between the sputum doxycycline concentrations and the degree of purulence. Though minocycline has also been suggested as a useful agent in chronic bronchitis its long-term prophylactic use is probably contraindicated by its toxic side effects (Lambert, 1975). Co-trimoxazole contains trimethoprim and sulphamethoxazole both with relatively long serum half-lives so that a twice daily regime is possible. The two constituents do not enter the sputum of bronchitic patients to the same extent, however. It has been demonstrated (Hughes, Bye & Hodder, 1972) that the trimethoprim concentration in sputum is about double that in serum whilst that of the sulphonamide component is only about half. This combination is nevertheless effective. The final choice must always be for the individual patient, however, and besides a compound’s antibacterial activity, its potential toxicity must also be considered. Furthermore the sensitivity of strains of haemophilus or *Streptococcus pneumoniae* may vary from one area to another and even from one year to another. In general terms, however, continuous chemoprophylaxis with a tetracycline or co-trimoxazole should be considered for the bronchitic subject with frequent winter exacerbations. If a scheme of rotating antibiotics on ‘patient demand’ therapy is to be employed, then ampicillin or amoxycillin is useful though their continued use for more than one month could lead to gastrointestinal side effects.

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References


**Diabetes and infection**

Diabetics are at risk of developing abscesses at the site of insulin injections, infected ulcers secondary to ischaemic and neuropathic changes in the feet, and candidiasis of the urogenital tract in the presence of uncontrolled glycosuria. It has also been widely considered that they are more prone to other infections than the non-diabetic though the evidence to support this assumption is not clear cut and the impression of a high infection rate may be partly due to the additional hazards of infection in diabetic patients. However, there are various abnormalities of cellular defence mechanisms which appear to increase the diabetic’s susceptibility to infection. Migration of polymorphonuclear (PMN) leucocytes is delayed (Mowat & Baum, 1971) and PMN phagocytosis is impaired. Although the impairment is probably multifactorial (Robertson & Polk, 1974) it can be related to poor diabetic control and the evidence would suggest that hyperglycaemia itself is the most important single factor (Bagdade, Root & Bulger, 1974).

It has also been demonstrated that although T and B lymphocyte subpopulations are normal in the well and poorly controlled diabetic, lymphocyte activity as measured by response to the mitogen phytohemagglutinin is depressed in poorly controlled subjects (MacCuish, Urbaniak, Campbell, Duncan & Irvine, 1974). The impairment is reversible and can also be directly related to the degree of hyperglycaemia (MacCuish, 1976). These *in vitro* findings are in keeping with the clinical observation that, as distinct from ketoacidosis, the development of severe
hyperosmolar, hyperglycaemic non-ketotic coma is often multifactorial (Gerich, Martin & Recant, 1971). It might be argued that the infective component is as much effect as cause. Thus a vicious circle situation appears to exist; not only can infection precipitate metabolic decompensation, but poorly controlled diabetics are rendered more susceptible not only to infection, but also to septicemia. Severe keto-acidosis is a life threatening condition. Its appropriate management demands not only an awareness of the underlying metabolic disturbance, but also of the initial precipitating cause. Recent studies have shown that bacterial infection is the single most common factor being present in up to 56% of episodes (Beigleman, 1971; Alberti, 1974). In one series significant bacterial infection occurred in 41% of 211 episodes (Campbell, Munro, MacCuish & Duncan, 1974), the incidence being particularly high in previously undiagnosed diabetics aged 45 years or more and previously diagnosed insulin dependent diabetics. Most infections arise from the urinary and respiratory tracts (including β haemolytic streptococcal sore throats) with skin sepsis and a mixture of other infections responsible for the remainder. As the vast majority of episodes develop outside hospital, in otherwise healthy diabetics, infection by resistant organisms or opportunists is unusual, but an 'epidemic' of keto-acidosis has been described during an influenzal outbreak (Watkins, Soler, Fitzgerald & Malins, 1970). The symptoms and signs of infection are often concealed by the severity of the metabolic upset and even septicemia can occur in the absence of a leucocytosis or of elevation in temperature.

With increasing awareness of the appropriate management of the biochemical disturbances, there has been a major reduction in the mortality from keto-acidosis. Most deaths can now be attributed to the underlying cause, myocardial infarction carrying a particularly poor prognosis. Severe infection, in particular septicemia, is a major contributing factor in 33 to 44% of deaths and is responsible for the majority of deaths in patients under the age of 45 (Beigleman & Warren, 1973; Campbell, Munro, MacCuish & Duncan, 1974). Although the presence of infection may only be detected by appropriate bacteriological sampling, the clinician cannot afford to wait for bacteriological confirmation before initiating therapy. It is the old story of the quick and the dead. If you are not quick, they are dead. In the most severely ill, whether there is clinical evidence of infection or not, chemotherapy should be commenced once bacteriological samples, including blood for culture, have been obtained.

Because vomiting is common and alimentary absorption is impaired, chemotherapy must be given parentally. Hypotension and peripheral circulatory collapse associated with the inevitable fluid and electrolyte depletion can markedly reduce the rate of intramuscular injection. When the infecting organism can be identified an appropriate narrow spectrum agent is indicated. Often this is not possible and broad spectrum cover is necessary. There is evidence to suggest that the poorly controlled diabetic is especially prone to gram positive infections (Robson, 1970) and the selected regime should effectively cover staphylococcal and streptococcal organisms. One effective combination is that of gentamicin with soluble penicillin.

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