HEALTH EFFECTS OF
PROJECT SHAD
BIOLOGICAL AGENT:

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[E. COLI]

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SPECIAL NOTE ON PSYCHOGENIC SEQUELAE OF PERCEIVED EXPOSURE TO BIOCHEMICAL WARFARE AGENTS

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

*Escherichia coli* [*E. coli*] is a Gram-negative rod-shaped facultatively anaerobic bacterium of the *Enterobacteriaceae* family whose members are sometimes referred to simply as enteric bacteria. Discovered in 1884 by Theodor Escherich, *E. coli* and its strains are probably the most widely studied of microorganisms. The species is well known as part of the normal human intestinal microflora, where its presence is typically harmless or benignly symbiotic. It has abundant uses in the laboratory, lately finding a new role as a useful cloning host in recombinant DNA technology. In Project SHAD, it was released atmospherically as a simulant to study biological decay rates; the strain is unspecified.

Many strains of *E. coli*, along with non-intestinal exposure to “commensal” bacteria from the intestines, can be harmful, even deadly, however. The microbiology and molecular pathology of the microbe’s virulence is an ongoing subject of intensive ongoing study. The effects of one factor in *E. coli* virulence, the endotoxin liposaccharide (LPS), is an area of particular note as it has, in some studies, shown the potential for long-term effects related to autoimmunity and fever regulation.

Currently, classification of the various infectious strains of *E. coli* is based on a mixture of several considerations – areas of colonization, clinical effects, serotype, and determinants of virulence.

For strains of *E. coli* with intraintestinal pathogenicity, the following are the most noted classes of strains and the pathogenic activity with which they are associated:

**Enterotoxigenic *E. coli* (ETEC)** - contaminates foods and water causing diarrhea.

**Enterohemorrhagic (EHEC) strain** -- synthesizes verotoxin (VT) (shiga-like toxin), which damage the intestinal lining, causing hemorrhagic colitis, with its uniquely severe bloody diarrhea. (CFSAN 2003)

**Enteroinvasive *E. coli* (EIEC)**: -- creates manifestations similar to the dysentery caused by *Shigella*, but does not synthesize shiga toxin

**Enteropathogenic *E. coli* (EPEC)** -- damages intestines by adhering to and altering the cellular structure of the lining

**Enteroaggregative *E. coli* (EAEC)** -- also adheres to the intestinal lining, and produces a toxin

**Enteroadherent *E. coli* (EAEC)** – colonizes and adheres to the small intestine and causes “traveler's diarrhea”.

The relatively new strain *E. coli* O157:H7 has been of special interest over the past two decades. The Centers for Disease Control (CDC) devotes a special notice to that strain. Strains that are pathogenic outside the intestinal tracts are called extra intestinal or uropathogenic *E. coli*.

*E. coli* is also a common nosocomial infection risk.
Definitive diagnosis is by culturing the body fluid of the infected area.

The effects of \textit{E. coli} are well-characterized. Acute food poisoning, manifested as nausea and diarrhea is the most commonly noted effect. “Traveler’s diarrhea” and the Mexican water-borne “Montezuma’s revenge” diarrhea are two very familiar examples. These conditions are usually self-limiting and last a few days.

Areas of greater concern in terms of seriousness and duration of effects include infections of the urinary tract and the abdomen and related complications. The spectrum of urinary tract infections (UTIs) ranges from asymptomatic bacteriuria to cystitis to acute and chronic pyelonephritis and renal abscess. The kidney infection pyelonephritis may lead to temporary or chronic renal insufficiency.

Although urinary tract infections are more commonly seen in women (where they can be chronic but not serious to overall life and health), they can also occur in men. They are often nosocomial, related to the use of catheters and other invasive/manipulative procedures. Acute and chronic prostatitis, the latter being difficult to treat, are possible manifestations and consequences of \textit{E. coli} UTIs.

Pathogenic \textit{E. coli} may progress into other systems from the area of colonization. This spread can happen through the blood as bacteremia, and then proceed into sepsis and septic shock. Blood dissemination can lead to infection in other areas of the host. In UTIs, \textit{E. coli} have been known to proceed to the kidney and induce pyelonephritis. This kidney infection can lead to acute or chronic renal challenge. Severe, complicated pyelonephritis is mainly seen among alcoholic, diabetic, and immunocompromised patients.

\textit{E. coli} pneumonia is usually encountered also as a secondary infection of UTI. Rarely is it known to have arisen from direct exposure, though there have been cases of community-acquired \textit{E. coli} pneumonia.

The nervous system may be directly invaded. Meningitis in neonates is a well-observed effect of \textit{E. coli} activity; meningitis in adults is, however, far rarer and usually connected with neuroinvasive procedures. (One case study, nevertheless, reports aspergillar sinusitis being associated with recurrent \textit{E. coli} meningitis episodes.)

The appearance of strain O157:H7 (EHEC) since about 1982 has given rise to a new concern over \textit{E. coli} exposure: namely the complications hemolytic uremic syndrome (HUS) and thrombocytopenic purpura (TTP). Strain O157:H7 infection usually involves a gastrointestinal episode of severe diarrhea with blood in the stool. But in about 10\% of these cases, in a matter of days or weeks, endothelial damage further induces microvascular lesions with platelet-fibrin hyaline microthrombi that occlude arterioles and capillaries. The aggregation of the platelets then causes consumptive thrombocytopenia.
In the HUS manifestation, the health effects are primarily limited to the kidneys with some possible central nervous system effects. TTP's effects are primarily of the central nervous system type; they typically include seizures arising from hypertensive encephalopathy. End stage failure and death are possible consequences of HUS; the overall death rate from HUS is 5-15%. Untreated TTP can have a mortality rate of 95%. Symptoms may include thrombocytopenia, fever, renal insufficiency, neurological deficit, microangiopathic hemolytic anemia (MAHA), headache, fatigue/malaise, altered mental status, and hemiplegia.

A lesser chronic complication of EHEC strain infection is the risk of irritable bowel syndrome after uncomplicated gastrointestinal infection.

Intra-abdominal effects tend to follow puncturing of the peritoneum. These effects, which often are polymicrobial, can lead to abscesses which are usually accompanied by a low-grade fever, and may proceed to septic shock, pylephlebitis of the portal vein, liver abscess, as well as cholecystitis and cholangitis. Partial obstructions in the biliary system can be a greater risk for infection than full obstructions. Peritonitis is a common consequence of \textit{E. coli} penetration of the peritoneum.

Other noted \textit{E. coli} infection effects include endophthalmitis (usually associated with diabetic patients suffering from UTI or pyelonephritis), osteomyelitis, endocarditis, septic arthritis, and skin, soft tissue and surgical wound injuries.

Special attention is called to the accumulation of study of lipopolysaccharide (LPS) endotoxin activity and possible associations it may have with long-term effects on the immune and immune regulatory systems. (LPS forms part of the outer cell wall of Gram-negative bacteria, including non-pathogenic laboratory strains like K-12.) Animal tests suggest that neonate exposure can lead to a diminution of fever response to a subsequent adult challenge from LPS. LPS has also been shown to have possible associations with the initiation of autoimmune joint disorders and in the induction of autoimmune diabetes.

Studies or reports of clinical psychogenic health effects resulting specifically from exposure to \textit{E. coli} have not been found. 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.”

Preventive measures center on proper hygiene. No standardized treatment for \textit{E. coli} infections exist; treatment is site and severity specific. Infection management usually includes intravenous hydration. The employment of antimicrobials in strain O157:H7 infection are not recommended because they may worsen the condition. Under development is the use of neutralizing human antitoxin antibodies which appear to have a protective role in HUS.
II. MICROBE & BACKGROUND

A few years after Louis Pasteur identified the association of bacteria and human disease, the celebrated Austrian pediatrician Theodor Escherich began examining the human body for microorganisms. In human feces from the colon, he found a rod-shaped microbe that he named *Bacterium coli*. It was later to be renamed for its discoverer as *Escherichia coli* (Bettelheim 1986).

*E. coli* is a Gram-negative fecal coliform member of the *Enterobacteriaceae* family (a class sometimes referred to as enteric bacteria). The most known association of *E. coli* with humans has been relatively benign, as a "commensal" inhabitant of the intestines. In these anaerobic conditions, this facultative anaerobe resorts to fermentation processes, producing gasses and acids from glucose (Go 2004; Todar 2002).

Called a "laboratory workhorse", *E. coli* has useful applications outside the body especially because it easily flourishes on inexpensive media containing little more than glucose (Kaper 2004). The nonpathogenic strain K-12 is widely used in activities ranging from classroom demonstrations of basic biological principles through sophisticated experiments in recombinant biology to industrial-scale batch cultivation for recombinant proteins production (Kaper 2004).

*E. coli* strains can also be significantly pathogenic, however. Pathogenic strains are classified according to such characteristics such as serotype, areas of colonization, clinical effects and determinants of virulence. Virulence factors include proteins (e.g. invasins, adhesins), toxins, siderophores, surface features (e.g. lipopolysaccharides, antigens), and other properties that enable the microbe to evade or undermine the host's defenses, to injure or invade the host's tissues and cells, or to bring about a noxious inflammatory response (Johnson 2003; Todar 2002).
Identification, and subsequent definitive diagnosis of \textit{E. coli} infection, is done by culturing the body fluids of the infected area on selective media, and, in some cases it includes serologic testing of antigens (CDC 1994).

The genomes of both the non-pathogenic strain \textit{E. coli} K-12 and the pathogenic strain \textit{E. coli} O157:H7 have been sequenced and published. This will contribute to genetically identifying virulence and in developing more effective therapies (Khan A, et al. 2003) (See https://asap.ahabs.wisc.edu/annotation/php/logon.php.)

