Though the series surveyed is still small, it is apparent that most if not all cases of carcinoma in situ are detected, but that certain glandular cancers and an occasional invasive squamous cancer might be missed.

The present instrument provides a 30-parameter measurement output per field in just under one second but its logic circuitry is not entirely appropriate to malignant cell scanning. A new instrument, more purpose built, is being constructed so that rapid scanning of linear cell tracks on film strip is possible. It is estimated that a three minute scan of around 50,000 cells should be possible if the problem of cell presentation and suitable contrast training is achieved.

It is suggested that a test profile may be necessary to detect the endometrial and other invasive cancers by adding the 6-phosphogluconate-dehydrogenase enzyme test to the cell samples of all women over the 45-age group.

LABORATORY TESTS IN VIRAL HEPATITIS

PATRICIA E. TAYLOR, A. J. ZUCKERMAN, AND W. D. BRIGHTON (London School of Hygiene and Tropical Medicine, and the National Institute for Medical Research, Hampstead Laboratories) Increasing evidence suggests that the Australia antigen is closely related to, if not identical, with the agent responsible for viral hepatitis (Levene and Blumberg, 1969; London, Sutnick, and Blumberg, 1969). This antigen was first described in 1964 by Blumberg who found that sera from two multiply transfused haemophiliacs contains an antibody which reacted with the serum of an Australian aborigine in immunodiffusion tests to form a single precipitin line. The aboriginal antigen was first considered to be another example of a serum protein pleomorphism, but this view was later modified with the discovery of its association with leukaemia, Down's syndrome, and hepatitis (Blumberg, Gerstley, Hungerford, London, and Sutnick, 1967). Soon after Blumberg's report, Prince (1968) described a similar closely related if not identical antigen, the SH antigen, in the blood of transfused patients during the incubation period and early acute phase of post-transfusion hepatitis.

A modified two-dimensional immunodiffusion technique, complement fixation, and immune electron microscopy are being used at the London School of Hygiene and Tropical Medicine to study the epidemiological distribution and morphological characteristics of the antigen. For all three tests, indicator sera containing antibody to the Australia-SH antigen have generally been obtained from patients who have been presumably hyper-immunized by receiving multiple transfusions of blood or plasma, some of it containing the Australia-SH antigen. On occasion, antibody to the antigen has also been found in persons who have not been transfused but who have had subclinical contact with cases of viral hepatitis.

The technique used for immunodiffusion and the source of reference reagents have already been described (Zuckerman and Taylor, 1969). With this technique, antigen has been found in approximately 40% of adult patients with acute viral hepatitis. Detectable antibody has not been found in sera collected from these patients during convalescence. The presence of the antigen is usually transient during the acute phase of the disease. However, fresh samples of serum collected in 1968 and 1969 from a blood donor who was identified in 1951 as a 'silent' carrier of the virus of serum hepatitis have been found to contain the antigen (Zuckerman and Taylor, 1969). This indicates that, on occasion, a long-term carrier state may develop. Furthermore, in two instances, both antigen and antibody have been present at the same time in the same specimen of serum.

A standard microtitre complement fixation system (Sever, 1962) is also being used for the detection of Australia-SH antigen. Preliminary results indicate that this technique is somewhat more sensitive than immunodiffusion. Very high antigen titres, up to 1:2,048 or more, are found. With some specimens, a prozone effect is noticeable.

Immune electron microscopic studies, carried out in collaboration with Mrs J. D. Almeida and Professor A. P. Waterson of the Royal Postgraduate Medical School, have revealed characteristic particles which correspond to the Australia-SH antigen (Almeida, Zuckerman, Taylor, and Waterson, 1969). The main antigenic constituent is a roughly spherical particle approximately 200 Å in diameter. A considerable degree of pleomorphism exists and many tubular and aberrant forms are seen. The tubular forms may extend up to several thousand Angstroms in length, along which can be seen a periodicity of approximately 30 Å. The diameter of these tubular forms is approximately 200 Å.

In addition to the above studies, intensive efforts are being made to cultivate the responsible agent of viral hepatitis in tissue cultures of human embryonic liver, primary cultures of differentiated parenchymal cells and as a continuous cell line made up principally of spindle-shaped cells. Cultures of tissue obtained from adult liver by percutaneous needle biopsy are also being used. In addition, immunofluorescent methods similar to those described by Millman, Zavatone, Gerstley, and Blumberg (1969) are being applied for the detection of antigen in hepatic cells obtained by needle biopsy of the liver from patients with the antigen in the serum. Future studies include the development of other serological methods, including passive haemagglutination and immunoelectrophoresis, for the study of the antigen.

REFERENCES


THE BACTERIOLOGY OF TRAVELLER'S DIARRHOEA

B. ROWE AND JOAN TAYLOR (Salmonella Reference

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The Association of Clinical Pathologists: 83rd General Meeting

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Laboratory, Colindale, London) The traveller newly arrived at his destination, particularly if a warm climate, is commonly affected by acute diarrhoea within 14 days, a condition usually referred to as 'traveller's diarrhoea'.

In 1965 a bacteriological study was made on 540 men belonging to an Army unit which moved by air from the United Kingdom to Aden.

