The Association of Clinical Pathologists: 88th general meeting

The 88th general meeting of the Association of Clinical Pathologists was held at the University of Sheffield on 13 and 14 April 1972. Abstracts of the scientific communications and of some of the papers given at the symposium follow. There was a guest lecture by Dr A. Usher of the Department of Forensic Pathology, University of Sheffield, who took as his title, 'Mainly murder'. There were two symposia, one on brucellosis, the other on myelomatosis, and some of these papers are also included in the form of abstracts.

Trimethoprim Levels in Cerebrospinal Fluid

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Although the combination of trimethoprim sulphamethoxazole has been used for treating meningitis (Morazaria, Walton, and Pickering, 1969) information about trimethoprim levels in cerebrospinal fluid (CSF) is scanty.

Preliminary results are presented in which cerebrospinal fluid was obtained by lumbar puncture at routine diagnostic air encephalography in patients selected for this procedure on clinical grounds. All patients were between the ages of 12 and 70 years, not pregnant, and not receiving treatment with thiazide diuretics or antibiotics. The trimethoprim was injected intravenously during one and a half minutes, and was administered within 60 minutes of the start of the procedure or at least 90 minutes before the lumbar puncture was performed. A third group of patients received oral Cotrimoxazole which was given the night before, and in some cases on the same morning also. Samples of cerebrospinal fluid were obtained within a space of from 15 to 30 minutes at the start and during the radiological investigation during which time all patients were anaesthetized.

Microbiological assay was performed using a sensitive organism (*Bacillus pumilus* strain CN 607) which was incorporated in the middle layer of a three-layered plate of nutrient agar containing wells into which standard solutions of trimethoprim (prepared in the same type of body fluid as that being assayed) and test fluids were placed; zones of inhibition

thus produced were compared graphically (Bushby and Hitchings, 1968). The results showed that a single intravenous dose of trimethoprim of 3.0 mg/kg body weight gave levels in cerebrospinal fluid within the first hour of 0.4 µg/ml or higher, and 0.5 µg/ml or higher in the second hour. Results following oral administration are presented on blood and cerebrospinal fluid obtained at intervals of between four and 18 hours after administration.

Within the limitations of the clinical procedure, these results suggest that trimethoprim levels are attainable which, in the presence of sulphonamides, are bactericidal for the majority of organisms likely to be found in cerebrospinal fluid.

References

- Bushby, S. R. M., and Hitchings, G. H. (1969). *Brit. J. Pharmacol.*, 33, 72-90.
Morzaria, R. N., Walton, I. G., and Pickering, D. (1969). *Brit. med. J.*, 2, 511-512.

Acquired Toxoplasmosis and its Laboratory Diagnosis

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Most acquired toxoplasmosis in man presents as an acute or subacute lymphadenopathy. It occurs most frequently in children, less frequently in 'teenagers', and still less frequently in adults. Any node, group of nodes, or groups of nodes may be involved. Those most commonly affected are the cervical ones.

Hodgkin's disease is often suspected, particularly when resolution of an enlarged node is delayed. Sometimes mesenteric lymphadenopathy is found at laparotomy for a suspected abdominal emergency, or a lump removed from the upper and outer quadrant of the breast proves to be an enlarged lymph node.

Occasionally, in addition to lymph nodes, another system is involved. In such patients the clinical picture is usually almost entirely due to the disease process in the other organ—encephalitis, pneumonitis, myocarditis, myositis, hepatitis, and bone marrow dysfunction. Often the first clue indicating toxoplasmosis is the histological appearance of the lymph nodes.

Toxoplasmic uveitis is a chronic manifestation and is usually confined to the choroid and retina. While it is nearly always the result of congenital infection it is sometimes due to acquired infection. Then the lesions may not be confined to the posterior tract; they may be in the anterior or in both.

A clinical diagnosis can be confirmed by any of the many antibody tests, particularly if a rising titre can be shown, or by isolating the parasite by mouse inoculation from part of a lymph node biopsy, or by finding the typical reactive changes on histological examination of the remainder of the biopsy, or by a combination of these methods.

Antibiotic-producing Commensals in Surgical Wounds and Dermatological Lesions

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Although antagonistic activities among microorganisms have been studied for over 100 years since Lister's first observations in 1871, their implications in the ecology of the human body have been strangely ignored. A notable area of this neglect is the skin whose normal commensals frequently produce antibiotic active against most Gram-positive bacteria as well as some Gram-negative species (Selwyn and Ellis, 1972).

In a preliminary bacteriological survey of various normal skin sites in 250 people, commensal *Micrococcaceae* strains produced moderate to wide inhibition zones against indicator organisms in 56 cases (22.4%). Yet the antagonistic organisms were actually predominant in only 22 cases. This suggested that such organisms possess little or no survival advantage in a healthy skin habitat. The situation seems to be different, however, if the skin is damaged or diseased.

Three series of patients were investigated: a dermatological group of 233 from whose lesions serial cultures of representative strains had been stored (Selwyn, 1965); a group of 90 surgical patients from whom pre- and post-operative cultures were obtained; and finally a series of 36 dermatological patients in whom successive cultures were examined from the nose, perineum, and normal skin, as well as from lesions receiving topical steroid treatment.

In the two dermatological series pre-existing or hospital acquired Gram positive pathogens were rarely found in lesions containing antibiotic-producing commensals on admission. Similarly, the presence of antibiotic producers on the skin of surgical patients appeared to protect operation wounds against colonization by exogenous organisms. Evidently commensals that produce antibiotics derive full ecological advantage only

diseased or damaged skin where they act as a valuable defence against infection.