The strain used in Project SHAD, where it was employed as simulant to evaluate environmental factors affecting biological agent degradation, has not been specified.
IV. HEALTH EFFECTS

The effects of *E. coli* are well-characterized. Its infectious strains are chiefly associated with the following conditions, among others:

Enteric (Gastrointestinal) infections  
Urinary tract infections (UTIs) (and complications)  
Intra-abdominal infections  
Bacterial meningitis

Additionally, there are significant risks that colonization by the pathogen may result, directly or secondarily, in bloodstream invasion or infection via bacteremia and septicemia, resulting in systemic dissemination and possibly fatal septic shock (Sarf et al 2003; Go 2004). High mortality (42%) has been associated with this kind of bacterial infection. Risk factors in such spread reflect a tendency for nosocomial acquisition of bacterial bloodstream infection. Undergoing hemodialysis has a relative risk factor of 208.7 in the induction of bacterial bloodstream infection. Advanced age, diabetes, cancer, lung disease, and alcoholism are other significant associations (Laupland 2004).

As further developed in this section, long-term effects are often associated with urinary tract infection, where recurrences occur and infections are often complex. Permanent renal deficiency and chronic prostatitis have been observed. Strain O157:H7 infections present long term risks in the form of two potentially deadly or permanently incapacitating conditions. Recurrent meningitis as a consequence of infection has also been observed, while the lipopolysaccharide endotoxin of *E. coli* may present possible long-term risks to the immune system.

**Gastrointestinal**

Acute food poisoning, manifested as nausea and diarrhea is the most commonly noted effect. “Traveler’s diarrhea” and the Mexican water-borne “Montezuma’s revenge” diarrhea are two very familiar examples resulting from encounters with enterotoxigenic *E. coli* (ETEC)-contaminated foods and water.

The enterohemorrhagic (EHEC) strain *E. coli* O157:H7 (discovered in 1982) has been of special interest in the past two decades, earning dedicated web pages at both the Centers for Disease Control (CDC) and the U.S. Food & Drug Administration (FDA) websites (CDC 1994; CFSAN 2003). Most noted for contaminating raw/undercooked ground beef, it can also affect other foods, such as alfalfa sprouts and unpasteurized fruit juices. It synthesizes verotoxin (VT) (also known as shiga-like toxin), which damage the intestinal lining, causing hemorrhagic colitis with its uniquely severe bloody diarrhea. (CFSAN 2003).

The four other classes of *E. coli* that are causative agents in GI diseases, with their effects, are (Go, 2004; Todar 2002):
Enteroinvasive *E. coli* (EIEC): causes symptoms similar to dysentery caused by *Shigella*, but do not synthesize shiga toxin

Enteropathogenic *E. coli* (EPEC): damage intestines by adhering and altering the cellular structure of the lining

Enteroaggregative *E. coli* (EAggEC): also adheres to the intestinal lining, and produces a toxin

Enteroadherent *E. coli* (EAEC): specifically colonizes the small intestine and is another cause of traveler's diarrhea

In most cases, these gastrointestinal conditions last for several days and are self-limiting.

**Complications of EHEC: HUS/TTP**

In about 10% of strain O157:H7 (EHEC) infections, in a matter of days or weeks following the GI effects, endothelial damage from the shiga-like toxin induces microvascular lesions with platelet-fibrin hyaline microthrombi that occlude arterioles and capillaries. The aggregation of the platelets causes consumptive thrombocytopenia (Go 2004; Garg et al. 2003; Dundas and Todd 2000; Karch. 2001). This process helps induce hemolytic-uremic syndrome (HUS) or thrombocytopenic purpura (TTP). HUS can also be a complication of non-gastrointestinal infections, such as UTIs; in such instances, they are not associated with prodromal diarrhea (Go 2004; Chiurchiu, et al. 2003)

Effects caused by HUS are primarily limited to the kidneys, ultimately leading to acute renal failure; they may also lead to permanent kidney failure (end stage renal failure) and death. The overall death rate from HUS is 5-15%, while 50% of those afflicted will have some degree of lasting renal impairment (Thorpe. 2004). A lesser chronic complication is the risk of irritable bowel syndrome after subsequent uncomplicated gastrointestinal infection. Additionally, the central nervous system may also be affected. In TTP, the central nervous system is major primary target, causing hypertensive encephalopathy that leads to seizures (Go 2004). Untreated TTP can have a mortality rate as high as 95%. Symptoms may include thrombocytopenia, fever, renal insufficiency, neurological deficit, microangiopathic hemolytic anemia (MAHA), headache, fatigue/malaise, altered mental status, and hemiplegia (Symantec 2001; Go 2004).

About 15% of children with gastrointestinal infections from strain O157:H7 may develop hemolytic uremic syndrome (Chiurchiu, et al. 2003).

**Urogenital**

The urinary tract is a common site of infection by *E. coli*. Uncomplicated urinary tract infections (UTIs) are caused by *E. coli* in greater than 90% of cases. They can often be nosocomial, arising from the use of catheters and other invasive or manipulative procedures (Johnson. 2003; Nassar. 2000; Go, 2004).
A great concern in regard to this type of *E. coli* infection is the possibility of its progressing into other systems. This can happen through the blood as bacteremia, and then proceed to sepsis and septic shock. A death rate in a mostly elderly hospitalized population was 16% for those experiencing such complications. Pneumonia is usually seen, however, as a secondary infection of UTI, rarely as a result from direct exposure, although there is a report of *E. coli* occurring in community acquired pneumonia (Bansal, et al 2004)

*E. coli* in urinary tract infections have been known to proceed to the kidney and induce pyelonephritis and damage renal tissue. Urinary tract infections (UTIs) can thus range from asymptomatic bacteriuria through cystitis to acute and chronic pyelonephritis, and renal abscess (Go 2004; Johnson 1991). Severe, complicated pyelonephritis is mainly seen among alcoholic, diabetic, and immunocompromised patients (Merrier. 2003; Egland 2002).

Urinary tract infections are more commonly seen in women where they can be chronic but not serious to overall life and health. In men, the infections are often associated with prostatic hypertrophy. The resulting chronic bacterial prostatitis can be either acute or chronic, the latter condition being difficult to manage (Nassar 2000; Go, 2004).

One invasive procedure, transrectal biopsy of the prostate, appears to have resulted in multiple fatal *E. coli* infections of the prostate (Hasegawa et al 2002).

**Intra-abdominal infections**

Punctures to the viscera will cause intra-abdominal infections, particularly if it releases the contents of the bowels where *E. coli* resides. Intra-abdominal infections are often polymicrobial and can lead to abscesses. Another source of intra-abdominal infections are obstructions, which allow bacteria to accumulate (Ayadi, et al 1998; Hasegawa et al 2002).

Characteristics of intra-abdominal infections caused by *E. coli* include intra-abdominal abscess, which is usually accompanied by a low-grade fever, and may proceed to septic shock; pylephlebitis of the portal vein; liver abscess; cholecystitis and cholangitis. Obstruction of biliary system can enhance the risk of an *E. coli* infection. Partial obstruction increases the risk of infection, bactibilia, and bacteremia. Partial obstructions in the biliary system have been shown to be a greater risk than full obstructions (Go 2004).

Peritonitis is a common consequence of *E. coli* penetration of the peritoneum (Go 2004).

**Other Systems**

In neonates, meningitis is frequently observed, but in adults, it is far less common, and usually connected with neuroinvasive procedures. One adult case history, however, tells
of aspergillar sinusitis being associated with recurrent *E. coli* meningitis episodes (Passeron, et al 2004).

Other effects noted are endophthalmitis (associated with diabetic patients suffering from UTI or pyelonephritis), osteomyelitis, bone loss, endocarditis, septic arthritis, and skin, soft tissue and surgical wound injuries (Johnson et al. 2003; Briggs, et al 2004; Jiang et al. 2002; Go 2004; Todar 2002.).

**Lipopolysaccharide (LPS)**

All Gram-negative bacteria, whether non-pathogenic *E. coli* laboratory strains like K-12 or highly pathogenic species, have a lipopolysaccharide (LPS) component as part of their outer cell wall. Lipopolysaccharide endotoxins elicit varying physiological and immunological reactions. Neonate animal tests suggest that early exposure to LPS can lead to a decrease in the central nervous system-mediated fever response to subsequent adult LPS challenge. LPS has also been shown to be possibly associated with the initiation of autoimmune joint disorders, the induction of autoimmune diabetes and bone resorption (Todor 2000; Balasa B, et al. 2000; Jiang et al. 2002).
V. PSYCHOGENIC EFFECTS

Studies or reports of clinical psychogenic health effects resulting specifically from exposure to *E. coli* have not been found. General psychogenic effects of perceived exposure to agents of biological (and chemical) warfare are examined in the supplement under this contract “Psychogenic Effects of Perceived Exposure to Biochemical Warfare Agents.”
VI. TREATMENT/PREVENTION

Preventive measures center on proper hygiene. Making sure food is fully cooked, proper washing of hands before and after high risk activity are the messages for the general public and for health care professionals (Go 2004; Todar 2002).

There is no standardized treatment for *E. coli* infections; treatment is site and severity specific. The infection management of strain O157:H7 infection includes intravenous hydration, and contraindicates antimotility agents. (Thorpe 2004; Tzipori et al. 2004) The use of antimicrobials are not recommended in most EHEC cases, because they may be harmful and/or or worsen the condition. Currently being developed is the use of neutralizing human antitoxin antibodies, which seem to have a protective role in HUS. (Tzipori et al. 2004)
VII. SECONDARY SOURCE INFORMATION

Information on *E. coli* infections is widespread and voluminous.

