreaks caused by S marcescens are very difficult to eradicate. An infection control program that includes molecular typing of microorganisms and the proper dissemination among staff members of the typing results is likely to be very effective in reducing NICU-acquired infections and in controlling outbreaks caused by S marcescens, as well as other multiresistant bacteria.


From 16 July through 27 September 1988, seven cases of nosocomial Serratia marcescens bacteremia occurred in a cardiac care unit. In all seven case patients, S. marcescens was isolated from blood cultures. Two of the seven had other microorganisms identified in the blood culture in which S. marcescens was recovered; one had Enterobacter cloacae, and one had Klebsiella pneumoniae. A case-control study was conducted to identify risk factors for bloodstream infection. Case patients were more likely than controls to have been exposed to an intra-aortic balloon pump pressure.
transducer (7 of 7 versus 6 of 21; $P = 0.001$) and to a pulmonary arterial pressure transducer (7 of 7 versus 8 of 21; $P = 0.005$). Cultures of in-use and in-storage transducers revealed bacterial contamination of the pressure-sensitive membranes of the transducers. *S. marcescens* blood culture isolates obtained from five of the seven case patients, as well as six *S. marcescens* isolates from cultured transducers, belonged to serotypes Oundetermined:H1 and Oundetermined:H18. E. cloacae isolates from one case patient and from two stored and two in-use transducers had identical antimicrobial susceptibility patterns. Review of cardiac care unit disinfection practices revealed that the transducers were not processed with high-level disinfection or sterilization between patient uses. We concluded that the transducers had served as reservoirs for this outbreak of bloodstream infection. Because intra-aortic balloon pumps with pressure transducers are being used more frequently in the management of critically ill cardiac patients, their role as infectious reservoirs should be considered in the investigation of nosocomial bacteremia.


An outbreak of Serratia marcescens bacteremia detected in the intensive care unit (ICU) of a tertiary care center on the last days of October, 1985, is described. The rate of primary *S. marcescens* nosocomial bacteremia during the pre-epidemic period (January-September 1985) was 6.25 per cent; and for the post-epidemic period compared with the epidemic were significantly different ($p <$ 0.0001). The outbreak strains belonged to the biotype A8b, which has been endemic in our hospital. The responsible organism exhibited an unusual antimicrobial resistance pattern associated to the presence of a specific plasmid (greater than 50 kilobases), which showed similar fragments after restriction endonuclease digestion. No specific risk factors were identified in the case-control study. The outbreak was probably related to a greater influx of infected patients, resulting in less careful infection control measures, due to the emergency situation which suffered the hospital after the earthquakes in 1985. The unusual high rate of blood isolation of *S. marcescens* at the ICU was the first sign of the outbreak. The prompt reinforcement of infection control policies facilitated its resolution.


Serratia marcescens has been reported as an organism which can cause rapidly spreading, antibiotic resistant nosocomial colonization and disease. We report here an outbreak of
colonization and disease due to S.marcescens involving 53 infants admitted to the Neonatal Intensive Care Unit (NICU) of the Uberlandia Federal University Hospital, Brazil, between December, 1997, and April, 1998. Thirty-eight infants were colonized without clinical signs of infection and 15 infants had clinical disease. Five infants developed septicemia (4 cases were fatal, including the presumed index case). Seven infants developed conjunctivitis, 1 developed both sepsis and conjunctivitis, 1 infant developed otitis, and 1 infant had a urinary tract infection. On univariate analysis, independent risk factors for S. marcescens clinical disease were: low birth weight (<;1,500g), incubator care, use of carbapenems, duration of hospitalization (>;/=7days), low Apgar score, and prematurity. All the isolates of S.marcescens showed the same antimicrobial susceptibility profile. The causative strains were resistant to oxyiminocephalosporins due to their production of extended-spectrum beta-lactamases. Cultures from the hands of 12 NICU health care professionals (HCWs), soap samples, ventilator reservoirs, and work and incubator surfaces failed to identify a reservoir of S.marcescens, but positive cultures were found in half of the sink drains. Containment of the outbreak was achieved by closure of the NICU new admissions, employment of strict hygienic measures, and careful nursing care of the infected and colonized infants. Rapid organism identification and initiation of control measures are important in containing such an epidemic at an early stage.

