THE ASSOCIATION OF CLINICAL PATHOLOGISTS

The 65th general meeting was held in London on September 29 and 30, and a joint meeting with the Association of Clinical Biochemists on October 1.

Abstracts of the papers follow:

Investigation of Virus Infections of the Central Nervous System

F. O. MacCallum (Virus Reference Laboratory, Colindale) said that a large number of known viruses can attack the central nervous system, sometimes causing inapparent infection, frequently meningitis or "non-paralytic" poliomyelitis, less often encephalitis or encephalomyelitis. Present techniques allow isolation of most of the known viruses more rapidly than tubercle bacilli but less rapidly than meningococci.

The full value of the virus laboratory will only be obtained if possible virus aetiology is considered in each patient investigated in hospital or at home and the appropriate specimens collected in the acute stage of the disease, not after all other tests have proved negative.

As no specific treatment for virus infections is available at present, tests which will identify possible bacterial pathogens obviously take priority, as does examination of the cerebrospinal fluid. If no organism is identified within 24 hours, then specimens for virus isolation and information on amounts of protein and cells in the cerebrospinal fluid, white blood count, temperature pattern, and a few pertinent points of clinical history should be provided for the laboratory. If the onset of the patient's illness is more than three weeks before admission, virus investigations are unlikely to be of value. (For specimens required and methods of investigation see Monthly Bulletin of the Ministry of Health and the Public Health Laboratory Service (1957) 16, 151.)

Virus may be found in throat, stools, and cerebrospinal fluid. Stools are the best source of virus in infections with polio (three types), Coxsackie (25–30 types), and ECHO viruses (more than 28 viruses). Throat swabs and particularly cerebrospinal fluid, when available, are necessary for mumps, L.C.M., loping ill, and herpes infections. Serum in the acute stage and 14–21 days from onset should be provided to verify the significance of the virus isolated, or for selected tests when no virus is isolated.

Hospital Conditions as a Factor in Hospital Cross-infection

L. Steingold and L. Vogel (London) reported that finding causes of hospital cross-infection, and devising methods of correcting faults so found, presented little difficulty. The difficulty lies in introducing such methods into the wards and theatres, and, even more, in seeing that they are continued indefinitely once they have been introduced. Over a whole hospital, this last seems to be impossible.

The reason for this appears to be poor staff morale. Staff are enthusiastic at first, but sooner or later lose interest and revert to their previous unsatisfactory techniques. A possible explanation lies in the conditions under which staff work in most hospitals. Advances in clinical techniques have not been accompanied by the necessary improvements in design, staffing, and equipment of hospitals.

The more obvious parts of a hospital are usually reasonably adequate. Thus, operations are usually performed in a reasonably adequate operating space, and patients are usually accommodated in reasonably adequate wards. The accommodation for other work, however, is often grossly inadequate. Thus, bathrooms, sluice rooms, dressing rooms, changing rooms, and storage facilities may be poor or absent. In addition cleaning and sterilization equipment may be out of date or makeshift.

It is felt that insanitary, unhygienic conditions like these result in insanitary, unhygienic practices.

Control of Staphylococcal Cross-infection in Three Surgical Wards

V. G. Alder and W. A. Gillespie (Bristol) said that cross-infection had been measured in three surgical wards for four years when 1.6% of wounds developed theatre staphylococcal infection, with suppuration. Initially, 40% of open, drained wounds were cross-infected by staphylococi in the wards, as demonstrated by repeated swabbing. Most ward wound infections were clinically "silent." The chief clinical manifestations of ward cross-infection were staphylococcal complications other than wound infection, e.g., pneumonia, enterocolitis, parotitis, furunculosis, from which 0.93% of patients suffered before special precautions were taken. Ward cross-infection was mainly due to multiple-resistant staphylococci.

The precautions tested were:
(a) Against Sources.—Prophylactic application of neomycin-chlorhexidine cream to noses of all patients, and chemoprophylaxis of open and drained wounds with a neomycin-bacitracin-polymyxin spray. (b) Against Vectors.—Disinfection of bedding, bath-water, barber's brushes, urine bottles, crockery, and nurses' hands.