Project SHAD "Glossary" information is cursory but addresses most key issue outcomes (Project 112 2004):

*E. coli* is one of the most common bacteria in man’s environment. Most animals and humans have it in their digestive systems, where it does no harm. *E. coli* can cause severe stomach cramps, diarrhea, bloody stools, and kidney failure. Some who are exposed to *E. coli* may experience mild irritation of the stomach and intestines that goes away without treatment, while for others the bacteria can be deadly.
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 style or substance are strictly those of the original source. This bibliography contains supplemental material on the subject in addition to references that are specifically cited in the text above.}


Sclerosing peritonitis (SP) is a severe life-threatening condition for patients undergoing continuous ambulatory peritoneal dialysis (CAPD). This report reviews our experience and that reported in the literature concerning the prevalence of SP in CAPD patients, predisposing factors, and in particular, the role of peritonitis, its clinical presentation, diagnosis, treatment, and prevention. A total of 1,288 end-stage renal disease (ESRD) patients entered our peritoneal dialysis (PD) program between September 1977 and September 1997, seven of whom (0.54%) developed SP. The annual incidence of SP was 0.37 per 1,000 patient years, male-to-female ratio was 2.5 (M/F:5/2), mean age was 39+/−16 (median, 37; range, 23 to 61) years, and the median duration on CAPD was 62 (range, 12 to 144) months. Five patients were on CAPD for > or =4 years and two for less than 4 years before they were diagnosed with SP. All SP patients presented with clinical symptoms suggestive of intestinal obstruction, and five patients had decreased solute or fluid removal and had to increase the daily dialysate volume (3/7) or the tonicity of the fluid (4.25%) (3/7) or to combine a regular hemodialysis (HD) session with CAPD (2/7). There was a mean weight loss of 5+/−6 (median, 2; range, 0 to 18) kg. All patients had an episode of peritonitis at a mean time of 2+/−1 (median, 1; range, 1 to 3) months before the diagnosis of SP. The peritonitis was due to Staphylococcus aureus in four and Staphylococcus epidermidis, fungi, and Escherichia coli in one each. The definitive diagnosis of SP was established by laparotomy in four patients or postmortem examination in one patient, while in the remaining two there was no surgical confirmation; however, we believe the diagnosis was extremely likely because of the presence of clinical and radiologic criteria for SP. After the diagnosis of SP, all patients had their catheters removed, CAPD was discontinued permanently, and they were transferred to HD. Although there are isolated case reports of successful outcomes after surgical intervention, especially in patients in whom a peritoneal "cocoon" is related to severe peritonitis, usually the prognosis following surgery is poor. Treatment with immunosuppressive agents has been reported to be beneficial in the treatment of SP, although this has not been confirmed by all investigators. Among our SP patients, five (72%) died of sepsis (3/5) in a mean period of 10+/−5 (median, 9; range, 6 to 17) months after the diagnosis of SP and two are still alive on HD. SP is a rare but serious complication of CAPD. Severe peritonitis, especially in patients on dialysis for more than
4 years, may lead to SP. As the prevalence of SP increases in patients on long-term CAPD, early detection is important because of the high morbidity and mortality associated with this condition.


Isogenic Escherichia coli strains, differing in their expression of K1 antigen and ColV plasmid, were studied for their ability to produce disease. Newborn rats were used to test the ability of these strains to colonize the intestine and to produce bacteremia and meningitis; adult rats were used to test their ability to produce urinary tract infection. Colonization of intestine and bladder by K1+ ColV+ *E. coli* was associated with rapid induction of bacteremia and higher mortalities compared with colonization with K1+ ColV- strains. These findings suggest that the ColV plasmid could play a role in the pathogenesis of human infections.


The case of a pregnant woman (16th week) needing an amniocentesis is reported. She rapidly developed a septic shock. Despite vaginal delivery, curettage and antibiotic therapy, the patient deteriorated with the onset of an acute respiratory distress syndrome and a typical disseminated intravascular coagulation. Bacteriological data showed positive blood cultures to Escherichia coli. Amniotic liquid was positive to the same *E. coli*. Cultures obtained from instruments, disinfectant solutions and gel used during the procedure were negative. On the contrary, amniotic and fetal cultures were positive to *E. coli* and *Clostridium perfringens*. She died 2 days later. The incidence of septic shock following amniocentesis is very low but we report the first case of fatal sepsis and multiorgan failure, due to *E. coli* and *C. perfringens*. The mechanisms of infection are discussed: contamination from the instruments, systemic dissemination of bacteria coming from an asymptomatic intra-amniotic infection, and inoculation of the placenta with a needle passing through the bowel.


To test the role of the microbial product lipopolysaccharide (LPS) as an environmental trigger of autoimmune diabetes, we employed transgenic (tg) BDC2.5/NOD mice that bear an islet-specific CD4(+) T cell repertoire (>95%), but do not develop the spontaneous diabetes that typifies the NOD (nonobese diabetic) strain. LPS administration provoked diabetes in BDC2.5/NOD mice by their 16th week of age. However, LPS administration in NOD mice did not accelerate their diabetes. This finding indicates that the frequency of islet-specific T cells influences LPS-mediated diabetes. Furthermore, in vitro LPS-cultured splenocytes from BDC2.5/NOD and BDC2.5-microMT (B-cell-deficient) mice effectively transferred diabetes into immunodeficient
NOD-scid/scid mice but not immunosufficient NOD mice. Therefore, B lymphocytes are not required for LPS-provoked autoimmune diabetes. Flow cytometric analysis then revealed that LPS-stimulation in vitro induced the expression of an IL-2 receptor (CD25) on CD4 T cells; this indicates that the activation of islet-specific T cells is a prerequisite to eliciting diabetes in this situation. Overall, these results point to microbial LPS as an etiopathogenic agent of autoimmune diabetes.

**Bansal S, et al 2004** Clinical and bacteriological profile of community acquired pneumonia in Shimla, Himachal Pradesh. *Indian J Chest Dis Allied Sci.* 46(1):17-22. BACKGROUND: Community acquired pneumonia (CAP) is a common clinical problem. The present study was designed to evaluate the clinical and bacteriological profile of CAP in Shimla. METHODS: Seventy patients with community acquired pneumonia were enrolled in this study. In all the patients blood culture, sputum culture, pleural fluid culture (if available) and serological studies for the detection of Mycoplasma pneumoniae specific IgM antibodies by enzyme linked immunosorbent assay (ELISA) were done. RESULTS: Of the 70 patients, 53 (75.6%) had an identifiable aetiology with 12 patients having evidence of mixed infection. No organisms could be isolated in 17 patients inspite of using serological methods for Mycoplasma pneumoniae, invasive procedures like bronchoscopic aspirations in addition to the conventional methods like sputum culture, blood culture and pleural fluid culture. The most frequent pathogen was Streptococcus pneumoniae (n = 19; 35.8%) followed by Klebsiella pneumoniae (n = 12; 22%), Staphylococcus aureus in (n=9; 17%), Mycoplasma pneumoniae (n = 8; 15%), Escherichia Coli (n = 6; 11%), beta-haemolytic streptococci (n = 4; 7.5%) and other Gram-negative bacilli (n = 5, 9%). CONCLUSION: Age, smoking and underlying co-morbid conditions specially chronic obstructive pulmonary disease (COPD) were significantly associated with the development of CAP (p < 0.01).

**Bettelheim 1986.** Commemoration of the publication 100 years ago of the papers by Dr. Th. Escherich in which are described for the first time the organisms that bear his name. *Zentralbl Bakteriol Mikrobiol Hyg [A].* 261(3):255-65.

The centenary of the publication by Dr. Th. Escherich of his papers on the colonization of the intestines of neonates by bacteria is commemorated. His papers are reviewed and discussed from the point of view of current knowledge. The organisms described by him as Bacterium coli commune and now known as Escherichia coli are particularly discussed and their role as enteropathogens assessed. Current work on these organisms is contrasted with studies on them over the last 100 years.

**Blot et al 2003** Absence of excess mortality in critically ill patients with nosocomial Escherichia coli bacteremia. *Infect Control Hosp Epidemiol.* 24(12):912-5. OBJECTIVE: To evaluate excess mortality in critically ill patients with Escherichia coli bacteremia after adjustment for severity of illness. DESIGN: Retrospective (1992-2000), pairwise-matched (1:2), risk-adjusted cohort study. SETTING: Fifty-four-bed ICU in a university hospital including a medical and surgical ICU, a unit for care after cardiac surgery, and a burns unit. PATIENTS: ICU patients with nosocomial *E. coli* bacteremia (defined as cases; n = 64) and control-patients without nosocomial bloodstream infection (n = 128).
METHODS: Case-patients were matched with control-patients on the basis of the Acute Physiology and Chronic Health Evaluation (APACHE) II system: an equal APACHE II score (+/- 2 points) and diagnostic category. In addition, control-patients were required to have an ICU stay at least as long as that of the respective case-patients prior to onset of the bacteremia. RESULTS: The overall rate of appropriate antibiotic therapy in patients with *E. coli* bacteremia was high (93%) and such therapy was initiated soon after onset of the bacteremia (0.6 +/- 1.0 day). ICU patients with *E. coli* bacteremia had more acute renal failure. No differences were noted between case-patients and control-patients in incidence of acute respiratory failure, hemodynamic instability, or age. No differences were observed in length of mechanical ventilation or length of ICU stay. In-hospital mortality rates for cases and controls were not different (43.8% and 45.3%, respectively; P = .959). CONCLUSION: After adjustment for disease severity and acute illness and in the presence of adequate antibiotic therapy, no excess mortality was found in ICU patients with *E. coli* bacteremia.


Fever is an integral part of the host’s defense to infection that is orchestrated by the brain. A reduced febrile response is associated with reduced survival. Consequently, we have asked if early life immune exposure will alter febrile and neurochemical responses to immune stress in adulthood. Fourteen-day-old neonatal male rats were given Escherichia coli lipopolysaccharide (LPS) that caused either fever or hypothermia depending on ambient temperature. Control rats were given pyrogen-free saline. Regardless of the presence of neonatal fever, adult animals that had been neonatally exposed to LPS displayed attenuated fevers in response to intraperitoneal LPS but unaltered responses to intraperitoneal interleukin 1beta or intracerebroventricular prostaglandin E(2). The characteristic reduction in activity that accompanies fever was unaltered, however, as a function of neonatal LPS exposure. Treatment of neonates with an antigenically dissimilar LPS (Salmonella enteritidis) was equally effective in reducing adult responses to *E. coli* LPS, indicating an alteration in the innate immune response. In adults treated as neonates with LPS, basal levels of hypothalamic cyclooxygenase 2 (COX-2), determined by semiquantitative Western blot analysis, were significantly elevated compared with controls. In addition, whereas adult controls responded to LPS with the expected induction of COX-2, adults pretreated neonatally with LPS responded to LPS with a reduction in COX-2. Thus, neonatal LPS can alter CNS-mediated inflammatory responses in adult rats.