During a 12 month period, the Waikato Hospital Newborn Intensive Care Unit experienced an epidemic of Serratia marcescens infection. Seventeen serious infections occurred, resulting in three deaths. A further 15 cases of minor infection were also noted. Although no point source of introduction was found, gut colonization proved to be the most important reservoir for nosocomial spread of the organism. At the peak of the outbreak, a 95% incidence of rectal colonization with S. marcescens was observed. Eradication was achieved within a 4 month period using cohort isolation of affected infants.

Streptococcus equi causes equine strangles, a purulent lymphadenopathy of the head and neck. An avirulent, non-encapsulated strain (Pinnacle) has been used widely in North America as an intranasal vaccine. The aim of the study was to create a specific mutation of the hyaluronate synthase (hasA) gene in Pinnacle to permanently abolish the production of capsule and provide an easily recognisable genetic marker. An internal fragment of hasA was generated by PCR and cloned into pTW100 (Microscience, UK). An encapsulated revertant of Pinnacle was then transformed with the recombinant plasmid by electroporation and cultured under conditions to promote homologous recombination. Among 90 spectinomycin resistant transformants observed, one non-mucoid (non-encapsulated) spectinomycin resistant colony was detected. The presence of plasmid sequence within the hasA gene was confirmed by the PCR. After six passages in antibiotic-free medium, four non-mucoid spectinomycin sensitive colonies were found. Sequence analysis of one of these clones, designated Pinnacle HasNeg, revealed loss of
the 3’ end of the hasA and the 5’ end of the hasB genes. This deletion mutant should serve as a useful candidate to replace Pinnacle since it cannot revert to a mucoid phenotype and can be distinguished genetically from wild type strains.


We sought to characterize the molecular epidemiology of gram-negative bacilli (GNB) causing infections in infants and associated with carriage on nurses’ hands after hand hygiene was performed. From March 2001 to January 2003, GNB caused 192 (34%) of 562 hospital-acquired infections in the 2 participating neonatal intensive care units (NICUs) and were isolated from the hands of 45 (38%) of 119 nurses. Five species—Klebsiella pneumoniae, Escherichia coli, Pseudomonas aeruginosa, Serratia marcescens and Enterobacter cloacae, all of which were typed by pulsed-field gel electrophoresis—caused 169 (88%) of 192 of GNB infections. Overall, 58% of infections were caused by unique strains not cultured from other infants or nurses, and 31% of infections were part of unrecognized molecular clusters. In contrast, only 9% of strains that caused infections were cultured from nurses’ hands. These data suggest that practices in addition to hand hygiene are needed to prevent horizontal transmission of GNB in the NICU.


p-Nitrophenylglycerol (PNPG) effectively inhibits swarming of the enterobacterium Proteus mirabilis. The underlying mechanism of inhibition is unclear. We have now found that both PNPG also inhibits motility and swarming in another enterobacterium, Serratia marcescens. While the peak promoter activities of the flagellar master operon (flhDCSm), the flagellin structural gene (hagSm) and the nuclease gene (nucASm) in *S. marcescens* increased with increasing PNPG concentration, the expression of these genes was delayed in accordance with the reduced growth rate. As the quorum-sensing system is involved in the regulation of swarming in *S. marcescens*, we also examined the effect of PNPG on the production of quorum-sensing signal molecules and found that their expression was delayed with a reduced level. PNPG, therefore, had a pleiotropic effect on all aspects of *S. marcescens* physiology relating to swarming. The underlying molecular mechanism remains to be elucidated.