Simultaneous application of all the precautions, in two wards, reduced open wound cross-infection by about two-thirds, and almost eliminated the other staphylococcal complications (pneumonia, etc.). There was a very marked reduction in multiple-resistant strains.
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In the third ward, a comparable improvement was obtained by disinfection of bedding and bath-water, together with nasal and wound chemoprophylaxis. The results suggested that the first three of these measures were of special value, but no single precaution was effective when used alone.

The same precautions were used successfully in outbreaks of staphylococcal infection in four other wards.

Punch Actinomycosis

H. I. WINNER (Charing Cross Hospital, London) described the case of a man who damaged the back of his right index finger hitting someone in the teeth. He was treated with penicillin for four days. Although the skin injury healed, the finger became swollen and painful, and remained so for three months. At the end of this time it became acutely inflamed. Radiographs now showed rarefaction of the head of the proximal phalanx. Open operation revealed much pus in the subcutaneous tissues, containing numerous "sulphur granules" in which Actinomyces israeli was identified.

After operation he was treated with penicillin and streptomycin for one week, thereafter with penicillin for four months. Uneventful cure followed.

Four similar cases have been found in the literature.

Investigations of the Serological Specificity of Atypical Acid-fast Bacilli

A. BECK (Paddington General Hospital, London) said that four cultures of photochromogenic mycobacteria which had been isolated repeatedly from patients with a disease resembling tuberculosis were compared serologically with the human tubercle bacillus strain H37Rv and with M. phlei and M. smegmatis. Antisera against these cultures were examined by the Middlebrook test using P.P.D. fractions of mycobacteria as antigens for red cell sensitization. Titration of these sera revealed marked cross-reactivity. By the use of absorption and inhibition techniques, however, a specific antigen could be demonstrated in photochromogens. In addition they were found to have a common antigen with the human tubercle bacillus strain H37Rv, and a third antigen which is shared by all the mycobacterial species examined.

These results supported the view that atypical acid-fast bacilli represent a special group of mycobacteria which is distinct from both tubercle bacilli and saprophytic mycobacteria.

Acute Mesenteric Lymphadenitis Due to Pasteurella pseudotuberculosis

N. S. MAIR and E. M. STIRK (Leicester) said that until a few years ago human infection with Past. pseudotuberculosis was generally regarded as rare. Between 1910, when the first case was described by Albrecht, and 1952, only 15 cases, most of them characterized by a severe typhoid-like illness, were reported in the medical literature.

In contrast with this severe but rare type of infection a benign and more frequent form is now recognized. About 170 cases have been reported in Germany and a few cases in Hungary and France. There are no references to similar cases in the English literature.

During the period May to October, 1959, 17 cases of mesenteric adenitis were investigated in Leicester for the presence of both virus and Past. pseudotuberculosis infection.

Specimens examined included mesenteric glands, appendix, throat swabs, faeces, and serum. Virus was not isolated from any of the specimens, but evidence of infection with Past. pseudotuberculosis was obtained in three patients. Past. pseudotuberculosis Type IA was isolated from the mesenteric glands of two of the cases, and all three cases showed serological evidence of infection with the organism. The mesenteric glands of two of the cases showed histological changes characteristic of pseudotuberculosis.

The source of infection could not be found in any of the cases, which did not appear to be epidemiologically related.

The Value of pH Adjustment of Urine in Chemotherapy of Urinary Tract Infections

W. BRUMPITT and A. PERCIVAL (London) described a method by which the effect of pH on the activity of antibiotics could be rapidly tested. This consists of buffering nutrient agar plates to pH 5.5, pH 7.0, and pH 8.0, and then carrying out sensitivity tests by the impregnated paper disc technique. These tests demonstrated that most antibiotics have an enhanced activity at acid or alkaline pH.

Growth, inhibition, and killing curves, carried out in nutrient broth, buffered to the appropriate pH levels and containing antibiotics, showed that the results found on solid media could be reproduced in broth.

For most antibiotics the favourable pH could be predicted, but not for all.

