

# The Association of Clinical Pathologists

The sixty-eighth general meeting was held at the University College of North Staffordshire, Leeds, from 12 to 14 April 1962. The following are abstracts of papers read at that meeting.

## CAUSES AND PREVENTION OF URINARY INFECTION FOLLOWING CATHETERIZATION OF FEMALE PATIENTS

K. B. LINTON, N. SLADE, G. G. LENNON, and W. A. GILLESPIE (Bristol) Infection may be caused by organisms from a contaminated catheter, or from the urethra. With indwelling catheters, organisms from contaminated collecting vessels may be carried to the bladder by ascending air bubbles; or organisms may enter between the catheter and the urethral mucosa.

Two methods of preventing infection during intermittent catheterization were studied. In obstetric patients, terminal disinfection of the bladder with chlorhexidine, as described by Paterson *et al.* (1960), reduced the infection rate from 28% to 5%. In repeatedly catheterized gynaecological patients, disinfection of the urethra with chlorhexidine jelly, before catheterization, reduced bacillary infections from 52% to 17%, but did not affect *Strep. faecalis*. *Strep. faecalis* was less virulent and, unlike Gram-negative bacilli, rarely caused pyuria.

Infection nearly always followed open drainage by indwelling catheter. The organisms were often antibiotic-resistant hospital strains. The infection rate was reduced to 38% by draining urine into closed vessels containing formalin, and to 15% when, in addition, the catheter was anchored so as to prevent to-and-fro movement in the urethra.

## REFERENCE

Paterson *et al.* (1960). *J. Obstet. Gynaec. Brit. Cwlth.*, 67, 394.

## TELLURITE-EGG-YOLK AGAR AS A SELECTIVE MEDIUM FOR STAPHYLOCOCCI IN CLINICAL BACTERIOLOGY

V. G. ALDER and W. A. GILLESPIE (Bristol Royal Infirmary) described the use of a tellurite-egg-yolk agar medium in clinical bacteriology. The medium was first described by Innes (1960) for isolating staphylococci from foodstuffs.

It was found useful for detecting staphylococci in clinical specimens containing mixed organisms, such as sputum, wound swabs, etc., and in assessing aerial contamination by staphylococci using settle plates. More staphylococci were isolated on tellurite-egg-yolk agar medium than on blood agar because the medium inhibited the growth of Gram-negative bacilli. The main disadvantage of tellurite-egg-yolk agar medium in clinical bacteriological use is that it is highly selective for *S. aureus*. It will therefore detect small numbers of staphylococci in a speci-

men such as sputum and everything else will be suppressed. The significance of the staphylococci present in the specimens may therefore be exaggerated. A full 24 hours' growth is needed for the main growth characteristics of *S. aureus* to develop on tellurite-egg-yolk agar medium. It is therefore a useful adjunct to other media but does not replace them.

## REFERENCE

Innes, A. G. (1960). *J. appl. Bact.*, 23, 108.

## A CASE OF JUVENILE ARTERITIS

H. M. CAMERON (Stobhill General Hospital, Glasgow) A case was presented in which a bizarre and unexplained haematological state was associated with an unusual pathological process of unknown aetiology.

The patient, a boy who suffered repeated infections from birth, had a moderate leuco-erythroblastic anaemia, associated with a persistent lymphocytosis. The liver and spleen were enlarged, and splenectomy was performed at the age of 2½ years to relieve discomfort. Examination of the spleen and a liver biopsy showed extramedullary haemopoiesis. Plasma proteins were normal.

Necropsy, with subsequent histology, showed a chronic arteritis affecting the coronary arteries, the abdominal aorta, the interlobar arteries of the kidney, and the pulmonary arteries. There was also inflammatory involvement of pulmonary veins and a coronary vein, and foci resembling Aschoff bodies were found in the heart. The marrow was hypercellular.

## THE PROTEINS OF SEMINAL PLASMA

M. SYMONS, E. REES, and G. H. GRANT (Shrewsbury) Double diffusion and immuno-electrophoretic techniques were used to analyse the bands found on paper electrophoresis of seminal plasma, bands with mobilities similar to albumin,  $\alpha_2$ -,  $\beta$ -,  $\gamma$ - and post- $\gamma$ -globulins. The results (mounted as lantern slides) showed that they consist in part of proteins originating from the blood plasma but mainly of proteins specific to the genital tract.

It was confirmed that seminal plasma (like normal urine) contains a number of relatively low molecular weight serum proteins.