Serratia marcescens SS-1 and its SpnR-defective isogenic mutant, SMdeltaR, produced an extracellular surfactant able to decrease surface tension of water from 72 to 37 dyne cm(-1) (SMdeltaR strain) and to 45 dyne cm(-1) (SS-1 strain). The biosurfactant also emulsified kerosene and diesel with a maximum emulsion index of 77% (diesel and kerosene) for the SMdeltaR strain, and 72% (kerosene) and 40% (diesel) for the SS-1 strain.
strain. Deletion of spnR gene appeared to enhance biosurfactant production. Model simulations suggest that biosurfactant production by the two strains was growth-associated. The SMdeltaR strain had a yield coefficient of 22-32% g dry cell(-1), which is 32-50% higher than that of the SS-1 strain.


Between 2 February and 16 April 1985, an outbreak of *Serratia marcescens* infection involving 10 male patients occurred in a cardiac surgery unit. All the patients had surgical wound infection, five also had osteomyelitis (four sternal, one costal), and another had peritonitis secondary to peritoneal dialysis. Three patients had concomitant bacteremia. All *Serratia* strains isolated produced a cherry-red pigment, and all had the same biochemical and antibiotic susceptibility pattern. An intensive search for the origin of the outbreak was initially unsuccessful, and it proved impossible to isolate *S. marcescens* from cultures of numerous samples taken from hospital personnel and from the environment. The fact that all patients were male and had been shaved for surgery by the same team of barbers led us to investigate the shaving procedures. We finally isolated a strain of pigmented *S. marcescens*, corresponding to that involved in the outbreak, from samples taken from the hands and equipment of the barbers. After suitable action had been taken, the epidemic terminated.

An in vitro model was developed to investigate the migration of a variety of bacteria of different characteristics through a gel system in the presence or absence of a wide range of polymer monofilament threads. The bacteria were unable to migrate through the gel from the point of inoculation in the absence of a solid substrate. Migration occurred along all thread types tested, including those used as IUCD marker tails and the extent of bacterial migration appeared to be determined primarily by the motility of the microorganisms. The implications of these findings in relation to the development of pelvic infections in IUCD wearers is discussed.


Parenteral nutrition therapy can achieve an anabolic state in patients who are unable to maintain normal nitrogen balance; however, it may be associated with infectious complications. Infections may be related to contamination of the cannula and the cannula wound, of the infusate, or of other parts of the parenteral nutrition system. A variety of microorganisms has been associated with these infections. The exact mechanisms that
initiate cannula-related infection are poorly understood. Susceptibility of the host, the method and site of cannula insertion, colonization of parenteral nutrition cannulas, use of parenteral nutrition systems for multiple purposes, cannula material, and other factors may all play some role. Controlling infections depend on many factors, including quality control processes to ensure sterility of parenteral nutrition solutions, attention to aseptic technique during cannula insertion, procedures to prevent in-use contamination, proper care of the cannula insertion site, and proper management of other parts of the parenteral nutrition system. In addition, infectious complications appear to be reduced by an organized team that follows infection control protocols. Many facets of parenteral nutrition therapy are based on data from uncontrolled clinical investigations. Well-designed, controlled clinical trials may provide data that will further minimize the risks associated with parenteral nutrition therapy.

Three commercial chicken hatcheries were sampled for environmental bacteria. Isolated bacteria were tested for resistance to commercial preparations of quaternary ammonia, phenolic, and glutaraldehyde liquid disinfectants. Bacterial isolates were exposed to several disinfectant dilutions bracketing the dilutions recommended by the manufacturer for 5-, 10-, and 15-min exposure periods before subculturing to broth medium. Approximately 8% of the isolates from two of three hatcheries were resistant to disinfectant concentrations at and above the manufacturers recommended dilution and time of exposure. Resistant bacteria included Serratia marcescens, Bacillus cereus, Bacillus thuringiensis, Bacillus subtilis, Enterococcus faecalis, Enterococcus faecium, Pseudomonas stutzeri, and Entrobacter agglomerans.