With the use of a number of harmless drugs, urinary pH can be varied over the range pH 5.5 to pH 8.5. Therefore, a trial was carried out to see whether adjustment of urinary pH to the optimum for an antibiotic improved the results of treatment.

Two similar groups of 103 patients, with acute urinary tract infections, were studied. One group was given the antibiotic of choice, based on ordinary sensitivity testing. The other group was given the antibiotic of choice, taking into account pH adjustment. In the latter group the urine was adjusted to the optimal pH before starting treatment. In both groups a five-day course of therapy was given.

By pH adjustment the cure rate (based upon bacteriological examination) was increased from 67 to 88%.

Finally, by pH adjustment and chemotherapy in 156 patients with acute urinary tract infections who had relapsed, cure was obtained in 125 (80%).

It is concluded that pH adjustment of the urine, combined with chemotherapy, gives improved results in the treatment of acute urinary tract infections, and
The Role of the Catheter in Causing Urinary Tract Infection in Pregnancy and the Puerperium

B. I. Davies and W. Brumfit (London) reported that in order to study the role of the catheter in causing infection 276 maternity patients were divided into three groups according to their catheterization history.

Group I contained 105 patients who had normal deliveries and were not catheterized.

Group II contained 66 patients who also had normal deliveries, but on whom a catheter was passed once.

Group III was composed of 105 patients in whom complications in labour necessitated catheterization.

Only patients whose urines on admission to hospital were uninfected were included in the series, and any subsequent infections were detected by frequent bacteriological and cytological examination of midstream urine specimens while they were in hospital, and, in addition, one month after discharge.

The sole criterion of infection was a urine bacterial count in excess of 100,000 organisms per millilitre. Such counts were usually, but not always, accompanied by leucocyte counts of 50 per c.mm. or more. Many infections were asymptomatic and would not have been suspected clinically.

The infection rates were: Group I, five out of 105 (4.75%); Group II, six out of 66 (9%); Group III, 24 out of 105 (22.8%). These results show that catheterization of the normal patient approximately doubles the risk of infection, whereas the complications of labour which compel the clinician to catheterize (Group III) greatly increase this danger. Certain of the reasons for catheterization carry an especially high risk, such as catheterization for retention of urine (40.6% infected), or investigation of puerperal pyrexia (36.4% infected), whereas catheterization preceding forceps delivery does not greatly enhance the danger (12.5% infected).

Of the 37 infections, 31 were caused by *Bact. coli*, the organism most commonly associated with primary, non-obstructive urinary tract infection.

Further Observations on Tumours of Salivary Tissue

J. Malcolm Cameron (Southern General Hospital, Glasgow) said that in a series of 401 examples of tumours of salivary tissue there were 315 cases of pleomorphic adenomata constituting 78.5% of the total. In addition there were 64 cases of carcinoma (16%) and 16 cases of adenolymphoma (4%).

The parotid gland accounted for just over 80% of the pleomorphic adenomata, 53.6% of which occurred on the right side, and there appeared to be a slight preponderance of females. Almost 60% occurred before the age of 40 years and 90% before 60 years of age. Most tumours grew slowly and intermittently and recurrences were noted in 30% following surgery.

Carcinoma occurred mainly between the fifth and eighth decade and again the parotid gland was the commonest site. The recurrence rate was much higher. All but one of the adenolymphomas occurred in the parotid gland, the one exception being in the right tonsil, bilateral adenolymphoma being found in four patients.

Attempts to produce tumours in experimental animals, similar to human pleomorphic adenomata, were described. In general these attempts were unsuccessful, as have been those of previous workers.

A Study of the Post-natal Anaemia in Erythroblastosis

P. S. Macfarlane, A. L. Speirs, and J. W. Whitelaw (Stirling) said that a series of 30 cases of neonatal anaemia due to Rh incompatibility, and including all grades of severity, had been studied. Full blood examinations were frequently performed and in most cases three specimens of bone marrow were examined.

It was concluded that although excessive red cell destruction is the prime cause of the anaemia another important aetiological factor is the inability of the marrow to produce red cells in the neonatal period. This is essentially a physiological condition, but it is acknowledged to be a significant factor in the causation of the anaemia of prematurity.

