The Association of Clinical Pathologists: 92nd general meeting

The 92nd general meeting was held at the University of Warwick, Coventry, from 3 to 5 April 1974. Abstracts of the scientific communications follow. The Guest Lecture was given by Dr C. F. Hawkins on 'Speaking at meetings'. Two symposia were held, one on 'Systemic manifestations of intravascular coagulation' (Chairman: Professor E. K. Blackburn), and the other on 'Jaundice' (Chairman: Professor G. H. Lathe).

Klebsiella aerogenes Infections in the Tropics

EVELYN FINNIE (*Public Health Laboratory, Coventry*) The purpose of this study was to assay the significance of the isolation of *Klebsiella* from the upper and lower respiratory tract in a group of Jamaican hospital patients.

An incidence of 13.5% of *Klebsiella aerogenes* isolation was encountered in a group of 200 persons showing evidence of upper respiratory tract infection compared to an isolation rate of 11.5% in a similar population showing no evidence of upper respiratory tract infection. Details of the biotypes and serotypes of *Klebsiella* isolated are considered.

In the lower respiratory tract an incidence of 19% isolation of *Klebsiella aerogenes* was encountered in a population sample of 200 cases showing evidence of respiratory tract infection ranging from acute bronchitis to lobar pneumonia and lung abscess formation and this was significantly greater than the control group showing an isolation rate of 10%. Thirty per cent of the *Klebsiella* isolates from 'normal' sputum and 38% from purulent sputum came from patients on antibiotics at the time of first isolation of *Klebsiella*.

No species of *Klebsiella* other than *Klebsiella aerogenes* was encountered during the period of this study. Considerable heterogeneity of biotype and serotype combination was found and no cases of cross infection were demonstrated.

Electron Microscopy of Faeces in Acute Gastroenteritis

T. H. FLEWETT, A. S. BRYDEN, AND HEATHER DAVIES (*Regional Virus Laboratory, East Birmingham Hospital, Birmingham*) Immunoelectron microscopy has been employed by Dr S. K. R. Clarke's group in

Bristol and Dr R. M. Chanock's group in Bethesda, Md, to detect parvovirus-like particles in faeces of infected volunteers. We thought it would be worthwhile to see what viral flora of faeces might be discernible by electron microscopy in acute gastroenteritis and other conditions. Suspensions of faeces in saline were clarified by centrifugation at 7000 rev/min for 30 min. The supernatants were centrifuged at 50 000 rev/min for one hour; the deposits were resuspended in a few drops of distilled water and examined in the electron microscope after negative staining. Fragments of bacterial cell walls and flagella were often seen.

Many different kinds of virus-like particles were observed. Many were obviously bacteriophages; the smaller particles might well have been of either human or bacterial origin. Two groups, adenoviruses and reovirus-like particles, were recognizable as being of human origin. Adenoviruses were seen in almost half the faeces from which they were isolated. The reovirus-like particles were found, often in great numbers, almost exclusively in faeces of young children and infants with acute gastroenteritis. The relationship of these viruses to the Reoviruses and Orbiviruses will be discussed, and attempts at isolation described.

Further Thoughts on Sulphonamide-trimethoprim Mixtures

R. W. LACEY, E. L. LEWIS, AND J. D. ANDERSON (*Department of Bacteriology, University of Bristol*) The exclusive use of trimethoprim with sulphamethoxazole in a single preparation has been justified on the following theoretical grounds: the prevention of resistance developing to the individual components, the increased therapeutic efficacy due to bacteriostatic

synergy between the components, and the bactericidal action attainable by the mixture only. The validity of each of these reasons is disputed. Since the introduction of trimethoprim/sulphamethoxazole preparations, the understanding of the origins of antibiotic resistance in general and of that to these agents in particular has increased. The infrequency with which trimethoprim resistance has appeared in sulphonamide-resistant organisms suggests that the use of trimethoprim alone would not provoke rapid development of resistance to it. Sulphamethoxazole and trimethoprim do not produce bacteriostatic synergy against most sulphonamide-resistant organisms in nutrient agar containing lysed blood. In broth, the bactericidal effect of the mixture appears to be nullified by the presence of minute amounts of thymidine. Despite inactivation of thymidine by the presence of lysed horse red cells, the majority of coliforms and *Proteus* spp are not destroyed in nutrient broth.

Effect of Urine from Individuals Receiving Either Co-trimoxazole or its Separate Components upon Urinary Gram-negative Bacteria

J. D. ANDERSON, M. A. SELLIN, AND R. W. LACEY (*Department of Bacteriology, University of Bristol*) Various authors have come to different conclusions on whether co-trimoxazole is predominantly bactericidal or bacteriostatic *in vitro*, and the extent to which its individual components (sulphamethoxazole and trimethoprim) are synergistic. Most arguments have centred on the efficiency of methods used to neutralize sulphonamide and trimethoprim inhibitors in laboratory media. The use of urine as a test medium avoids speculation on the clinical significance of tests with laboratory media.

Twenty-eight isolates of *Enterobacteriaceae* were obtained from inpatients and outpatients with significant urinary tract infections. The effect of co-trimoxazole or its separate components was then determined upon shake cultures of these organisms in urine obtained from healthy subjects. Co-trimoxazole did not have a significant bactericidal effect upon any of the organisms. Trimethoprim alone had a bactericidal effect upon about one quarter of the organisms. Sulphamethoxazole thus appears to antagonize the bactericidal effect of trimethoprim in urine.