We showed previously that large numbers of T lymphocytes accumulate within a few days in the kidneys of rats with ascending pyelonephritis induced with Escherichia coli or Pseudomonas aeruginosa. CD4+ T cells propagated from the lesions exhibited MHC-restricted proliferative responses to formalin-fixed bacteria of the species used to induce infection. In the present study we investigated further the nature of the antigens responsible for the T cell proliferation and studied the ability of different bacterial strains and species to produce proliferative responses. We found that heat-killed bacteria were more stimulatory than formalin-fixed bacteria, and that soluble supernatants of heat-killed organism were also effective. The stimulatory effects of supernatants were destroyed by trypsin and the responses were MHC-restricted. Twelve different E. coli strains, with or without characteristics of uropathogenicity in humans, were all highly stimulatory to T cells derived from a kidney infected with a single E. coli strain. Strains of Klebsiella pneumoniae, Enterobacter aerogenes, and Serratia marcescens--species of Enterobacteriaceae closely related to E. coli--were also stimulatory, whereas more distantly related bacteria--Proteus, Morganella, and P. aeruginosa--were not. T cells propagated from kidneys infected with P. aeruginosa responded to supernatants of this organism, but not to E. coli supernatants. We conclude that a protein antigen (or antigens) shared by strains of E. coli and related Enterobacteriaceae, but not by other gram-
negative bacteria, produce MHC-restricted proliferative responses of CD4+ T cells that infiltrate rat kidneys infected with E. coli.


Cross-infection by contaminated equipment is a potential hazard associated with conscious sedation with nitrous oxide and oxygen. Nosocomial infections have occasionally been linked with the use of unsterile inhalation devices; microbial contamination of sterile nasal hoods routinely occurs during administration of nitrous oxide; and in vitro experiments indicate that subsequent use of contaminated nasal masks may lead to aspiration of microorganisms. Although the incidence of respiratory disease after such contamination is unknown, it is clear that disinfection of the nitrous oxide apparatus between patients is desirable. A simple cleaning method involving alkaline glutaraldehyde is described that provides adequate disinfection of the rubber goods used in the administration of gas. Superiority of this technique over previously recommended cleaning methods is shown.

Numerous broad-spectrum beta-lactam antimicrobial agents have been introduced into medical practice since 1985. Although several of these compounds have advanced, infectious disease therapy resistances to them has also emerged world-wide. In 1997, a Japanese 22 medical center investigation was initiated to assess the continued utility of these agents (oxacillin or piperacillin, ceftazidime, cefepime, cefpirome, cefoperazone/sulbactam [C/S], imipenem). The participating medical centers represented a wide geographic distribution, and a common protocol and reagents were applied. Three control strains and a set of challenge organisms were provided to participant centers. Etest (AB BIODISK, Solna, Sweden) strips were used in concurrent tests of these organisms and a qualitative determination of participant skills in the identification of resistant and susceptible phenotypes was established. The quantitative controls demonstrated 97.7-99.2% of MIC values within established QC limits, and the qualitative (susceptibility category) controls documented a 97.3% agreement of participant results with that of reference values (1,320 total results). Only 0.2% of values were false-susceptible errors. After the participant quality was assured, a total of 2,015 clinical strains were tested (10 strains from 10 different organism groups including methicillin-susceptible Staphylococcus aureus and coagulase-negative staphylococci [CoNS], Escherichia coli, Klebsiella spp., Citrobacter freundii, Enterobacter spp., indole-positive
Proteae, Serratia spp., Acinetobacter spp., and Pseudomonas aeruginosa). The staphylococci were uniformly susceptible to all drugs tested except ceftazidime (MIC90, 24 micrograms/ml) that had a potency six- to 12-fold less than either cefepime or cefpirome. Only 3.7 and 45.1% of S. aureus and CoNS were susceptible to ceftazidime, respectively. Among E. coli and Klebsiella spp. the rank order of antimicrobial spectrum was imipenem = “fourth-generation”; cephalosporins >; ceftazidime >; C/S >; piperacillin. Possible extended spectrum beta-lactamase phenotypes were identified in 2.9-8.6% of these isolates. Isolates of C. freundii, Enterobacter spp., Proteae, and Serratia spp. that were resistant to ceftazidime and piperacillin remained susceptible to imipenem (0.0-4.5% resistance) and cefepime (0.0-5.0%). Acinetobacters were inhibited best by C/S (99.5% susceptible) and least susceptible to piperacillin (MIC90, >; 256 micrograms/ml; 21.7% susceptible) activity. P. aeruginosa isolates were most susceptible to cefepime (83.6%) and this zwitterionic cephalosporin also had the lowest level of resistance (9.1% of MICs at >; or = 32 micrograms/ml). Several multi-resistant organisms were identified in participant medical centers including S. marcescens strains resistant to cefepime, imipenem, or both observed in six hospitals. Clonal spread was documented in two medical centers; one hospital having two distinct epidemic clusters. Also a multi-resistant E. cloacae was found in two patients in the same hospital. Evaluations of carbapenem resistance in four species discovered only two strains (in same hospital) among 40 P. aeruginosa isolates (5.0%) with a metallo-enzyme, with nearly all of the remaining strains inhibited by an Ambler Class C enzyme inhibitor (BRL42715) indicating a hyperproduction of a chromosomal cephalosporinase. These results indicate that most newer beta-lactams remain widely useable in medical centers in Japan, but emerging often clonal, resistances have occurred. The overall rank order of antimicrobial spectrum against all ten tested bacterial groups favors the “fourth-generation”; cephalosporin, cefepime (96.4% susceptible) as an equal to imipenem (95.9%) >; C/S (90.9%) = cefpirome (90.0%) >; ceftazidime (75.1%) = penicillins, either oxacillin or piperacillin (76.4%).