It seemed possible that the marrow inactivity might be due to nutritional deficiency and folic acid treatment was tried with only limited success. The alternative explanation is that at birth, when the marrow is invariably responding fully to the haemolysis, there is present in the baby’s blood a marrow-stimulating factor which later becomes deficient.

To test this hypothesis the Rh antibodies were absorbed from plasma obtained at exchange transfusion and the plasma was administered intravenously during the phase when red cell production was in abeyance. Significant reticulocyte responses were obtained. Similar results have been obtained using fresh frozen plasma.

These studies offer evidence that an important factor in the cause of the anaemia in erythroblastosis is deficiency of an erythropoietic stimulating factor.

The Practical Value of an Electronic Blood Cell Counter in a Routine Laboratory

C. H. Wrigley (Winchester) reported on an electronic blood cell counter installed two years ago at the Winchester laboratory. The machine is of the fluid flow type, first developed by Crosland-Taylor and later manufactured under the trade name E.E.L.

It was not considered that an electronic counter for counting red cells only was financially justifiable in a routine laboratory.

There had been two main difficulties in using the machine for counting leucocytes, but these had now been overcome.
The difficulties were: (a) The mechanical design of the jet chamber originally made adjustment of the jets difficult, but this had now been remedied by the manufacturers; (b) precipitation of a protein-like substance, which caused frequent blocking of the jets. This was overcome by adding ammonia to the circulating fluid, making the concentration 0.04%. During the last 12 months this machine regularly averaged 25 leucocyte counts per day. The time saved by the machine more than compensated for that spent on routine maintenance. Its great value is in relieving the technicians of the fatigue of visual counting.

It is considered that any laboratory carrying out more than 15 white cell counts on an average per day will benefit from one of these machines.

The Adhesiveness of Platelets

J. R. O'Brien (Portsmouth) described the following methods in the investigation of the adhesiveness of platelets in native whole blood to various surfaces:

Adhesion to Damaged Cells.—(a) The Ivy bleeding time (which may be influenced by other factors as well as platelet adhesiveness); (b) tissue cultures of human amnion cells grown in sheets were damaged by heating. Native blood was trickled over these cells and the number of platelets adhering was counted.

Adhesion to Glass.—Native whole blood was forced at a constant rapid speed through a tube packed with glass beads. The decrease in the platelet count of blood issuing from the beads compared with an initial count was a measure of how many platelets had stuck.

Aggregation.—Aggregation of one platelet to another to form clumps in native plasma was observed visually.

The platelets in blood from heparinized and "dindevan"-treated patients and from all the coagulation defects studied adhered normally to glass, and these patients have a normal bleeding time.

The following substances inhibited all three test systems in vitro: Cocaine, benadryl, quinine, cetyl tetra-ammonium bromide, cetyl pyridinium bromide (both positively charged detergents), and sodium citrate. The first two systems only were inhibited by sodium salicylate. Cocaine, benadryl, and quinine did not interfere with the clotting mechanism.

It was concluded that platelet aggregation is probably essential for clot retraction; that platelet adhesion is calcium dependent; that clotting and adhesion to cells or to glass are independent phenomena; that at least part of the mechanism of aggregation, which takes time, is different from that of immediate adhesion; that the adhesion of platelets in whole blood to glass and to damaged cells can be prevented by some chemicals. Those chemicals investigated were actively anti-adhesive in vitro only at concentrations that would be lethal in vivo. Since the rapid adhesion of platelets to "damaged" endothelial cells is probably an essential step in thrombus formation, it is possible that a harmless drug with anti-adhesive properties might prevent thrombosis.

Indigenous Amoebiasis

W. P. Stamm (R.A.F., Halton) drew attention to the chronic insidious nature of the clinical symptoms of the majority of cases of intestinal amoebiasis and to the further difficulty in diagnosis caused by an incidence of carriers of E. histolytica in the United Kingdom between 5 and 10%.

He thought that the fact that civilian routine laboratories did not report such a high incidence was due to direct microscopy of faeces not being practised as a routine and to inexperience in faecal protozoology of pathologists and technicians.