References

- Selwyn, S., and Ellis, H. (1972). Skin bacteria and skin disinfection reconsidered. *Brit. med. J.*, 1, 136.
 Selwyn, S. (1965). The mechanism and prevention of cross-infection in dermatological wards. *J. Hyg. (Lond.)*, 63, 59.

Proteus Urinary Infections in Childhood

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Quantitative urine culture by the dip-inoculum technique of Mackey and Sandys (1965) has shown that the pattern of infection in male children is quite different from that of female children. Among boys under the age of 14 *Proteus mirabilis* is the causative organism in about 75% of cases of active urinary infection. By contrast only 15% of infection in girls is due to *Proteus*, the dominant pathogen being *Esch. coli*.

Proteus mirabilis was found in the preputial sacs of 20/51 boys under 10, without overt urinary infection. In nine instances preputial infestation was associated with the presence of *Proteus* in urine collected without retraction of the foreskin. Although the degree of bacteriuria arising in this way should not often reach levels typical of active infection, nevertheless infestation of the prepuce by *Proteus* may be the source of active infection in boys, thus providing a reason for the contrasting incidence of *Proteus* infection in the two sexes.

Reference

- Mackey, J. P., and Sandys, G. H. (1965). *Brit. med. J.*, 2, 1286.

Experimental Pertussis Infection in the Vaccinated and Unvaccinated Marmoset: Similarities to Natural Infection in the Child

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Isolates of *Bordetella pertussis* from children were type 1,2,3; 1,2; 1,3; or a mixture of these. Type 1 (apparently a degraded form) was rarely isolated and always grossly outnumbered by other serotypes. Fresh isolates of all four types were avirulent for mice, intracerebrally, but readily colonized the marmoset nasopharynx. Within three days of pernasal inoculation with type 1, the marmoset

colonization had changed to type 1,2 (? rough to smooth mutation).

No marmoset coughed or vomited, or 'whooped', though some became catarrhal. But, like children, they developed circulating antibodies consistent with the agglutinogens in the infecting strain or in a killed vaccine.

Three pairs of marmosets were challenged pernasally with type 1,3 (now prevalent in children). Those previously vaccinated with 1,2,3 eliminated the 1,3 challenge in 10 to 13 days, whilst those vaccinated with 1,2 harboured 1,3 organisms for 22 to 24 days. In unvaccinated animals (with no antibody 2) the 1,3 infection changed to 1,2,3 after two weeks, then to 1,2 after three to four weeks, and persisted until six weeks from challenge.

Three other pairs were challenged with type 1,2,3. Those previously vaccinated with 1,2,3 eliminated the infection in two to two and a half weeks; one, vaccinated with 1,2 took two and a half weeks, but the infection in the other changed to 1,3 and persisted for five weeks. In unvaccinated animals, the 1,2,3 infection changed to 1,3 after two weeks and persisted for five weeks (11 weeks in one animal).

Similar changes of serotype have been found in the child; and, as in these marmosets, type 1,2,3 vaccine appears more effective than 1,2 vaccine in protecting the child.

Brucellosis: the Situation in Britain

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About 600 cases of human brucellosis occur annually, according to the only reports available. They are virtually all contracted from drinking infected milk or contact with infected cattle. One third of the dairy herds of Britain are infected and the Ministry of Agriculture, Fisheries and Food has embarked upon a scheme to eradicate the disease from cattle. Sub-clinical infection with *Brucella abortus* affects dairy farmers and herdsmen and their families, slaughterhouse men, and veterinary surgeons at some time in their lives, and creates difficulties of diagnosis if it is made by serology alone. The disparity between the annual number of cases (328 for the years 1968-71) in Scotland, where there are only between 5000 and 6000 dairy herds, and in England and Wales (270 for the same period), where there are over 80 000 herds, may be perhaps due to the reporting of serological

findings without a clinical assessment of the patient being made, since reports show that infection in Scottish herds is no higher than that in herds in England and Wales. Legislation is strict; under the Agricultural Act of 1970 anyone selling a cow, otherwise than for slaughter, known to be a reactor, can be fined £400, and the MOH has wide powers under the Food and Drugs Act 1955 and the Milk and Dairies (General) Regulations of 1959 to order pasteurization of milk which he knows to be infected.

Brucellosis in South West Eire

BRIDGET V. FOLEY (*St Finbarr's Hospital, Cork*)

In 1964 Brucellosis eradication commenced in the 26 counties using a milk ring survey of churn samples. The incidence of brucellosis was found to resemble that of tuberculosis, being low in the west and north west and high in the dairy areas of Leinster and the south, areas of greater cattle concentration and habitual movement of dairy cattle. The use of S.19 vaccine was confined to 3-6-month-old calves to ensure protection for herds that would be mature before eradication was complete. In 1966 full-scale eradication commenced in Donegal and movement of cattle in and out of the country was controlled. Market value compensation was given for reactor animals.

In 1968 a complete ban was put on the use of S.19 vaccine, and the 45/50 vaccine was substituted. Later that year eradication extended to Sligo, Leitrim, Monaghan, Cavan, and in 1968 these five counties were brucellosis free. Wholesale clearance is going on along a line from Dublin to Mayo; other counties will not have eradication for some time and this includes our area of the south west.

The first investigation was undertaken in 1967 on three groups of people occupationally exposed to possible infection, ie, veterinarians, dairy farmers, and butchers, using Kerr's questionnaire and doing three sera tests (standard agglutination test, Coombs AHG and CF tests). Seventy-four or 92.5% of the 80 veterinarians, 45 or 44.1% of the 102 farmers, and nine or 18% of the butchers had positive titres. Thirteen veterinarians who were in administration work show that positive titres persist for many years.

The second investigation was carried out in connexion with an epidemic due to *Brucella abortus* in a girls' boarding