Section of Epidemiology & Preventive Medicine

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Causes and Prevention of Sepsis Due to Gram-negative Bacteria

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Ecology of the Infecting Organisms

Most of our ideas about the epidemiology and prevention of septic infections in hospital were formed at a time when interest was almost exclusively in staphylococcal disease. In the first place, therefore, it seems desirable to summarize the main ways in which the epidemiology of disease due to Gram-negative organisms differs from that of staphylococcal sepsis.

Sources of Infection

Disease-producing staphylococci are almost invariably of human origin, derived from the nose or skin of a carrier or from a septic lesion. The immediate source of infection may be the patient himself, but self-infection in hospital patients is often with a strain acquired at a carrier-site after entering hospital.

While some septic infections are caused by Gram-negative bacteria from the normal gut flora, others are due to an entirely different class of 'free-living' Gram-negative organisms, usually found in soil, water and other damp places. As with staphylococci, self-infection is common and may be caused either by organisms that were present in the patient's bowel when he entered hospital or by organisms, including 'free-living' types, acquired by the gut or skin after admission to hospital. Extraneous infection may also be with bowel-type organisms from other patients or with 'free-living' organisms from environmental sources.

Fig 1 shows the groups of Gram-negative bacilli that are important causes of septic infection in hospitals. On the left are those that form part of the normal bowel flora, and on the right are the 'free-living' organisms. *Escherichia coli* and the members of the proteus group are exclusively bowel organisms and many of the klebsiellas probably have a similar ecology. *Pseudomonas aeruginosa* is found in the gut of 4–6% of normal persons (Shooter *et al.* 1966, Stoodley & Thom 1970), and is also very widely distributed in nature. There are other enterobacteria, such as the enterobacter-serratia group, as well as several pseudomonads, flavobacteria and related organisms, that are entirely 'free living' but may cause severe disease in man under appropriate conditions.

Indeed, it is becoming increasingly difficult to make a clear distinction between animal pathogens, plant pathogens and 'free-living' organisms in this group. *Ps. aeruginosa* is a major animal pathogen, but apparently identical strains cause disease in sugar cane, tobacco and lettuce (Elrod & Braun 1942); *Ps. cepacia* (syn. *Ps. multivorans*), first described as a cause of 'sour skin' in onion bulbs (Ballard *et al.* 1970), is widespread in soil and drinking water and has caused several outbreaks of wound sepsis and urinary tract infection in man (Bassett 1971); and *Flavobacterium meningosepticum*, which causes outbreaks of meningitis of newborn infants, is one of a large

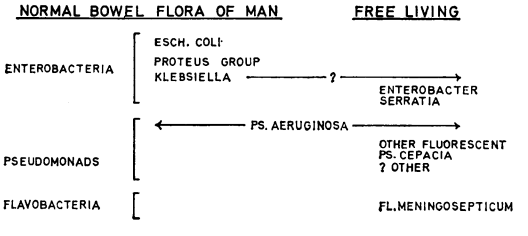

Fig 1 *Ecology of some Gram-negative bacilli that cause sepsis in hospitals*

group of similar organisms regularly found in tap outlets and elsewhere in hospital wards, as well as in brook water and soil (Olsen 1969).

Survival and Multiplication

Gram-positive cocci survive drying well, persist in dust and on dry surfaces, and are regularly found in the air of occupied rooms, but they do not multiply in the hospital environment. The Gram-negative organisms, on the other hand, suffer an immediate loss in numbers of 90–99% within a few minutes of drying (Lowbury & Fox 1953), though the survivors persist almost as well as do staphylococci. Thus, the number of Gram-negative organisms in the air and dust is usually only a tiny proportion of those present in the 'wet' sources from which they came. All the Gram-negative organisms survive well in moist places and the 'free-living' strains have simple nutritive requirements and a wide temperature-range for growth. They will therefore multiply at room temperature in fluids apparently devoid of organic material. Many of the enterobacter-serratia group and the fluorescent pseudomonads (but not *Ps. aeruginosa*) will also grow at refrigerator temperature (3–5°C). Some pseudomonads can use unlikely materials such as phenolic and quaternary ammonium compounds as sources of carbon and energy for growth.

Many Gram-negative bacteria are said to be exceptionally resistant to disinfectants, but in fact they are almost as easily killed by many 'conventional' disinfectants as are other non-sporing bacteria. Nevertheless, in hospitals these organisms are often found not only to survive but also to multiply in chemically disinfected equipment and in the disinfectants themselves. The disinfectants used in hospital are, unfortunately, often not 'conventional' and are sometimes used to treat objects that are almost impossible to disinfect by any chemical means. Places where disinfectants are ineffective are also usually places in which the Gram-negative survivors can multiply, so the consequences of incomplete destruction are much more serious than they are with Gram-positive organisms.

Patterns of Infection

There are three common situations in which sepsis due to Gram-negative bacilli occurs in hospital.

(1) *Common-source outbreaks:* These occur when an organism contaminates a piece of equipment or a fluid and is transferred by this means directly to a number of patients. In nearly every case the organism appears to have multiplied in the environmental reservoir and it is therefore the 'free-living' organisms that are responsible for most of these outbreaks. The organism may be injected into or inhaled by the patient, but in many cases, particularly in newborn infants and very debilitated patients, it appears to be sufficient for the organism to be ingested or deposited on the skin (*see* Bassett 1971).

(2) *Hyperendemic situations:* In certain departments of the hospital there are concentrations of patients who are all highly susceptible to infection at a particular site, e.g. burns wards and urological surgery departments. Here the infected patients provide a rich source of organisms; infection is spread from patient to patient by contact in the strains, especially of *Ps. aeruginosa*, proteus and klebsiella organisms, persist endemically for months or years and may cause high infection-rates (*see* Lowbury 1971).

(3) *Sporadic infections:* Many infections acquired in hospital, particularly with *Ps. aeruginosa*, are apparently sporadic, and those occurring in a particular ward are usually due to a variety of different types of the organism (Darrell & Wahba 1964). There is evidence that many of these are self-infections with organisms from the patient's own gut. Nevertheless, many of these organisms are of types seldom found in the gut of patients outside hospital (*see* Shooter 1971).

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Common-source Outbreaks

Common-source outbreaks of sepsis due to Gram-negative organisms arise because of the persistence or multiplication of the organisms in items of equipment or in solutions used in hospitals. This paper reviews forty-three such outbreaks, selected from the published reports of the last twenty years to illustrate the many different