He emphasized the difficulties in identification of E. histolytica and illustrated with lantern slides appearances of E. histolytica when stained in faecal smears and histological sections by some of the methods most suitable for routine use.

He drew attention to amoeboma in the differential diagnosis of abdominal tumours, and warned against operating on a patient who had been overseas and presented with an abdominal tumour, without a careful examination of stool specimens.

He concluded by pointing out that although clinical amoebiasis was undoubtedly commoner in the United Kingdom than was generally recognized, symptomless infections were even more common and a zealous search for amoebae not followed by good clinical judgment could easily result in amoebophila amongst doctors and a consequent amoebophobia in their patients.

Eosinophilia and Tropical Disease

J. K. Mason (R.A.F., Halton) said that many of the conditions characterized by tropical acquisition, a prolonged course, and an associated eosinophilia, presented with vague clinical symptoms and might often be first indicated in the laboratory.

The finding of an eosinophilia in a person returned from overseas does not necessarily imply a tropical origin but should always excite a search for such a cause. The most frequently responsible organisms are the helminths. Of the intestinal nematodes, ascaris, ankylostoma and strongyloides were discussed in relation to symptoms and the occurrence of eosinophilia.

Infestation with filarial worms gives rise to a profound eosinophilia. Common methods of presentation in Europeans were described.

The occurrence of schistosomiasis in Europeans was discussed. The diagnosis should be made in all persons returning from an endemic area presenting with haematuria until it can be disproved. The diagnosis of the acute and chronic disease was discussed.

Tropical eosinophilia was described as a differential diagnosis of other chronic pulmonary diseases.

The frequent difficulty of demonstrating the causal organism in a case of unexplained eosinophilia was stressed and a plea made for a very thorough parasitic investigation in every case.
Pyrexia of Unknown Origin of Tropical Origin

R. Mortimer (R.A.F., Halton) said that the most important tropical disease likely to be encountered in the U.K. is malignant tertian malaria, which in its pernicious forms, particularly cerebral malaria, is still killing patients. The possibility of malaria should always be considered in any patient with a fever who had arrived in the U.K. from the tropics via central Africa about 10 to 14 days previously, with perhaps a history of an unscheduled night stop en route. There is usually no difficulty in demonstrating parasites in blood films in such cases, and, if found, the results should be phoned at once to the ward so that treatment can begin with the minimum delay. All patients with pernicious malignant tertian malaria should be treated as emergencies with intravenous or intramuscular chloroquine or intravenous quinine. Delay in treatment or treatment by mouth may result in tragedy. Case histories were described of deaths due to the various failures of diagnosis, treatment, and management, and the recognition of other types of malaria was discussed. Emphasis was placed on the need to think in terms of multiple diagnoses in relation to tropical diseases, and the presentations of kala azar, relapsing fever, brucellosis, and amoebic liver abscess and their clinicopathological diagnosis, were discussed. The pitfall of not considering syphilis, which in the tropics is often florid in character, was mentioned. In conclusion a plea was made for a more positive approach to the possibility of tropical disease occurring in patients in the U.K.

Diseases Encountered in Immigrants

K. R. Hill (Royal Free Hospital, London) said that, of 250,000 immigrants in the U.K., more than half were West Indians. Two main aspects of their background are (1) racial pattern, and (2) dietary malnutrition.

Negroes are preponderant but are mixed with Anglo-Saxon, Celtic, Chinese, East Indian, and Mediterranean immigrants. Sickle cell disease is present in 5 to 10% of the populace. Sickle cell anaemia (genotype S.S.) is easily recognized, but the trait (S.A. or S.C.) may be complicated by other haemoglobinopathies. All immigrants should have their blood tested for sickling.

Leukaemias, aplastic, hypochromic, and megaloblastic anaemias are common, but pernicious anaemia is rare. (This last statement may not be valid.)

Dietary malnutrition is reflected in kwashiorkor and hepatic veno-occlusive disease. Cirrhosis is shown in 3 to 4% of necropsies, and primary hepatic carcinoma associated with cirrhosis in 16% of all primary carcinoma.