Yamasaki et al. 1984. A clinical survey of bacteria isolated from urine specimens of patients with various urological disease. Hinyokika Kiyo. Vol. 30(12): 1899-1909. We have clinically surveyed the distribution and disk sensitivity of bacterial strains obtained from urine of patients with various urological disease at our department during three (1975-1977) and four (1980-1983) years. Escherichia coli was the most frequently isolated (29.4%) from the outpatients, followed by Staphylococcus epidermidis (17.5%), Pseudomonas cepacia (11.2%) and Serratia marcescens (11.2%). Pseudomonas cepacia was the most frequently isolated (28.0%) from the inpatients, followed by Staphylococcus epidermidis (16.3%) and Serratia marcescens (15.9%). Pseudomonas cepacia which has been increasing was first isolated in 1977 and Serratia marcescens in 1976. They have become the main bacteria causing infections in our hospital. Pseudomonas cepacia was frequently isolated after postoperative prophylactic chemotherapy and Serratia marcescens in the late period of admission. The majority of Pseudomonas cepacia was resistant to all agents except chloramphenicol and doxycycline. Serratia marcescens was also resistant except to gentamicin and doxycycline. In Escherichia coli species, resistant strains increased gradually but they have good sensitivity to gentamicin, dibekacin, colistin and doxycycline. Staphylococcus
epidermidis isolated from outpatients had good sensitivity to all agents but increased in incidence of resistant strains isolated from inpatients.


We have detected Campylobacter species which are now recognized as major pathogens of acute diarrheal disease in humans using polymerase chain reaction (PCR) and a nonradioactive labeled DNA probe. Diagnosis of Campylobacter enteritis without doing culture from stool samples is of great benefit in the laboratory. Two oligonucleotide primers (20 mer) complementary to a unique sequence of the DNA encoding ribosomal RNA (rRNA) of Campylobacter jejuni for PCR were synthesized by solid-phase phosphoramidite method. Amplified target DNA of 275 base pairs could be resolved on ethidium bromide-stained gels, and hybridized with an oligodeoxynucleotide probe (28 mer) conjugated to alkaline phosphatase. In identification experiments, it was shown that the nonradioactive probe was hybridized to clinical strains of C. jejuni (104), C. coli (5), C. laridis (5), C. hyointestinalis (1) and C. fetus subsp. fetus (1) with an accuracy of 99-100%, while it was not for Helicobacter pylori. Further, there was no evidence of amplification in strains of K. pneumoniae, *S. marcescens* and E. coli. Using direct detection to stool specimens, this method could be performed in C. jejuni in 39 of 43 culture-positive specimens (91%), and in 19 of 141 culture-negative specimens (13.5%), respectively. The results of this comparative study suggested that the DNA probe assay became a rapid and reliable technique to confirm culture of Campylobacter species.