Twenty-three women with non-obstructive acute pyelonephritis due to Escherichia coli were prospectively studied during 880 patient months, mean observation time 38 months. Each patient had between 1 and 4 new episodes of *E. coli* bacteriuria during the study period (altogether 49 recurrences). All *E. coli* isolates were typed by biochemical fingerprinting. Twenty-six of the recurrences were caused by an *E. coli* strain identical to one of those that had previously appeared. Sixteen of these infections were caused by a strain identical to the one that gave rise to the original acute pyelonephritis. Ten further
recurrences were due to an *E. coli* strain that had previously caused symptomatic or asymptomatic bacteriuria during the observation period. Despite appropriate treatment and repeated negative urine cultures post-treatment, infections caused by identical *E. coli* strains occurred up to 35 months after the initial episode of acute pyelonephritis. We suggest that the infecting *E. coli* strain may survive in the fecal flora or is harboured in the patient's surroundings, and after recolonizing the patient, these strains may give rise to further urinary tract infections.


In order to assess the clinical features, aetiology, treatment and outcome of post-neurosurgical and post-traumatic Gram-negative bacillary meningitis (GNBM) we performed a retrospective review of all adult patients admitted to the Department of Neurosurgery who had Gram-negative bacilli cultured from cerebrospinal fluid (CSF) following a neurosurgical procedure or traumatic head/spinal injury. During the 12 y of the review 33 patients had CSF isolates of Gram-negative bacilli that were thought to be significant. The median patient age was 47 y (range 22-77 y) and 21 (64%) were male. Klebsiella pneumoniae, Enterobacter cloacae and Escherichia coli were the most common isolates. Minimal inhibitory concentrations (MIC) measured for half the patients' isolates resulted in 5 regimen changes, including 2 patients with E. cloacae meningitis in whom cephalosporin susceptibility decreased during cephalosporin treatment. Our recommended initial treatment was intravenous ceftriaxone and amikacin, subsequently tailored by susceptibility results; approximately half the patients remained on the antibiotics they started and half were changed to an alternate regimen, most often a carbapenem. Five patients (15%) died, 1 dying after cure of his GNBM. There were no failures in those who received more than 12 d of appropriate treatment: treatment for at least 14 d after the last positive CSF culture guaranteed cure. Initial ceftriaxone and amikacin subsequently changing to susceptibility driven alternatives, often a carbapenem, resulted in cure of 85% of our patients with GNBM.

**Cadwgan et al 2002** Three years experience of adults admitted to hospital in north-east Scotland with *E. coli* O157. *Scott Med J.* 47(5): 112-4. To describe the epidemiology, clinical features, treatment and outcomes of adults with *E. coli* O157 infection presenting to Aberdeen Royal Infirmary over a three year period. METHODS: A retrospective casenote review. RESULTS: Thirty-two confirmed cases of *E. coli* O157 infection were admitted between 1997 and 2000. The median age was 58 years (range 16-93). Ten patients (31%) were from the city of Aberdeen and 22 (69%) from surrounding rural areas. Twenty-seven patients (85%) presented between May and October. The source of infection was unknown or unconfirmed in all cases. Bloody diarrhoea was present in 30 (94%). Leucocytosis was present in 18 (63%) but only four patients (13%) had a fever. Six of the 32 patients (19%) developed Haemolytic-Uraemic Syndrome (HUS) of whom 2 died. Ten patients received antibiotics of whom two developed HUS. Twenty-seven of the 32 (85%) had made a full recovery by time of discharge, three (9%) had impaired renal function and two (6%) died in hospital. CONCLUSION: *E. coli* O157 infection tends to occur sporadically in rural areas in North East Scotland. It is not usually
associated with fever. Infection occurs more commonly in the summer and autumn. HUS complicates infection in almost one fifth of patients.


About 15% of children with Shiga toxin (Stx) producing *Escherichia coli* (STEC) primarily of serotype O157:H7, gastrointestinal infection, and watery or bloody diarrhea, may develop hemolytic uremic syndrome (D+ HUS). Usually D+ HUS is not complicated by bacteremia and patients recover spontaneously without antibiotic treatment. We report here an adult case of a STEC O157:H7 urinary tract infection complicated by bacteremia and HUS that was not preceded by diarrhea (D- HUS). Cases of D- HUS need to be carefully examined for foci other than the gastrointestinal tract, and patients with *E coli* bacteremia should receive early antibiotic treatment as would any patient with sepsis.


Univariate and multivariate analyses were applied to determine risk factors for the progression of *Escherichia coli* O157:H7 enteritis to hemolytic uremic syndrome (HUS). Both clinical and laboratory variables were assessed for 118 pediatric patients (28 HUS; 90 enteritis only). Verotoxins 1 and 2 were produced by 89% of *E. coli* strains whereas verotoxin 2 only was produced by 11%. Although a greater frequency of strains producing verotoxin 2 only occurred in HUS isolates (p = 0.11), toxin phenotype was not significantly associated with risk after multivariate analyses. HUS patients with or without neurological manifestations had similar frequencies of the two toxin phenotypes among their isolates. Significant associations for young age (RR = 0.984; 95% CI = 0.971-0.998) and prolonged use of antidiarrheal agents (RR = 44.11; 95% CI = 8.48-229.4) with HUS were apparent. A lesser chance of progression was observed for patients whose strains possessed a 4 kb plasmid (RR = 0.27; 95% CI = 0.08-0.94). Our results are consistent with the hypothesis that progression to HUS is dependent upon both bacterial virulence factors and the clinical characteristics of the individual patient.

blood stream infections in 2000 at Royal Darwin Hospital in the tropical north of Australia. RESULTS: Significant isolates were grown from 257 sets of blood cultures. Staphylococcus aureus was the most common isolate overall (28%); 26% of these were methicillin-resistant (MRSA). Escherichia coli was the most common cause of community-acquired bacteraemia. Burkholderia pseudomallei caused 32% of community acquired, bacteraemic pneumonia; 6% of bacteraemias overall. Vancomycin-resistant enterococci were not isolated. Crude mortality rates (13% overall; 9% attributable mortality) were lower than in most comparable studies. CONCLUSIONS: The major difference between these findings and surveys performed elsewhere is the presence of B. pseudomallei as a significant cause of bacteraemic community-acquired pneumonia. Our results demonstrate the effects of local environmental and patient characteristics on the range of organisms causing blood stream infections, and emphasize the important role of local microbiology laboratories in guiding empiric antibiotic therapy.


Seventeen years after its recognition, outbreaks and sporadic infections attributed to Escherichia coli O157 continue to increase. Acute gastrointestinal, and the systemic complications haemolytic uraemic syndrome (HUS) and thrombotic thrombocytopenic purpura (TTP), are frequent and severe. Current challenges that face clinicians are the early recognition of infection, identification of risk factors for poor prognosis, determination of appropriate monitoring for the development of complications, establishment of a therapeutic strategy and, finally, advice for patients about their long-term prognosis. Clinical features which, in combination, have been shown to distinguish E. coli O157 infection from other enteric pathogens are a history of bloody diarrhoea, visibly bloody stools, absence of fever, a leucocyte count greater than 10 x 10(9) l(-1) and abdominal tenderness on physical examination. The most consistent risk factors for the development of HUS/TTP are the extremes of age and a raised leucocyte count. Bloody diarrhoea and 'antimotility' drugs are also likely to be important risk factors. Recent evidence from the central Scotland outbreak suggests that individuals who are taking drugs that reduce gastric acidity or antibiotics at the time of infection with E. coli O157, or who have a short incubation period, may also be at increased risk of progression to HUS/TTP. Clinical management, in particular the role of antibiotics in gastrointestinal infection, remains controversial, and retrospective assessment of the 1996 outbreaks from central Scotland and Japan only adds to this controversy. Therapeutic plasma exchange is a promising treatment for adults who develop HUS/TTP, but its role has yet to be determined definitively, either in a randomized controlled trial or by an international register of cases. Significant chronic sequelae of infection occur, particularly irritable bowel syndrome after uncomplicated gastrointestinal infection, and renal failure after HUS/TTP. Their frequency and severity are likely to become evident over the next decade.