Tuberculosis is very common and fungus diseases may be encountered.

Syphilis and gonorrhoea are very common; S.T.S. is positive in 30% of hospital cases. The early stages of yaws are unlikely to be encountered, but the later stages of scarring and deformity may cause confusion.

The Negro has a fibrous diathesis and there is a high incidence of keloids, fibromyomata, and osteogenic fibromata of the jaw.

Lymphogranuloma venereum is common and the L.G.V.C.F.T. is positive in 30%. This test, and S.T.S., should be carried out in all immigrants.

Atherosclerosis, particularly of the coronary arteries, is common; myocardial infarction is uncommon. Hypertension is very prevalent and this is associated with a high incidence of nephritis. Streptococcal infections are prevalent and rheumatic fever not uncommon.

The West Indian does not withstand operative trauma very well and post-operative circulatory collapse is not uncommon. This may be related to the fact that the adrenals (cortices) are about two-thirds those of Europeans. At operation there is often a hyperglycaemia which may be related to an unstable carbohydrate metabolism. A special Jamaican type of diabetes has been described. Malaria may be encountered, as may be microfilaria, as an incidental finding in the blood.

Pathogenesis of the Malabsorption Syndrome

A. C. Frazer (The Medical School, Birmingham) said that the primary aetiologic factor in the malabsorption syndrome may be faulty intraluminal preparation for absorption, due to lack of pancreatic enzymes or bile salts, or incoordination of gastrointestinal function. A secondary enteropathy may be superimposed in such patients, due to electrolyte imbalance or bacterial infestation. A primary enteropathy may arise from gluten intolerance, folic acid deficiency, bacterial infestation, or small intestinal disease, or to a combination of two or more of these factors.

A deleterious agent can be demonstrated in wheat gluten which inhibits small intestinal motility by interference with acetylcholine release. This substance is ultrafiltrable, heat-stable, resistant to peptic/tryptic digestion, but its action is destroyed by incubation with small intestinal mucous membrane extract. Gluten or appropriate fractions cause deterioration in patients in remission on a gluten-free regimen. Gluten intolerance may be a major or a secondary aetiologic factor.

Folic acid deficiency is an important feature of sprue; the cause of the folic acid deficiency has not yet been satisfactorily established. Folic acid deficiency may occur as a secondary complication of gluten-induced enteropathy.

Bacterial infestation of the small intestinal lumen may be a major factor, as in gastro-colic fistula and blind-loop syndromes; it may also play an important part in other forms of the malabsorption syndrome.

Small intestinal disease, such as regional enteritis, lymphatic obstruction, or Whipple's disease, may be associated with the malabsorption syndrome.

Whatever the cause of the malabsorption, unabsorbed food materials pass into the lower reaches of the bowel and give rise to increased bacterial
activity. The flora modify many of the faecal constituents. In some cases significant amounts of fat and nitrogen that are not of direct dietary origin may be found in the stools.

The Use of Fat Labelled with $^{131}$I in the Diagnosis of Steatorrhoea

M. Lubran (West Middlesex Hospital, London) said that absorption of fat from the intestine could be investigated satisfactorily by measuring the faecal radioactivity for four days after the oral administration of 10 $\mu$C of $^{131}$I-triolein. Of 183 tests carried out simultaneously with a six-day chemical fat determination, complete agreement between the two tests was found in 139 (76%) of tests and borderline agreement in a further 44 (13.7%). The radioactive and six-day chemical fat tests are about equally effective in detecting steatorrhoea. However, because of the fluctuations in the faecal excretion of fat in steatorrhoea, it may be necessary to carry out daily faecal fat measurements for a prolonged period. Radioactive fats are not suitable for long-continued measurements.

Blood levels of radioactivity following oral $^{131}$I-triolein are not a satisfactory guide to steatorrhoea because of the wide range of values in normals and the normal values obtained in some patients with steatorrhoea. Urinary radioactivity measurements are also unsatisfactory in the diagnosis of steatorrhoea. Administration of $^{131}$I-oleic acid and measurement of blood radioactivity after a previous abnormal curve with $^{131}$I-triolein may be of limited value in the diagnosis of pancreatic disease. Simultaneous administration of $^{38}$Br-oleic acid and $^{131}$I-triolein and the study of the ratio of $^{38}$Br to $^{131}$I in the blood two, four, and six hours later provides a promising test of pancreatic function.