We applied infrequent-restriction-site PCR (IRS-PCR) to the investigation of an outbreak caused by 23 isolates of Acinetobacter baumannii in an intensive care unit from November 1996 to May 1997 and a pseudoepidemic caused by 16 isolates of Serratia marcescens in a delivery room from May to September 1996. In the epidemiologic investigation of the outbreak caused by A. baumannii, environmental sampling and screening of all health care workers revealed the same species from the Y piece of a mechanical ventilator and the hands of two health care personnel. IRS-PCR showed that all outbreak-related strains were genotypically identical and that three strains from surveillance cultures were also identical to the outbreak-related strains. In a pseudoepidemic caused by *S. marcescens*, IRS-PCR identified two different genotypes, and among them one genotype was predominant (15 of 16 [93.8%] isolates). Extensive surveillance failed to find any source of *S. marcescens*. Validation of the result of IRS-PCR by comparison with that of field inversion gel electrophoresis (FIGE) showed that they were completely concordant. These results suggest that IRS-PCR is comparable to FIGE for molecular epidemiologic studies. In addition, IRS-PCR was less laborious and less time-consuming than FIGE. To our knowledge, this is the first report of the application of IRS-PCR to A. baumannii and *S. marcescens*.

From July 1996 to June 1997, 22 adult patients with Serratia marcescens bacteremia were retrospectively studied at China Medical College Hospital. All patients had severe underlying disease, most commonly diabetes mellitus. Eighteen (82%) patients had nosocomial infection. Clinical syndromes included primary bacteremia (68%), pneumonia (14%), urinary tract infection (9%), suppurative thrombophlebitis (5%) and surgical wound infection (5%). Twelve patients had central venous catheters in place at the onset of bacteremia, but only one case met the definition of catheter-related infection. In 14 (64%) patients, portal of entry of S. marcescens infection was unknown. Five (23%) patients had concurrent polymicrobial bacteremia. The overall mortality rate was 50% (11/22). Seven (32%) of the 22 patients died of S. marcescens bacteremia. All isolates were resistant to ampicillin and cephalothin and susceptible to imipenem. Ninety-five percent of strains were susceptible to moxalactam, 68% to amikacin, 55% to ceftazidime, 45% to aztreonam, 32% to ceftriaxone, 27% to gentamicin, 18% to cefoperazone and cefotaxime, and 9% to piperacillin. MICs of various antibiotics demonstrated that ciprofloxacin and imipenem had good activities against S. marcescens, with MIC90 of 0.19 microg/mL and 1.0 microg/mL, respectively. Due to increasing multidrug resistance, choosing appropriate antimicrobial agents such as moxalactam, imipenem, and ciprofloxacin should be highly recommended for the treatment of S. marcescens infections.


Agrobacterium radiobacter is a gram-negative bacillus, which is recognized as an emerging opportunistic human pathogen. To our knowledge, there have been only 25 cases of A. radiobacter bacteremia reported. In most of these, A. radiobacter was associated with long-term indwelling plastic central venous catheters. We describe a 78-year-old man who had a history of chronic obstructive pulmonary disease with long-term use of a corticosteroid. He was admitted to the China Medical College Hospital with pneumonia caused by Serratia marcescens. His general condition gradually improved after initiation of appropriate treatment. Unfortunately, he developed A. radiobacter bacteremia while hospitalized in the medical intensive care unit. With the onset of this infection, the patient had a high fever, leukocytosis, raised C-reactive protein level, and positive blood cultures for A. radiobacter. A central venous catheter-related infection was suspected because of redness and localized tenderness at the catheter site. The patient gradually recovered after removal of the catheter and appropriate antimicrobial treatment with latamoxef 1.5 g intravenously every 8 hours for 10 days.