The specific seminal proteins were analysed by the use of antisera raised in rabbits by immunization with seminal plasma. Double diffusion analyses with these antisera suggested that the principal specific seminal

plasma proteins arise from the prostatic or seminal vesicle glands, that none of the specific proteins produced by these two types of gland are similar, and that the testis, epididymis, and bulbo-urethral glands contribute little if any to the soluble proteins of seminal plasma. In normal seminal vesicle fluids collected at necropsy some six components were distinguished, and in normal prostatic fluids collected at operation or necropsy some seven components, two of which, apparently of high molecular weight, were present in semen only in traces.

Comparative immuno-electrophoretic analyses of seminal plasma, prostatic fluid, and seminal vesicle fluid indicated the origin of many of these secreted seminal proteins and showed that the intense  $\beta$  band seen on paper electrophoresis was due to at least six components, the two principal ones arising one from the prostate the other from the seminal vesicles.

#### SECRETORY PROPERTIES OF PHAEOCHROMOCYTOMAS

M. K. ALEXANDER, D. F. BARROWCLIFF, A. P. PRIOR, R. ROBINSON, and P. SMITH (Warwick) The secretory properties of phaeochromocytomas were investigated in 13 patients with those tumours by studying their urinary excretion of 3-O-methyl catechols. The results suggested that the composition of the secretion discharged by these tumours may be more variable than is generally thought.

All the tumours secreted excessive amounts of noradrenaline: seven out of 13 also secreted large amounts of adrenaline. In three cases, more adrenaline than noradrenaline was secreted. Three patients also excreted the 3-O-methyl derivative of N-dimethyl noradrenaline, a catecholamine not previously described in man.

A malignant phaeochromocytoma secreted both adrenaline and noradrenaline. Six months after the primary tumour had been removed, functionally active secondary growths had developed which secreted only noradrenaline. The patient who had this tumour excreted increased amounts of methoxytyramine. In a larger series of 30 phaeochromocytoma patients whose urinary phenolic acids were studied, he was the only patient who excreted obviously increased amounts of homovanillic acid and the only patient with a malignant tumour. Since methoxytyramine and homovanillic acid are dopamine metabolites, these results suggest that malignant phaeochromocytomas secrete excessive amounts of dopamine.

The possible diagnostic significance of this finding requires further experimental work. It is suggested that the urines of all patients with phaeochromocytomas should be examined for dopamine metabolites.

#### CHEMICAL TESTS FOR PHAEOCHROMOCYTOMA

J. KELLEHER and G. WALTERS (Wolverhampton) Many patients with phaeochromocytoma present with sustained hypertension and with no special features to suggest phaeochromocytoma. To diagnose these cases it is necessary to estimate catecholamines or their metabolites more or less routinely in hypertension. The results of such estimations are not always easy to inter-

pret, since excretion of catecholamines and their metabolites has been found on occasion to be increased up to four times normal in the absence of a tumour. We have seen 11 such cases. This problem can often be resolved by carrying out further tests, but in some cases it is necessary to estimate both catecholamines and at least one metabolite since either may be raised to diagnostic levels when the other is within the false positive range. In patients who have no signs to indicate when secretion is occurring, the diagnosis can only be excluded by repeated examinations, and we suggest that in such cases several qualitative tests by a comparatively simple method such as Hingerty's method for catecholamines, is preferable to an accurate quantitative result if this can only be done once.

### SYMPOSIUM ON THE USE OF RADIOACTIVE ISOTOPES IN THE CLINICAL LABORATORY

#### THE ESTABLISHMENT OF A CLINICAL ISOTOPE LABORATORY

M. G. NELSON (Belfast) Nowadays tracer techniques using radioisotopes are being increasingly employed as diagnostic tools in clinical medicine. As a consequence many hospitals are contemplating the establishment of some facilities for utilizing radioisotopes diagnostically. As we have established such a unit in our hospital, our experience might be of value to others in indicating the organization and requirements for such a service.

We have developed our radioactive isotope service as a division of the hospital laboratory, making a fifth discipline in clinical pathology. The basic needs for such a service are:

- 1 A section to store, to check, to dispense, and to issue radioisotopes. This is called a hot room.

- 2 A section to assay radioactivity in biological fluids. This is called a radioactive assay laboratory.

These first two sections are clearly laboratory responsibilities.

- 3 A section to carry out clinical measurements on patients. Here 'uptake' counts are performed over the whole body or over body organs. This is called a radioactive uptake laboratory.

Dependent upon the work-load the unit may also require, apart from the space for clinical measurement, a waiting room and a room for dispensing doses. This latter section is a clinical unit with laboratory attachments. As patients are dealt with in this section it requires medical and nursing services.

The planning, instrumentation, and radiation protection needed for each section was described. The organization is based on technical responsibility being placed on the biophysicist, administration on the clinical pathologist, and policy on a radioactive isotope committee with broad representation. Studies of the work-load in relation to technical staff indicate the possibility of 30 assay procedures and eight uptake counts per technician per week.