**CONTEXT:** The long-term renal prognosis of patients with diarrhea-associated hemolytic uremic syndrome (HUS) remains controversial. **OBJECTIVES:** To quantify the long-term renal prognosis of patients with diarrhea-associated HUS and to identify reasons for different estimates provided in the literature. **DATA SOURCES:** We searched MEDLINE and Experta Medica (EMBASE) bibliographic databases and conference proceedings, and we contacted experts until February 2003. We also searched the Institute for Scientific Information index and reference lists of all studies that fulfilled our eligibility criteria. The search strategy included the terms hemolytic-uremic syndrome, purpura, thrombotic thrombocytopenic, *Escherichia coli* O157, longitudinal studies, kidney diseases, hypertension, and proteinuria **STUDY SELECTION:** Any study that followed up 10 or more patients with primary diarrhea-associated HUS for at least 1 year for renal sequelae. **DATA EXTRACTION:** Two authors independently abstracted data on study and patient characteristics, renal measures, outcomes, and prognostic features. Disagreements were resolved by a third author or by consensus. **DATA SYNTHESIS:** Forty-nine studies of 3476 patients with a mean follow-up of 4.4 years (range, 1-22 years at last follow-up) from 18 countries, 1950 to 2001, were summarized. At the time of recruitment, patients were aged 1 month to 18 years. In the different studies, death or permanent end-stage renal disease (ESRD) ranged from 0% to 30%, with a pooled incidence of 12% (95% confidence interval [CI], 10%-15%). A glomerular filtration rate lower than 80 mL/min per 1.73 m2, hypertension, or proteinuria was extremely variable and ranged from 0% to 64%, with a pooled incidence of 25% (95% CI, 20%-30%). A higher severity of acute illness was strongly associated with worse long-term prognosis. Studies with a higher proportion of patients with central nervous system symptoms (coma, seizures, or stroke) had a higher proportion of patients who died or developed permanent ESRD at follow-up (explaining 44% of the between-study variability, P = .01). Studies with a greater proportion of patients lost to follow-up also described a worse prognosis (P = .001) because these patients were typically healthier than those followed up. One or more years after diarrhea-associated HUS, patients with a predicted creatinine clearance higher than 80 mL/min per 1.73 m2, no overt proteinuria, and no hypertension appeared to have an excellent prognosis. **CONCLUSIONS:** Death or ESRD occurs in about 12% of patients with diarrhea-associated HUS, and 25% of survivors demonstrate long-term renal sequelae. Patients lost to follow-up contribute to worse estimates in some studies. The severity of acute illness, particularly central nervous system symptoms and the need for initial dialysis, is strongly associated with a worse long-term prognosis.


46-year-old man refer to us because of hemospermia. The prostatic gland was normal in size and consistency at rectal examination. Serum prostate specific antigen was 7.04 ng/ml. Magnetic resonance imaging showed an area of low signal intensity on T2-weighted images in the left peripheral gland, possibly indicative of carcinoma.
Transrectal prostate biopsy was performed after intravenous administration of piperacillin. He developed chills and fever (39 degrees C) the next morning following biopsy. He was taken unconscious into the hospital where a diagnosis of septic shock caused by Escherichia coli was made. Five days later, he died. His general condition deteriorated notwithstanding intensive treatment. Postmortem blood cultures were positive for a piperacillin resistant Escherichia coli. Histological examination of the biopsies showed a benign prostatic hyperplasia. Autopsy showed diffuse tissue damage in the heart, lung, liver and kidneys. The prostate had numerous microabscesses. Currently, transrectal prostate biopsy is considered a generally reliable procedure to detect adenocarcinoma of the prostate. Our case seems to the sixth case report of fatal complications.

Heinrichs DE, et al 1998 Molecular basis for structural diversity in the core regions of the lipopolysaccharides of Escherichia coli and Salmonella enterica. Mol Microbiol. 30(2):221-32. Bacterial lipopolysaccharides (LPS) are unique and complex glycolipids that provide characteristic components of the outer membranes of Gram-negative bacteria. In LPS of the Enterobacteriaceae, the core oligosaccharide links a highly conserved lipid A to the antigenic O-polysaccharide. Structural diversity in the core oligosaccharide is limited by the constraints imposed by its essential role in outer membrane stability and provides a contrast to the hypervariable O-antigen. The genetics of core oligosaccharide biosynthesis in Salmonella and Escherichia coli K-12 have served as prototypes for studies on the LPS and lipo-oligosaccharides from a growing range of bacteria. However, despite the wealth of knowledge, there remains a number of unanswered questions, and direct experimental data are not yet available to define the precise mechanism of action of many gene products. Here we present a comparative analysis of the recently completed sequences of the major core oligosaccharide biosynthesis gene clusters from the five known core types in E. coli and the Ra core type of Salmonella enterica serovar Typhimurium and discuss advances in the understanding of the related biosynthetic pathways. Differences in these clusters reflect important structural variations in the outer core oligosaccharides and provide a basis for ascribing functions to the genes in these model clusters, whereas highly conserved regions within these clusters suggest a critical and unalterable function for the inner region of the core.

Seventy six children, 18 boys and 58 girls, aged 0-15.9 (median 1.0) years, with acute pyelonephritis were prospectively studied with a technetium-99m dimercaptosuccinic acid (DMSA) scan during infection and two months later. Fifty nine of these children were also studied two years after the infection. Seventeen children with a normal DMSA scan during infection or at two months after infection, or both, were not investigated by a DMSA scan at two years after acute pyelonephritis. A micturition cystourethrogram was performed in all the children after two months. Changes on the DMSA scan were found in 65 (86%) children during acute pyelonephritis, in 45 (59%) children at two months, and in 28 (37%) children at two years after infection. Vesicoureteric reflux (VUR) was found in 19 (25%) children at two months. Renal scarring was significantly correlated with the presence of gross VUR and recurrent pyelonephritis, but 62% of the scarred
kidneys were drained by non-refluxing ureters. Children with scars were older at the time of acute pyelonephritis than those without scars but no difference was found between the groups with regard to duration of illness, levels of C reactive protein and maximum white cell count, glomerular filtration rate, nor renal concentration capacity at the time of infection. It is concluded that renal scarring after acute pyelonephritis in children is more common than has been previously thought. Although children with gross VUR and recurrent pyelonephritis are at the greatest risk, renal scarring is more often seen without these risk factors.


Bacteria or their products may cause chronic inflammation and subsequent bone loss. This inflammation and bone loss may be associated with significant morbidity in chronic otitis media, periodontitis, endodontic lesions, and loosening of orthopedic implants caused by lipopolysaccharide (LPS)-contaminated implant particles. Currently, it is not clear how bacteria or endotoxin-induced bone resorption occurs and what cell types are involved. Here we report that Porphyromonas gingivalis, a periodontal pathogen, and Escherichia coli LPS induce osteoclastic cell formation from murine leukocytes in the absence of osteoblasts. In contrast, stimulation with parathyroid hormone had no effect. These multinucleated, tartrate-resistant acid phosphatase-positive cells were positive for receptor activator of NF-kappaB (RANK), the receptor for osteoprotegerin ligand (OPGL), also known as RANK ligand (RANKL). Blocking antibodies demonstrated that their formation was dependent upon expression of OPGL and, to a lesser extent, on tumor necrosis factor alpha. Mononuclear cells represented a significant source of OPGL production. In vivo, *P. gingivalis* injection stimulated OPGL expression in both mononuclear leukocytes and osteoblastic cells. Thus, these findings describe a pathway by which bacteria could enhance osteolysis independently of osteoblasts and suggest that the mix of cells that participate in inflammatory and physiologic bone resorption may be different. This may give insight into new targets of therapeutic intervention.


One or more putative enteroaggregative Escherichia coli (EAEC) virulence factors (aggA, aggR, aspU, or aafA) were identified in 60 (70%) of 86 EAEC isolates from travelers with diarrhea compared with a rate of 7 (8%) of 90 in patients with diarrhea who were infected with nonadherent *E. coli* (odds ratio, 27.36; 95% confidence interval, 11.30 to 65.91). The presence of aggR or one or more virulence factors in EAEC from patients with diarrhea was associated with a statistically increased concentration of interleukin-8 (IL-8) in feces compared with that in EAEC negative for these factors: for aggR positive
(9 of 12 [75%]; median, 800 pg/ml) versus aggR negative (5 of 18 [28%]; median, 0), P < 0.05; and for isolates positive for > or =1 virulence factor (13 of 21 [62%]; median, 360 pg/ml) versus those negative for > or =1 virulence factor (1 of 9 [11%]; median, 0), P < 0.05. Other fecal cytokines (IL-1beta and IL-1ra) were found in increased concentrations (P < 0.05 when at least one EAEC virulence factor was present compared with the concentrations when EAEC negative for multiple virulence factors was found in patients with diarrhea. Putative virulence factors were commonly found in EAEC from patients with diarrhea, and the pathogenicity of many strains was suggested by showing an association between the presence of plasmid-borne virulence factors and the presence of fecal cytokines. The different patterns of virulence factors of EAEC revealed several clusters demonstrating diversity among the isolates from the various regions.


The most frequent and best-studied agent of urinary tract infection (UTI) is Escherichia coli, which serves as a useful model pathogen for understanding microbial virulence in relation to UTI pathogenesis. The E. coli strains that cause most UTIs and other extraintestinal E. coli infections represent a highly specialized subset of the total E. coli population. The enhanced virulence potential of such strains, which collectively are known as uropathogenic E. coli or extraintestinal pathogenic E. coli (ExPEC), is thought to be caused mainly by their multiple virulence factors. These virulence factors include diverse adhesins, siderophores, toxins, polysaccharide coatings, and other properties that assist the bacteria in avoiding or subverting host defenses, injuring or invading host cells and tissues, and stimulating a noxious inflammatory response. Although the true evolutionary basis for ExPEC is unknown, the virulence factors of ExPEC serve as useful epidemiologic markers and in the future may provide effective targets for anti-UTI interventions.


Uropathogenic strains of Escherichia coli are characterized by the expression of distinctive bacterial properties, products, or structures referred to as virulence factors because they help the organism overcome host defenses and colonize or invade the urinary tract. Virulence factors of recognized importance in the pathogenesis of urinary tract infection (UTI) include adhesins (P fimbriae, certain other mannose-resistant adhesins, and type 1 fimbriae), the aerobactin system, hemolysin, K capsule, and resistance to serum killing. This review summarizes the virtual explosion of information regarding the epidemiology, biochemistry, mechanisms of action, and genetic basis of these urovirulence factors that has occurred in the past decade and identifies areas in need
of further study. Virulence factor expression is more common among certain genetically related groups of *E. coli* which constitute virulent clones within the larger *E. coli* population. In general, the more virulence factors a strain expresses, the more severe an infection it is able to cause. Certain virulence factors specifically favor the development of pyelonephritis, others favor cystitis, and others favor asymptomatic bacteriuria. The currently defined virulence factors clearly contribute to the virulence of wild-type strains but are usually insufficient in themselves to transform an avirulent organism into a pathogen, demonstrating that other as-yet-undefined virulence properties await discovery. Virulence factor testing is a useful epidemiological and research tool but as yet has no defined clinical role. Immunological and biochemical anti-virulence factor interventions are effective in animal models of UTI and hold promise for the prevention of UTI in humans.