Cases of diarrhoea commenced about four days after arrival; the incidence reached a peak at 10 days and then dropped off to 14 days. In the subsequent weeks cases of diarrhoea continued to occur but no peak incidence was found. Thirty-eight soldiers suffered an attack of diarrhoea during their first 14 days after arrival. Faecal specimens were investigated from 35 of these subjects. A new serotype of Escherichia coli 0148K ? H 28 was isolated in the acute phase from 19 subjects (54-3 %).

Two cases (5-7 %) suffered from gastroenteritis due to a Salmonella and in the remaining 14 (40 %) of cases E. coli of various O groups were found which could not be related to diarrhoea. The peak of the isolations of E. coli 0148K ? H 28 corresponded with the peak incidence of the cases of diarrhoea. This serotype was not isolated from a healthy subject in Aden nor has it been found in the United Kingdom, except in a case of laboratory infection associated with this work.

This work suggests that in Aden in 1965 this specific serotype of E. coli caused the diarrhoea in about 54 % of the cases of traveller's diarrhoea.

ANTIBACTERIAL ACTION OF COMBINATIONS OF COLISTIN AND THE SULPHONAMIDES

N. A. Simons (Chase Farm Hospital, Enfield) The activity of colistin in vitro combined with sulphamethoxazole against 184 strains of Gram-negative bacteria was investigated. Seventy-four of the organisms were Pseudomonas aeruginosa, 37 Escherichia coli, 21 Proteus spp, 30 Klebsiella aerogenes, 12 Shigella spp, and 10 Salmonella spp. All the strains of Proteus were sensitive to sulphamethoxazole and resistant to colistin, but the activity of sulphamethoxazole was enhanced by colistin. Seventy of the 74 Ps. aeruginosa were sensitive to sulphamethoxazole as were 27 of the 37 Esch. coli, 24 of the 30 Klebsiellae, eight of the 12 Shigellae, and all 10 of the Salmonellae. All of the organisms other than Proteus were sensitive to colistin whose activity against sulphamethoxazole-sensitive organisms was enhanced by the sulphonamide. Sulphamethoxazole did not enhance the activity of colistin against sulphamethoxazole-resistant organisms. Investigations carried out on 29 of the organisms showed that with sensitive strains colistin was bactericidal, sulphamethoxazole was only bacteriostatic, and combinations of the two drugs were bactericidal.

CHANGES IN ANTIBIOTIC SENSITIVITY OF STAPHYLOCOCCI IN A NON-HOSPITAL POPULATION DURING THE PAST 20 YEARS

D. J. Goldie, V. G. Alder, and W. A. Gilhespie (Bristol) The proportion of antibiotic resistance in Staph. aureus isolated from skin sepsis and nasal carriers outside hospital has been determined periodically since 1949. Penicillin resistance, originally less than 4%, began to increase in 1952, reached 57% in 1967 and has not changed significantly since. Resistance to other antibiotics was first observed in 1957 when it quickly rose to 17%; this was due to the spread of multiresistant type 80 staphylococci from hospitals in which it was behaving epidemically. By 1967 the proportion of multiresistance had fallen again to 8% and has not changed significantly since. Methicillin resistance, first looked for systematically in 1969, has not been found.

The failure of phage group III multiresistant staphylococci to proliferate outside hospitals, though prevalent inside them, perhaps may be explained by their relative inability to colonize noses and their susceptibility to drying (as discussed in the next paper).

In 1969, 6% of non-hospital staphylococci and 44% of hospital staphylococci were resistant to sulphonamide. None were resistant to trimethoprim. Treatment of infections by such strains with sulphonamide-trimethoprim mixtures might promote the development of resistance.

THE SURVIVAL OF STAPHYLOCOCCUS AUREUS ON SKIN

R. W. Lacey, V. G. Alder, and W. A. Gilhespie (Bristol) Experiments were performed to determine whether some strains of Staph. aureus consistently survive longer than others on the skin. Suspensions containing known numbers of cocci were dried on the forearms of volunteers and the survivors counted after five hours by an adhesive label technique.

In preliminary experiments, day-to-day and person-to-person variations in survival of single strains were sufficient to mask possible differences between strains. To overcome this, mixtures of three staphylococci were inoculated, one of which was a standard strain with which the survival of the others could be compared. The component colonies of the mixture on recovery from the skin were distinguished by two independent properties on milk agar, pigmentation and colony size; lipase-negative strains gave larger colonies than lipase-positive strains.

As a group, strains isolated from primary skin sepsis and strains in phage groups I and II survived longer than other strains. Although it was not known whether the source or the phage pattern was primarily associated with long survival, it was concluded that length of survival on skin may be related to the production of cutaneous sepsis.

Similar differences were found when the strains were dried on glass, but were diminished by increasing atmospheric humidity. Hence variation in the survival of strains on dry skin can be explained, in part at least, by differences in their susceptibility to desiccation.

STUDIES ON STAPHYLOCOCCI FROM COLONIZED VENTRICULO-ATRIAL SHUNTS

R. J. Holt (Queen Mary's Hospital for Children, Carshalton, Surrey) Bacterial colonization of the shunt associated with indolent bacteraemia is a major complication in children with ventriculo-atrial shunts for the relief of