There is an advantage in the centralization of the

radioactive isotope diagnostic service in a hospital. This saves duplication of equipment and makes the service available to all the hospital clinicians.

It is possible to establish a hospital isotope division in a modest way and to develop it. The requirements for even a minimal service are (a) official permission from the Medical Research Council to use radioactive isotopes for diagnostic purposes on patients; (b) laboratory space for instruments, washup, and shielded storage, which must be separate from the routine laboratory service; (c) basic counting equipment which can be used both for assay procedures and clinical measurements on patients. This consists of a collimated probe type scintillation detector and appropriate scaler; (d) a member of the medical or laboratory staff trained in the clinical use of radioisotopes and the counting equipment.

#### USE OF RADIOACTIVE POTASSIUM, SODIUM, AND OTHER AGENTS

M. LUBRAN (West Middlesex)  $^{24}\text{Na}$  is used to measure the 24-hour exchangeable sodium and 24-hour corrected sodium space,  $^{42}\text{K}$  measures the 24-hour exchangeable potassium,  $^{82}\text{Br}$  the 24-hour bromide space, and  $\text{H}_2\text{O}$  the total body water. Sodium and bromide spaces are closely related to extracellular fluid volume. Exchangeable sodium and potassium are best expressed in terms of total body water and then show less variation with sex and age than when expressed in terms of body weight. Simultaneous measurements of exchangeable sodium and potassium, bromide space and total body water can be made, giving data from which intracellular as well as extracellular ionic concentrations can be calculated.

#### THE PRACTICAL USES OF RADIOACTIVE IRON AND $\text{B}_{12}$

G. WETHERLEY-MEIN (St. Thomas's Hospital, London) In reviewing and evaluating the various uses of these isotopes in the clinical laboratory, it was emphasized that in the vast majority of patients a satisfactory diagnosis on which logical treatment can be based can be obtained by the use of established haematological techniques such as the M.C.H.C., reticulocyte count, and marrow examination. In a small number of patients the diagnosis will remain obscure and it is in these that analysis of the mechanism of anaemia in terms of red cell production, red cell destruction, blood volume, blood loss, and capacity to absorb iron and  $\text{B}_{12}$  is indicated.

The various available techniques using radioactive iron and radioactive  $\text{B}_{12}$  were considered and it was suggested that those most suitable for the investigation of the individual patient were the  $^{59}\text{Fe}$  utilization over seven to 10 days,  $^{59}\text{Fe}$  surface pattern, and the Schilling  $^{58}\text{Co}$   $\text{B}_{12}$  absorption technique. Against the background of a complete haematological examination these techniques, particularly if combined with a  $^{51}\text{Cr}$  red cell survival study, should make a considerable contribution to the resolution of problem cases.

#### IODINATED FATS AND PROTEINS IN THE STUDY OF GASTRO-INTESTINAL FUNCTION

M. LUBRAN (West Middlesex)  $^{131}\text{I}$ -triolein is easily prepared and may be used to study intestinal absorption of fat by measuring faecal, urinary, or blood radioactivity following an oral dose. Urinary radioactivity measurements are of little value in the diagnosis of steatorrhoea. Blood activity reflects fat absorption but normal activity curves may occur in patients with severe steatorrhoea. Methods of correcting these curves to improve their reliability introduce fresh uncertainties. Measurement of faecal radioactivity is the best guide to fat absorption and correlates well with chemical fat determination. However, most information is given by carrying out chemical and radioactive tests at the same time.  $^{131}\text{I}$ -oleic acid may be given to patients with poor absorption of triolein to diagnose pancreatic insufficiency. Comparison of the resulting curves is sometimes inconclusive because of the occasional poor correlation of plasma activity and fat absorption. Simultaneous administration of  $^{131}\text{I}$ -triolein and  $^{82}\text{Br}$ -oleic acid and the measurement of the ratio of  $^{82}\text{Br}$  to  $^{131}\text{I}$  in the plasma (double tracer test) give more reliable information on pancreatic insufficiency.  $^{131}\text{I}$ -labelled human albumin is given intravenously to study protein loss into the gastrointestinal tract. An anion exchange resin is given by mouth at the same time to pick up protein digestion products and prevent their reabsorption. The resulting faecal radioactivity measures the intestinal protein loss.

#### LABORATORY CONTROL OF ORAL ANTICOAGULANT TREATMENT

L. POLLER (Manchester) Both the 'extrinsic' and 'intrinsic' systems of thromboplastin formation are impaired during oral anticoagulant treatment. The Quick test measures only the extrinsic system. Results with the P and P and Thrombotest are different, but there is no evidence that this is due to sensitivity to additional clotting factors.