Multiple Escherichia coli isolates from four adults with extraintestinal infections underwent molecular phylotyping and virulence profiling. A patient with secondary peritonitis had two low-virulence *E. coli* strains from phylogenetic groups A and D. In contrast, three patients with invasive extraurinary infections (septic arthritis/pyomyositis, nontraumatic meningitis/hematogenous osteomyelitis, and pneumonia) each had a single high-virulence phylogenetic group B2 strain resembling typical isolates causing urinary infection and/or sepsis, i.e., extraintestinal pathogenic *E. coli*.

Few microorganisms are as versatile as *Escherichia coli*. An important member of the normal intestinal microflora of humans and other mammals, *E. coli* has also been widely exploited as a cloning host in recombinant DNA technology. But *E. coli* is more than just a laboratory workhorse or harmless intestinal inhabitant; it can also be a highly versatile, and frequently deadly, pathogen. Several different *E. coli* strains cause diverse intestinal and extraintestinal diseases by means of virulence factors that affect a wide range of cellular processes.

Enterohemorrhagic *Escherichia coli* (EHEC) are the most common cause of postdiarrheal hemolytic-uremic syndrome (HUS). The most important EHEC serotype implicated worldwide is O157:H7. However, several so-called non-O157 EHEC serotypes have emerged. After a mean incubation period of 3 days, patients develop watery diarrhea accompanied by cramping abdominal pain. During the next days, in most patients watery diarrhea changes to bloody diarrhea. One week after the onset of diarrhea, in about 15% of infected patients under 10 years of age EHEC infection results in a systemic complication, HUS. Shiga toxins (Stxs) are considered the major virulence factors of EHEC involved in the pathogenesis of HUS. It is generally believed that after intestinal infection with EHEC, Stxs cross the intestinal barrier and bind to endothelial cells. At this
point they presumably injure the host cell by inhibition of protein synthesis, stimulation of prothrombotic messages, or induction of apoptosis. The B subunit of Stx binds to the membrane receptor globotriaosylceramide (Gb3). Gb3 facilitates the endocytosis and intracellular trafficking of the toxin. The Stx A subunit hydrolyzes a specific adenine residue of the 60S ribosomal subunit of mammalian cells. As a consequence, Stx shuts down the protein machinery of the susceptible cell. The HUS is the net effect of a variety of interacting factors, including background risk of acquisition, host factors (such as age), virulence characteristics of the infecting EHEC strain, and exogenous factors. All known EHEC virulence determinants are located on mobile genetic elements, and this has an important impact on the evolution of these pathogens. The evolution of EHEC has a dynamic component that includes different genetic mechanisms. The recent progress in understanding the pathogenesis and epidemiology of EHEC infections forms a basis for the development of future strategies to prevent EHEC infections in humans.


Shiga toxin producing Escherichia coli (STEC) is a newly emerged pathogen that has been the focus of immense international research effort driven by its recognition as a major cause of large scale epidemics and thousands of sporadic cases of gastrointestinal illness. It produces a severe bloody diarrhoea that is clinically distinct from other types of diarrhoeal diseases caused by other enteric pathogens. One of the most important areas of current exploration concerns how STEC enters our food chain, an investigational avenue that begins with the ecology of STEC in animals and in the environment. A variety of foods have been identified as vehicles of STEC-associated illness and this makes the organism one of the most serious threats to the food industry in recent years. The pathogenesis of STEC is multifactorial and involves several levels of interaction between the bacterium and the host. STEC strains carry a set of virulence genes that encode the factors for attachment to host cells, elaboration of effective molecules and production of two different types of Shiga toxins. These genes are found in the locus of enterocyte effacement (LEE), lamboid phages, and a large virulence associated plasmid. The publication of the complete genome sequence of Esch. coli O157:H7 chromosome offers a unique resource that will help to identify additional virulence genes, to develop better methods of strain detection and in the understanding of the evolution of Esch. coli through comparison with the genome of the non-pathogenic laboratory strain Esch. coli K-12. These research efforts in turn, should lead to development of new potent and cost effective anti-Stx therapies or vaccines and thereby major improvement in human health world-wide.


BACKGROUND: Chronic alcoholism and malnutrition are uncommon causes of complicated acute pyelonephritis (APN). CASE REPORTS: Since 1997, we have seen 5 patients with chronic alcoholism (3 women and 2 men, mean age 53.4 +/- 13 years) without cirrhosis, diabetes or renal failure who developed severe APN in a state of malnutrition (albumin 22 +/- 3 g/l, total cholesterol 0.86 +/- 0.2 g/l). Diagnosis was made 14.6 +/- 9 days after onset of atypical symptoms which the patients neglected. There was

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Health Effects of Escherichia coli [E. coli]
a major bacterial inoculum: Escherichia coli 10(6.2 +/- 2) (3 multisusceptible and 2 amoxicillin-resistant strains); positive blood cultures in 3 cases. The imaging study showed bilateral diffuse lesions with focal swelling and kidney enlargement, without obstacle, abscess, or papillary necrosis. All patients had severe acute renal failure (maximum serum creatinine: 582 +/- 210 mumol/l; 3 patients underwent dialysis). Mean duration of antibiotic therapy was 40 +/- 7 days (i.v.: 22 +/- 3 d). Renal scarring occurred since creatinine clearance was 33 +/- 22 ml/min 2 months after the initial episode. One patient progressed to end-stage renal failure. CONCLUSION: In malnourished alcoholic patients, APN may be unusually severe due to late diagnosis leading to the risk of irreversible renal damage and severe chronic renal failure.


**OBJECTIVE:** Although bloodstream infection commonly results in critical illness, population-based studies of the epidemiology of severe bloodstream infection are lacking. We sought to define the incidence and microbiology of severe bloodstream infection (bloodstream infection associated with intensive care unit admission within 48 hrs) and assess risk factors for acquisition and death. **DESIGN:** Population-based surveillance cohort. **SETTING:** Multidisciplinary and cardiovascular surgical intensive care units. **PATIENTS:** All adults with severe bloodstream infection in the Calgary Health Region (population approximately 1 million) during 2000-2002. **INTERVENTIONS:** None. **MEASUREMENTS AND MAIN RESULTS:** Three hundred forty patients had 342 episodes of severe bloodstream infection (15.7 per 100,000 population/year). Several demographic and chronic conditions were significant risk factors for acquiring severe bloodstream infection (relative risk, 95% confidence interval) including age > or =65 yrs (7.0, 5.6-8.7), male gender (1.3, 1.1-1.6), urban residence (2.4, 1.2-5.6), hemodialysis (208.7, 142.9-296.3), diabetes mellitus (5.9, 4.4-7.8), alcoholism (5.6, 3.8-8.0), cancer (7.5, 5.3-10.3), and lung disease (3.8, 2.6-5.4). The most common etiologies were Staphylococcus aureus, Escherichia coli, and Streptococcus pneumoniae (3.0, 3.0, and 1.9 per 100,000/year, respectively). The case-fatality rate was 142 of 340 (42%) for an annual mortality rate of 6.5 per 100,000. Increased Acute Physiology and Chronic Health Evaluation II score (odds ratio, 1.1 per point; 95% confidence interval, 1.1-1.2) and presence of a comorbidity (odds ratio, 2.5; 95% confidence interval, 1.4-4.3) were significant independent predictors of death. **CONCLUSIONS:** Bloodstream infections are commonly severe enough to require management in an intensive care unit and are associated with a high mortality rate. Identification of risk factors for severe bloodstream infection may allow targeting of preventive efforts to individuals at greatest potential benefit.


Escherichia coli O157:H7 infection is one of the more intriguing emerging infectious diseases of the industrialized world. The clinical importance of this organism first came to light in the 1980s and has been associated with significant morbidity and mortality in the United States. The infection is more common in industrialized countries than developing ones and is most closely associated with asymptomatic colonization of cattle.
Fecal oral transmission is the rule, with the inoculum needed for infection much smaller than that required for *E. coli*-related travelers’ diarrhea. The organism can survive for months in the environment, and cross contamination is common. Watery diarrhea that progresses to bloody diarrhea without prominent fever is the classic presentation. The classic biopsy finding is similar to that of ischemic colitis, with acute inflammation and hemorrhage involving the superficial mucosa with preservation of the deeper crypts. *E. coli* O157:H7 has powerful Shigella-like toxins that are encoded by bacteriophages and can trigger thrombotic complications such as the hemolytic uremic syndrome or thrombotic thrombocytopenic purpura. The very young and the elderly are most at risk for serious disease and complications. Treatment with antibiotics has been reported to increase the risk for complications, but the evidence supporting this conclusion is unconvincing, with many variables affecting outcome in any one patient.


We reviewed 75 episodes of *Aeromonas* spp. bacteraemia observed at our institution in 1979-2002, with special reference to episodes occurring in elderly patients (> or = 65 y) and to nosocomial episodes. In addition, we compared monomicrobial bacteraemic episodes caused by *Aeromonas* spp. (n = 54) with those caused by *Escherichia coli* (n = 108) and *Pseudomonas aeruginosa* (n = 108), to assess differences in clinical presentation and outcome. The 75 episodes of *Aeromonas* spp. bacteraemia occurred mainly in males (72%), suffering from chronic liver disease (36%) or neoplasm (33%). They had an abdominal origin in 52% of cases, were recorded as primary bacteraemia in 40%, and showed a 30-d case fatality rate of 36%. 22 episodes (29%) were nosocomial, 36 (48%) occurred in elderly patients and 21 (28%) were polymicrobial infections. In comparison with *Aeromonas* spp., *E. coli* bacteraemia was more often associated with less severe underlying conditions, a community-acquired infection (74%), and a urinary tract (52%) or abdominal (27%) origin and had a 30-d case fatality rate of 24%. *P. aeruginosa* bacteraemia occurred mainly in patients with severe underlying conditions, was associated with nosocomial infection (69%), and had a 30-d case fatality rate of 43%. In conclusion, *Aeromonas* spp. bacteraemia is a serious infection that should be considered in patients with chronic liver disease or neoplasm. It may occur in the elderly and as a nosocomial infection, and differs in clinical findings from bacteraemia due to other common pathogens. Severe bloodstream infections: a population-based assessment.