Volunteers were given therapeutic doses of either co-trimoxazole or equivalent amounts of its individual components. Urine from these individuals was found to have a similar effect upon the test organisms as synthetic mixtures of these various antimicrobials in normal urine.

There appears therefore to be a good case for further clinical trials to compare trimethoprim and co-trimoxazole in the treatment of urinary tract infections.

Benign Tumours of the Kidney in Infancy

A. H. CAMERON (*The Children's Hospital, Birmingham*) The salient features of six apparently benign tumours of the kidney are present. All occurred in infancy and were detected by abdominal palpation. All were large and one was initially considered to be an inoperable nephroblastoma. Some were solid and some were cystic. The histological appearances vary. Some have a well differentiated fibromatous pattern and others consist of simple cysts lined by inactive epithelium. More cellular areas are seen and dysplastic features may be encountered. The literature is briefly reviewed with particular reference to the confusing terminology in current use. The relationship of these tumours to renal dysplasia and nephroblastoma is briefly discussed.

References

- Bolande, R. P., Brough, A. J., and Iant, R. J. (1967). Congenital mesoblastic nephroma of infancy. *Pediatrics*, **40**, 272.
Fowler, M. (1971). Differentiated nephroblastoma: solid, cystic or mixed. *J. Path.*, **105**, 215.

The Effect of Vitamin C on the Blood Vessels

CONSTANCE R. SPITTLE (*Pinderfields General Hospital, Wakefield*) Following a chance observation that I could reduce my serum cholesterol with vitamin C, a study was done on other healthy people, and a group

of patients who had had a coronary thrombosis. It was found that while the serum cholesterol of young healthy people went down after vitamin C, in patients with coronary artery disease it tended to rise. This was attributed to mobilization of arterial cholesterol, and previous experimental evidence supported this. Vitamin C acts on the other fat fractions also: the lipoproteins, lipoprotein lipase activity, and the triglycerides. It also provides the ground substance for the arterial walls. Thus, a balance exists between vitamin C and fat. If the balance permanently favours vitamin C, the cholesterol will always be delivered to the liver, the β -lipoproteins will remain low, the lipoprotein lipase activity will be high, so the triglycerides will be low, and the arteries will be well supplied with ground substance, so they will remain clean. If the balance favours the fats, there will be a gradual accumulation of cholesterol in the arteries, the other fat fractions will gradually become abnormal, and the arteries will lose their ground substance, so atherosclerosis will result.

Direct proof of this hypothesis is impossible, but it is possible to show the powerful protective action of vitamin C against thrombosis in the veins. The results of a double-blind study are shown. Clinical deep vein thrombosis has now disappeared from our surgical wards.

Investigation of Cutaneous Inflammatory Response in Polycythaemia Vera

M. L. GHOSH, G. HUDSON, AND E. K. BLACKBURN (*Department of Haematology, University of Sheffield*) Changes in the inflammatory response to a simple skin abrasion, made under aseptic conditions, may be of value in studying haematological disorders such as malignant lymphoma (Ghosh, Hudson, and Blackburn, *Brit. J. Haemat.*, **25**, 293, 1973). In the present investigation, patients with established polycythaemia rubra vera, together with control subjects, have been studied by this technique.

The number of cells present in the exudate at 48 hr was a prominent feature in untreated polycythaemia. As compared with the control (10%), there was a significantly higher percentage of granulocytes (23%) and a correspondingly reduced percentage of macrophages. In the peripheral blood of these patients, the total white cell and neutrophil counts were significantly higher than in normal controls. Statistical analysis showed that

there was a relationship between the blood and skin window cell counts in respect of both neutrophils and eosinophils. In polycythaemic patients in remission, the skin window results were generally similar to the controls except in that basophils were increased.

The results provide no evidence of a quantitative defect in the cutaneous inflammatory reaction in polycythaemia vera, but suggest that the mechanisms underlying the basophilia may be worth investigating further.

The Influence of Oral Contraceptives on the Ratio of Factor VIII Activity to Factor VIII Related Protein

PENELOPE STABLEFORTH, MARGARET A. HOWARD, DANIELLE C. MONTGOMERY, MARY REAVLEY, ELAINE WILSON, WENDY L. CHURCHILL, KATHERINE M. DORMANDY, AND R. M. HARDISTY (*Hospital for Sick Children, London, and Royal Free Hospital, London*) Determination of the ratio of factor VIII activity to factor VIII related antigen (factor VIII RA) has proven to be a useful means of detecting carriers of haemophilia A.

Bouma *et al*¹ and Van Royen *et al*² have shown that during the last trimester of pregnancy the ratio of VIII activity to VIII RA is lowered due to an excessive increase in the level of VIII RA.

Oral contraceptives, like pregnancy, cause an increase in VIII activity but as the effect of oral contraceptives on VIII RA levels was not known, the present investigation was initiated between the Hospital for Sick Children and the Royal Free Hospital, London.

Twenty-four normal women taking oral contraceptives, age matched with normal women not taking the 'pill', were bled on three occasions at seven-day intervals.

The PT, PTT, and factor VIII activity were measured on fresh blood, and the VIII RA was measured by the Laurell technique using two different rabbit antibodies.

Early results indicate no appreciable difference between these two groups.

This suggests that, unlike pregnancy, oral contraceptives do not alter the ratio of VIII activity to VIII RA making it possible to diagnose haemophilia carriers taking oral contraceptives.

References

- ¹Bouma B. N., Sixma J. J., Van Mourik, J. A., and Mochtar, I. A. (1973). *Neth. J. Med.*, **16**, 54.