There appear to be three intensities of treatment represented by the 10 to 30% activity range: most intense therapy with the Quick test (using our own batches of human brain thromboplastin), intermediate with the P and P test, and least intense with the Thrombotest.

Much of the difference between the results arises from the use of saline dilution curves in the Quick test.

The Thrombotest gives reliable results with finger-prick blood samples although there are a number of disadvantages—contact-activation, duration of test, expense, and poor definition of end-point with group A bloods. Equally reliable results with finger-prick blood samples without these disadvantages are obtained with a combined home-made reagent consisting of adsorbed plasma, calcium, and brain. The therapeutic range with this reagent, like the Thrombotest, appears to be within the limits of 5 to 20% activity.

THE DIAGNOSTIC VALUE OF  
SERUM FOLIC ACID LEVELS USING  
*LACTOBACILLUS CASEI*

E. W. BALL and C. GILES (Stoke-on-Trent) Serum folic acid was estimated by a modification of the method of Waters and Mollin. The range in normal subjects is 4.6 to 12  $\mu\text{g./ml}$ . Results below the normal range are obtained consistently in megaloblastic anaemia of pregnancy and in intestinal malabsorption. During normal pregnancy the mean level is lower than in normal controls, and falls progressively as pregnancy proceeds. Epileptics receiving anticonvulsant therapy also have low levels: this is not due to the epilepsy nor to interference with the biological assay. In pernicious anaemia and iron-deficiency anaemia the levels are similar to those in normal controls. Many pregnant women and treated epileptics have very low serum folic acid levels, without developing megaloblastic anaemia; some additional factor must be involved.

Although not perfect, this test appears to be the simplest and best at present available for the routine detection of folic acid deficiency.

MALIGNANT CYTOLOGY AND THE  
CLINICAL PATHOLOGIST

T. D. S. HOLLIDAY (Chester) reviewed his experience of malignant cytology, using the Papanicolaou technique, over the past eight years. He examined 2,809 specimens, of which 364 (13%) were reported as malignant. Approximately one half of the specimens were sputa and one quarter cervical smears. Nearly 99% of malignant diagnoses were followed up. Malignancy was confirmed in 92% of these. Confirmation was by histological section in 45%, at necropsy in 7%, and by clinical means in 48%. The criteria for clinical confirmation were: Laparotomy, bronchoscopy, cystoscopy, radiological findings in conjunction with clinical course, or supporting clinical features followed by subsequent progression of disease, resulting in metastases or death, or necessitating radiotherapy.

Follow-up of negative sputum specimens showed the incidence of false negatives to be 31%. The average time spent in making positive diagnoses was eight minutes, and in making negative diagnoses 5.4 minutes. For comparison the average time spent on the microscopy of histological specimens was four minutes. Of sputa reported as malignant 27% were reported within two

minutes, 42% within five minutes, and 60% within 10 minutes. Prolongation of time spent increased the positive yield to an ever decreasing extent. It was deduced that 50 minutes microscopy was required to detect one malignant smear. Malignant cytology should be practised in conjunction with histology, and records, filing of slides, and regular follow-ups were vital to building up experience. Malignant cytology appeared to be worthwhile and was not unduly time-consuming.

PLUMBISM IN THE POTTERY INDUSTRY

A. J. MCCALL and C. R. KNAPPETT (Stoke on Trent) Several cases of lead poisoning were found during recent years in workers handling high solubility lead fluxes. Workers in a colour transfer factory were examined and though none showed serious effects from lead absorption, several workers showed anaemia with a haemoglobin level of less than 12.5 g./100 ml. due to lead. An undesirably high level of lead absorption was present in workers engaged in the process of 'flouring and dusting' transfers to remove excess powdered colour containing lead flux. The process was associated with a high lead content in air concentrations which were greatly reduced after improvements in ventilation.

THYROID AUTO-ANTIBODIES IN PERNICIOUS ANAEMIA

J. L. MARKSON and J. M. MOORE (Glasgow) The relationship between pernicious anaemia and Hashimoto's thyroiditis was investigated by testing the serum of patients with pernicious anaemia for the presence of thyroid auto-antibodies.

In a series of 78 patients with pernicious anaemia, the tanned red cell agglutination test was positive in 24% of males, in 25% of females, and, in titres of 1 in 2,500 or greater, in 9% of females; the thyrotoxic complement fixation test was positive in 26% of females. With the exception of the overall figure for the tanned red cell agglutination test in females the incidence of positive tests in these patients was significantly greater than in comparable controls. With the precipitin test a positive result was obtained in four women with pernicious anaemia while all the controls were negative.

It is considered that these results indicate an increased incidence of Hashimoto's thyroiditis in pernicious anaemia and that this relationship with a disease of disordered immunity may be relevant to the pathogenesis of pernicious anaemia.