Acute pyelonephritis is frequent. Its usual signs and symptoms comprise renal pain, fever, inflammation, and pyuria. Simple acute *E. coli* pyelonephritis is frequent in the young female and in most cases is a benign condition. A typical pyelonephritis may be painless, or without high fever, or lacking bacterial growth in the urine due to previous inappropriate treatment. Severe, complicated pyelonephritis is mainly observed in diabetic, alcoholic or immunocompromised patients. In occasional cases, a common form of pyelonephritis may progress to formation of a renal abscess requiring drainage. When secondary to urinary tract abnormalities, pyelonephritis may be complicated with septicemia and can induce early and severe renal tissue damage. This form warrants...
emergency urologic treatment. Simple pyelonephritis of the young female without febrile UTI history requires little imaging. Conversely, extensive imaging workup is mandatory in the male, the elderly, when treatment is not rapidly effective or in case of early relapse. In some cases, acute pyelonephritis leads to the development of cortical scars, the long-term prognosis of which remains to be determined.


A 57-year-old woman, known to have diabetes mellitus, presented with a one-week history of fever, dysuria, and left flank pain. Computed tomography showed extensive left renal parenchymal destruction and a large gas collection. Urine culture revealed growth of Escherichia coli. The diagnosis of emphysematous pyelonephritis was confirmed at left nephrectomy. The clinical manifestations of emphysematous pyelonephritis, types of gas-forming renal infection, and their radiological findings are discussed.


Urinary tract infections (UTIs) are commonly encountered in medical practice and range from asymptomatic bacteruria to acute pyelonephritis. Enterobacteriaceae with *E. coli* being the most prevalent, are responsible for most commonly acquired uncomplicated UTIs and usually respond promptly to oral antibiotics. In contradistinction, more resistant pathogens cause nosocomially acquired infections which often require parenteral antibiotic therapy. Patients with acute bacterial prostatitis, usually caused by Enterobacteriaceae present with a tender prostate gland and respond promptly to antibiotic therapy. Chronic bacterial prostatitis on the other hand, is a subacute infection characterized by recurrent episodes of bacterial UTI where the patient presents with vague symptoms of pelvic pain and voiding problems. Treatment is protracted and may be frustrating. Nonbacterial prostatitis and chronic pelvic pain syndrome produce symptoms similar to those of chronic bacterial prostatitis. Treatment is not well defined due to their uncertain etiologies. Most episodes of catheter associated bacteruria are asymptomatic, where less than 5% will be complicated by bacteremia. The use of systemic antibiotics for treatment or prevention of bacteruria is not recommended, particularly in the geriatric age group, since it helps select for resistant organisms. Prevention thus remains the best option to control it. Few patients without catheters who have asymptomatic bacteruria develop serious complications and therefore routine antimicrobial therapy is not justified with only two exceptions: before urologic surgery and during pregnancy.


Recurrent meningitis due to Escherichia coli is an extremely rare infection in adult patients. Most cases have been complications of neurosurgery. We report on the case of a 43-year-old man with 4 recurrent spontaneous episodes of *E. coli* meningitis related to aspergillar sphenoidal sinusitis. Surgical treatment of sinusitis cured the patient.

Long-term outcome of acute pyelonephritis (AP) in adults is unknown. We evaluated the frequency of renal damage 10-20 years after hospitalization for AP in adult women and the utility of technetium Tc 99m-labeled dimercaptosuccinic acid (Tc 99m-DMSA) scanning for detection of renal scars; 63 of 203 women hospitalized with AP during 1982-1992 were included in the study. Tc 99m-DMSA scanning detected renal scarring in 29 women (46%). Multivariate analysis showed that pregnancy and hypoalbuminemia (albumin level, <3.2 g/dL) at hospitalization were independent risk factors for subsequent development of renal scars. At follow-up, hypertension was observed in approximately one-fifth of patients, regardless of renal scarring status. Four women with scars had a glomerular filtration rate of ≤75 mL/min; none of them developed severe renal impairment. In conclusion, the risk of developing renal scarring after AP in adult women is high. However, clinically relevant renal damage is rare 10-20 years after AP. Tc 99m-DMSA scanning is useful for detecting renal scars in adults but is not routinely needed in practice.


BACKGROUND: Emphysematous pyelonephritis (EP) is a rare but life-threatening condition of the upper urinary tract, characterized by the presence of gas in the renal parenchyma and perirenal space. The vast majority of patients with EP (90%) are known to have diabetes, with Escherichia coli being the most common causative pathogen. CASE REPORT: We present a case of fatal bilateral EP in a patient with diabetes, with an unusual radiological finding of gas around the spinal cord and in the psoas muscle, with renal parenchymal sparing. Our case serves as an important reminder of this life threatening entity in diabetic patients, which is not well recognized by clinicians because of its rarity.


Emphysematous pyelonephritis is defined as the presence of gas-producing bacteria in the kidney and in peri-nephretic areas. Even if it is rare, the mortality rate of this affection is between 50% and 90%. The *E. coli* is responsible in 60% of the cases. We report a case of a 50 years old male patient, with under diagnosed diabetics, how is admitted with pains in the left flank, fever, troubled urine, hematuria and worsening of general state. The diagnostic of emphysematous pyelonephritis was confirmed by CT Scan. In spite of adapted antibiotherapy to the renal function, insulinotherapy and correction of hydro-electrolytic troubles, the patient died with septic shock associated to digestive bleeding. Based on this case and a review of the literature, the authors describe the different features of this disease. Only an urgent nephrectomy after a short reanimation can improve the prognostic.
Schurman DJ, et al 1977 Experimental *E. coli* arthritis in the rabbit. A model of infectious and post-infectious inflammatory synovitis. *J Rheumatol.* 4(2):118-28. Rabbit knee joints challenged with *E. coli* 06 underwent a self-limited infection lasting several weeks followed by a prolonged post-infectious inflammatory arthritis. The *E. coli* used did not possess collagenolytic activity nor did a variety of common aerobic clinical isolates. Articular cartilage destruction occurred by two basically different mechanisms: u) direct invasion of pannus at the juxtaarticular margins, and 2) fibrillation in cartilage to cartilage contact areas. Weekly measurement of intra-articular pH and temperature were correlated with bacteriologic findings and groww and microscopic pathologic events.

Shah AA, et al 2004 Characteristics, epidemiology and clinical importance of emerging strains of Gram-negative bacilli producing extended-spectrum beta-lactamases. *Res Microbiol.* 155(6):409-21. Beta-lactam antimicrobial agents represent the most common treatment for bacterial infections and continue to be the leading cause of resistance to beta-lactam antibiotics among Gram-negative bacteria worldwide. The persistent exposure of bacterial strains to a multitude of beta-lactams has induced dynamic and continuous production and mutation of beta-lactamases in these bacteria, expanding their activity even against the newly developed beta-lactam antibiotics. These enzymes are known as extended-spectrum beta-lactamases (ESBLs). The majority of ESBLs are derived from the widespread broad-spectrum beta-lactamases TEM-1 and SHV-1. There are also new families of ESBLs, including the CTX-M and OXA-type enzymes as well as novel unrelated beta-lactamases. In recent years, there has been an increased incidence and prevalence of ESBLs. ESBLs are mainly found in strains of *Escherichia coli* and *Klebsiella pneumoniae* but have also been reported in other Enterobacteriaceae strains and *Pseudomonas aeruginosa*. Infections with ESBL-producing bacterial strains are encountered singly or in outbreaks, especially in critical care units in hospitals, resulting in increasing cost of treatment and prolonged hospital stays. Not only may nursing home patients be an important reservoir of ESBL-containing multiple antibiotic-resistant organisms, but ambulatory patients with chronic conditions may also harbor ESBL-producing organisms.

Shapiro 2004 Hemolytic Uremic Syndrome *Emedicine.* http://www.emedicine.com/emerg/topic238.htm Last Updated: June 18, 2004

Skerk V, et al. 2002 Aetiology of chronic prostatitis. *Int J Antimicrob Agents.* 19(6):471-4. A total of 388 patients with symptoms of chronic prostatitis and inflammatory findings in expressed prostatic secretion (EPS) or in a urine sample collected immediately after prostate massage, were examined over a 2 year period at the Outpatient Department for Urogenital Infections, University Hospital for Infectious Diseases 'Dr Fran Mihaljevic', Zagreb, Croatia. The infective aetiology was determined in 276 (71.13%) patients. *Chlamydia trachomatis* was the causative pathogen in 109 patients, *Trichomonas vaginalis* in 52, *Escherichia coli* in 26, enterococci in 25, Proteus mirabilis in 14, *Klebsiella pneumoniae* in six, *Streptococcus agalactiae* in eight, *Ureaplasma urealyticum* in seven patients with chronic prostatitis. Other patients had a mixed infection.
Spontaneous bacterial peritonitis occurs in 30% of patients with ascites due to cirrhosis leading to high morbidity and mortality rates. The pathogenesis of spontaneous bacterial peritonitis is related to altered host defenses observed in end-stage liver disease, overgrowth of microorganisms, and bacterial translocation from the intestinal lumen to mesenteric lymph nodes. Clinical manifestations vary from severe to slight or absent, demanding analysis of the ascitic fluid. The diagnosis is confirmed by a number of neutrophils over 250/mm³ associated or not to bacterial growth in culture of an ascites sample. Enterobacteriae prevail and Escherichia coli has been the most frequent bacterium reported. Mortality rates decreased markedly in the last two decades due to early diagnosis and prompt antibiotic treatment. Third generation intravenous cephalosporins are effective in 70% to 95% of the cases. Recurrence of spontaneous bacterial peritonitis is common and can be prevented by the continuous use of oral norfloxacin. The development of bacterial resistance demands the search for new options in the prophylaxis of spontaneous bacterial peritonitis; probiotics are a promising new approach, but deserve further evaluation. Short-term antibiotic prophylaxis is recommended for patients with cirrhosis and ascites shortly after an acute episode of gastrointestinal bleeding.