The d-Xylose Excretion Test and its Use in the Diagnosis of Malabsorption

W. T. Cooke and Dorothy Fowler (Birmingham) said that the five-hour urinary excretion of d-xylose after the oral ingestion of 25 g. of d-xylose was a useful test in the diagnosis of disorders of the small intestine. Their mean value for 37 fasting normal subjects under the age of 65 years was 7.2 g. (S.E. 0.27) and for nine normal subjects over 64 years 2.9 g. (S.E. 0.10). Thus, a low result in patients 65 years and over is of little diagnostic significance. The normal results of the other workers were shown and the possible reasons for the discrepancies found discussed. The lower limit of normal was set at 4.2 g. d-xylose in the five-hour urine, i.e., 7.2–2.0 S.D. Results from 194 patients were presented. Of these, 49, under 65 years of age, had xylose excretions of less than 4.2 g. Thirty-two of the 49 were "idiopathic steatorrhoea," most having been confirmed by jejunal biopsy. The 17 remaining patients under 65 years of age who had five-hour urine xylose excretions less than 4.2 g. were discussed. Two were aged 61 and 64 years respectively, another was suffering from tropical sprue, one had a past history of steatorrhoea, and four were excreting between 3.8 and 4.0 g. xylose. Fourteen patients with "idiopathic steatorrhoea" had five-hour d-xylose excretion results of 4.2 g. and over. Of these, five had been on gluten-free diets for one year or more and had responded well. The other nine were discussed. Of 15 patients with pancreatitis, only one, a woman of 68 years, excreted less than 4.2 g. Results from patients with various other gastro-intestinal disorders were discussed.

Comparisons of five-hour urine xylose excretions with faecal fat excretion and folic acid excretion tests were presented.

Total Body Electrolytes in Intestinal Disease

J. P. Nicholson and J. F. Zilva (Westminster Hospital, London) had measured the total exchangeable sodium and potassium values in 19 patients suffering from intestinal diseases, particularly ulcerative colitis. The experimental method and determination of normal values were described.

Generally speaking, the exchangeable sodium values were within the normal range whilst the exchangeable potassium values were well below the normal limits. The picture is complicated by the fact that steroids are frequently used in the treatment of these conditions.

Further information may be obtained by considering the two values in conjunction, i.e., the sum of sodium and potassium, and their ratio.

The mechanisms involved were discussed and some suggestions put forward as to the way in which the potassium loss might be minimized.

Blood Volume and Plasma Protein Levels Before and After Gastrectomy

Alexander Swan, Geoffrey T. Allen, and Norman C. Tanner (London) said that blood volumes were estimated by the dye method using Geigy blue pre-operatively, nine or ten days post-operatively, and again six or seven months after operation, in a series of cases of partial gastrectomy and vagotomy and a small number of those of pyloroplasty and radical gastrectomy. Plasma proteins were also determined in a large proportion of these cases. The following trends were observed.

1. Patients with peptic ulcer are, as a rule, underweight and show a deficit of blood volume which is due more to shortage of red cells than to that of plasma.

2. The red cell deficit is further aggravated by the operative blood loss and tends to persist, being still demonstrable six to seven months after operation. Patients who received blood transfusion (two pints on the average) at or immediately after partial gastrectomy showed no appreciable reduction of the total red cell volume (T.R.C.V.) after operation as well as higher T.R.C.V. levels than cases operated on without blood transfusion six months after.

3. Haemoglobin and haematocrit values do not adequately reflect either the pre-operative T.R.C.V. deficit or its post-operative variations, at times showing
a change in the opposite direction to that of T.R.C.V.

(4) A small number of cases with the dumping syndrome gave no reason for belief that this condition is associated with a reduced blood volume.