A case-control study was conducted on an epidemic of bacteremia and meningitis caused by Serratia marcescens in the neonatal intensive care unit and special care nursery of a general hospital in Mexico City, Mexico. A 19.9% incidence of bacteremia and meningitis was recorded in contrast to 1.4% and 3.7% during preepidemic and post-
epidemic periods; a 69% mortality rate was observed. Peripheral IV catheters and the use of mixed IV fluids prepared in the wards were the major risk factors (P less than 0.001). Rectal and nasopharyngeal cultures were positive in 68% of asymptomatic neonates and hand cultures were positive in 16.7% of personnel. Strains were resistant to all aminoglycosides and broad-spectrum penicillins, and belonged to the A5/8 biogroup. Containment of this outbreak was difficult because of failure to identify colonized infants early in the epidemic and because of persistent carriage of S marcescens by personnel. Comparisons between this hospital and tertiary care centers in Mexico suggest that in developing countries nosocomial infections could be of greater magnitude in secondary than in tertiary level centers.


During attempts to create a realistic model of fatal bacteremia due to Pseudomonas aeruginosa during immunosuppression, it was found that the invasive as well as the disseminated phase of infection could be mimicked by gentle instillation of 10(8) colony-forming units of P. aeruginosa into the intact conjunctival sac of agranulocytic rabbits. Within 48 hr animals developed conjunctivits leading to severe necrotizing vasculitis and fatal bacteremia. Twelve of 26 strains from patients with P. aeruginosa infections were virulent, causing death in 50%--100% of animals. Nine (75%) of 12 isolates from blood but only two (15%) of 13 isolates from sputum and urine were highly lethal. Neither proteolytic enzyme production nor serum resistance alone accounted for virulence. No infection developed in animals and normal leukocyte counts or in neutropenic animals given Escherichia coli, Klebsiella pneumoniae, or non-aeruginosa pseudomonads. A rare vasculitic lesion was observed in animals inoculated with Serratia marcescens. This model, which illustrates the distinctive features of P. aeruginosa infection, is so simple and reproducible that it should be useful for evaluation of the efficacy of drugs and immunization against Pseudomonas in the compromised host.


Trospectomycin (TSP; U-63366F) is a novel spectinomycin (SP) analogue with broad-spectrum antibacterial activity. The in vitro activity of the analogue was compared to that of SP against approximately 400 bacterial isolates. The in vivo activity of the compound was assessed using experimental infection models for both Gram-positive and Gram-negative facultative bacteria. The preliminary human pharmacokinetics of TSP were evaluated following single-dose i.v. or i.m. administration. TSP was more active in vitro than SP (2 to 32-fold) against strains of numerous bacterial species, including staphylococci, streptococci, Haemophilus influenzae, Branhamella catarrhalis, Neisseria gonorrhoeae, Proteus spp., Bacteroides spp., Gardnerella vaginalis and Chlamydia trachomatis. The activity of TSP for most species of the family Enterobacteriaceae was comparable to that of SP. TSP was more active than SP (2 to 32-fold) in curing experimental infections due to streptococci, Salmonella typhi, Serratia marcescens, Klebsiella pneumoniae and Haemophilus influenzae. TSP was well-absorbed following
both i.v. and i.m. administration. Pharmacokinetic analysis of microbiological assay data for the 1000 mg dose yielded the following mean values for the i.v. and i.m. routes, respectively: Cmax = 81.2, 28.7 micrograms/ml; serum half-life = 2.2, 2.2 h; Tmax = 25, 75 min; and AUC = 156.6, 116.2 h micrograms/ml. Pharmacokinetic analysis of assay data derived using the more sensitive HPLC assay revealed the biphasic nature of trospectomycin elimination, highlighted by a short apparent serum half-life (2.2 h) and a prolonged tissue half-life (approximately 36 h). TSP inhibits a variety of clinically important organisms, including agents of sexually transmitted diseases and pelvic inflammatory disease, and demonstrates favourable pharmacokinetic properties. (ABSTRACT TRUNCATED AT 250 WORDS)