DBA/1 mice develop a chronic peripheral arthritis after immunization with type II collagen termed collagen-induced arthritis. We have localized the main arthritogenic determinants of CB11, a CNBr-generated arthritogenic fragment of chick type II collagen (CII), using 3 smaller peptide fragments of CB11 generated by endoproteinase LysC, LysC1 (CII 124-290), LysC2 (CII 291-374) and LysC3 (CII 375-402) and a panel of monoclonal antibodies (mAb) specific to CB11. MAb specific to the arthritogenic region of CB11 were also used to study the synergistic effect of *E. coli* lipopolysaccharide (LPS) on antibody-mediated arthritis in naive DBA/1 mice. LysC2 contained a minimum essential arthritogenic fragment of type II collagen: LysC2 induced arthritis by active immunization, also, a combination of four mAb specific to LysC2 passively transferred arthritis to naive mice. A single i.p. injection of LPS (50 micrograms/mouse) reduced the threshold values of the arthritogenic dose of mAb from 1 mg to 50 micrograms/clone per mouse, and decreased the number of mAb required for inducing arthritis from 4 to 2 clones. These observations suggest that LysC2, an 84 amino acid residue fragment, contains the main arthritogenic determinants within chick CB11. Importantly, LPS, a strong inducer of pro-inflammatory cytokines, negates the required multiple epitope specificity of autoantibodies in the passive transfer model and acts synergistically in the induction of arthritis by autoantibody.

upper urinary tract infection caused by haemolytic E coli in a female Birman cat is presented. Ultrasonographic examination of the kidneys documented changes in size, outline, echogenicity and architecture. Ultrasound guided fine needle aspiration of fluid from the renal pelvis was used to make the diagnosis. Fluid was submitted for culture and sensitivity and based on the results, antimicrobial therapy was initiated. The treatment was monitored over a 406-day follow-up period. Despite extensive treatment with specific antibiotics and supportive therapy, recurrence of urinary tract infection occurred.

Large-scale outbreaks of Shiga toxin-producing Escherichia coli (STEC) infection have revealed the great disease-causing potential of this organism, especially among children and elderly persons. Approximately 5%-10% of people with STEC infection will develop hemolytic-uremic syndrome (HUS), approximately 10% of those who develop HUS will die or have permanent renal failure, and up to 50% of those who develop HUS will develop some degree of renal impairment. Important concepts in understanding the pathogenesis and prevention of STEC-associated HUS are emerging, although no specific therapy yet exists. Optimal management of STEC infection includes intravenous hydration, avoidance of antimotility agents and antimicrobials, and monitoring for sequelae. Antimicrobials may have a potentially harmful role, possibly by inducing intestinal production of Shiga toxin during the diarrheal phase of illness. A recent clinical trial evaluating an intraluminal Shiga toxin-binding agent to ameliorate HUS showed no improvement in outcome. Interventions to prevent HUS from developing in STEC-infected children are under investigation. Prevention of exposure to STEC remains important, and animal vaccines to prevent stool shedding of STEC among food animals are in development.

Todar 2002 Todar's Online Textbook of Bacteriology. url: http://textbookofbacteriology.net/E.coli.html

Hemolytic uremic syndrome (HUS) is a disease that can lead to acute renal failure and often to other serious sequelae, including death. The majority of cases are attributed to infections with Escherichia coli, serotype O157:H7 strains in particular, which cause bloody diarrhea and liberate one or two toxins known as Shiga toxins 1 and 2. These toxins are thought to directly be responsible for the manifestations of HUS. Currently, supportive nonspecific treatment is the only available option for the management of individuals presenting with HUS. The benefit of antimicrobial therapy remains uncertain because of several reports which claim that such intervention can in fact exacerbate the syndrome. There have been only a few specific therapies directed against neutralizing the activities of these toxins, but none so far has been shown to be effective. This article reviews the literature on the mechanism of action of these toxins and the clinical manifestations and current management and treatment of HUS. The major focus of the article, however, is the development and rationale for using neutralizing human antibodies to combat this toxin-induced disease. Several groups are currently pursuing
this approach with either humanized, chimeric, or human antitoxin antibodies produced in transgenic mice. They are at different phases of development, ranging from preclinical evaluation to human clinical trials. The information available from preclinical studies indicates that neutralizing specific antibodies directed against the A subunit of the toxin can be highly protective. Such antibodies, even when administered well after exposure to bacterial infection and onset of diarrhea, can prevent the occurrence of systemic complications.

**Vandenbos 2004** Escherichia coli bacteremic urinary tract infections. Clinical aspects and pronostic factors *Presse Med.* 31;33(13):847-51. **OBJECTIVE:** To describe patients with bacteremia from urinary tract infection caused by Escherichia coli and investigate risk factors for mortality. **METHOD:** Retrospectively study of the files of patients with bacteremic urinary tract infection caused by *E. coli* and admitted via the Emergency Department of the University Hospital in Nice between 01/01/1997 and 12/31/2000. Inclusion criteria included at least one blood and urine culture positive for *E. coli* during the first 48 hours and age above 15 years. **RESULTS:** There were 118 patients in the population (71% female). Mean age was 73 years and median age 79 years. The majority of patients (90%) were hospitalized in a medical department. Initially the clinical picture was sepsis in 80% of patients, severe sepsis in 15% and septic shock in 5%. Lethality was 16%. In 40% of cases death occurred within the first 48 hours. Risk factors for mortality in multivariate analysis were initially severe clinical status and male sex. **CONCLUSION:** The population was aged and mortality was high for an infection presumed to be relatively benign. Age was not a risk factor for mortality, contrary to male gender.

**van der Vliet HJ, et al 2004** Myocardial air collections as a result of infection with a gas producing strain of Escherichia coli. *J Clin Pathol.* 57(6):660-1. Certain strains of Escherichia coli have been shown to cause gas accumulation in--for example, emphysematous pyelonephritis. This paper describes a patient with intramyocardial air collections resulting from an intramyocardial infection with gas forming E coli.

**Weidner W, Schiefer HG. 1991** Chronic bacterial prostatitis: therapeutic experience with ciprofloxacin. *Infection.* 19 Suppl 3:S165-6. Ciprofloxacin was used for the treatment of refractory chronic bacterial prostatitis. 17 men with symptoms of prostatitis for more than one year who had not responded to treatment courses of six weeks trimethoprim-sulfamethoxazole or trimethoprim alone received 500 mg ciprofloxacin twice daily per os for two weeks. Up to one year follow-up proved eradication of Escherichia coli in seven of ten and of other pathogens in two of five cases. In a second study, 16 patients with proven chronic bacterial prostatitis who had failed on pretreatment with co-trimoxazole, trimethoprim or norfloxacin, respectively, received 500 mg ciprofloxacin twice daily for four weeks. *E. coli* was the causative organism for all cases. After a median follow-up of 30 (21-36) months, ten out of 16 patients are clinically cured with permanent eradication of the causative organism. In two men a second treatment course with ciprofloxacin is considered successful. Two patients stopped treatment for central nervous system complaints.

We describe an unusual complication of acute pyelonephritis in a 45-year-old diabetic female. She was admitted to our hospital due to fever and flank pain which had developed 10 days earlier. Urinalysis showed many WBC and urine culture revealed *Escherichia coli*. After adequate antibiotic treatment, clinical symptoms abated but renal failure and leukocyturia persisted. Abdominal CT showed bilateral focal bacterial nephritis and renal biopsy disclosed chronic granulomatous interstitial nephritis. On the 80th hospital day she was discharged with a serum creatinine of 299 mumol/l. In the outpatient clinic, renal dysfunction and leukocyturia persisted up to 1 year. In conclusion, this case raises the possibility of a chronic interstitial process of acute pyelonephritis.


1. We investigated the role of bacterial lipopolysaccharide (LPS) in the reactivation of autoimmune disease by using collagen-induced arthritis (CIA) in mice in which autoimmunity to the joint cartilage component type II collagen (CII) was involved. 2. CIA was induced by immunization with CII emulsified with complete Freund's adjuvant at the base of the tail (day 0) followed by a booster injection on day 21. Varying doses of LPS from *E. coli* were i.p. injected on day 50. 3. Arthritis began to develop on day 25 after immunization with CII and reached a peak on day 35. Thereafter, arthritis subsided gradually but moderate joint inflammation was still observed on day 50. An i.p. injection of LPS on day 50 markedly reactivated arthritis on a dose-related fashion. Histologically, on day 55, there were marked oedema of synovium which had proliferated by the day of LPS injection, new formation of fibrin, and intense infiltration of neutrophils accompanied with a large number of mononuclear cells. The reactivation of CIA by LPS was associated with increases in anti-CII IgG and IgG2a antibodies as well as various cytokines including IL-12, IFN-gamma, IL-1beta, and TNF-alpha. LPS from *S. enteritidis*, *S. typhimurium*, and *K. neumoniae* and its component, lipid A from *E. coli* also reactivated the disease. Polymyxin B sulphate suppressed LPS- or lipid A-induced reactivation of CIA. 4. These results suggest that LPS may play an important role in the reactivation of autoimmune joint inflammatory diseases such as rheumatoid arthritis in humans.