(5) Plasma globulins rose after partial gastrectomy (10 days after). This was accompanied by a marked fall in the albumin fraction, so that the total plasma proteins fell. Six months after operation the total albumin circulating mass tended to rise to levels exceeding the pre-operative, whereas the globulins dropped almost to the pre-operative state. This was not reflected in the protein concentration figures, those of the albumin remaining far below the pre-operative levels.

Separation and Determination of Some Basic Substances in Urine by Ion Exchange Chromatography

S. Tompsett (Edinburgh) said that the cation exchange resin, "dowex 50 × 12," has been used for the separation of a number of basic substances from urine as a preparatory to colorimetric analysis or identification by paper chromatography. Concentration may be achieved, and by using gradient elution (varying concentrations of hydrochloric acid) specificity is increased. Some reference was also made to elution by ammonia.

The use of the anion exchange resin, "dowex 1," for the separation of some basic substances from urine was also referred to.

A New Approach to the Estimation of Ammonia in Blood

J. C. B. Fenton (St. Bartholomew's Hospital, London) gave a brief review of the analytical techniques used for blood ammonia estimation. Almost all methods used for the isolation of ammonia depend upon the volatility of this compound in alkaline solution. It is generally agreed that some ammonia is falsely produced under these conditions, and it has never been positively shown that the ammonia estimated in blood is not entirely an artefact derived from the alkaline hydrolysis of unstable nitrogenous substances. The lack of agreement as to what constitutes a normal value reflects the generally unsatisfactory state of the topic.

An alternative technique which circumvents some of these objections was put forward. This employs ion exchange at a neutral pH of separated heparinized plasma. The ammonium ion can be isolated by adsorption on to a sulphonic acid type ion exchange resin in the sodium cycle and eluted by a strong solution of sodium chloride. After treating the eluate with aluminium hydroxide the ammonia content is estimated by means of an indophenol blue colour reaction. The technique is sensitive and levels down to 10 μg. NH₃ nitrogen/100 ml. can be estimated with ease.

The whole process of separation of the plasma and ion exchange is carried out under ice-cold conditions. Under these circumstances no rapid rise in the ammonia content of plasma over the course of several hours has been found. Normally the ammonia content of plasma appears to be less than 50 μg./100 ml.

Lipaemia, Coagulation, and Thrombolysis in Ischaemic Heart Disease

D. C. O. James, J. Drysdale, J. D. Billimoria, and N. F. MacLagan (Westminster Hospital, London) reported comparisons of lipaemia, coagulation, and thrombolysis made between 28 normal subjects, 24 with angina pectoris and 34 with myocardial infarction. All subjects were in the age group 40 to 70 years. The normals were healthy subjects showing no evidence of ischaemic heart disease, hypertension, nephritis, diabetes mellitus, xanthomatosi, or thyroid disease and all had a normal E.C.G. The tests were carried out under standard conditions, with and without inclusion of butter in the test breakfast.

Under fat-free conditions the lipaemia in normal males under 40 years of age was significantly higher than in normal females under 40. Significant differences from normal were noted in the pathological groups; thus the angina pectoris group showed a higher lipaemia, a shorter Stypven time, and a longer thrombolysis time, while the myocardial infarction group showed similar trends but the differences from normal were less significant.

The differences due to inclusion of 1 ½ oz. of butter in the test breakfast were not sufficiently significant to justify the use of fat-feeding tests in the investigation of ischaemic heart disease.

The effects of anticoagulants (phenylindanedione) were studied, and these caused a decrease in the lysis time. The time interval between myocardial infarction and the tests did not seem to influence the results.

The results as a whole indicate some disturbance of plasma lipids and of coagulation and thrombolytic mechanisms in ischaemic heart disease which were much more significant in angina pectoris than in myocardial infarction.

17-Hydroxycorticosteroid Excretion in Patients with Peptic Ulceration

A. G. Green and C. N. Pulvertaft (York) described how, using a modified Appleby, Gibson, Norymberski, and Stubbs technique, the excretion of total 17-hydroxycorticosteroids (17-HCS) had been studied in patients suffering from peptic ulceration and in normal controls.

The mean excretion of 17-HCS for 90 men with active duodenal ulcers was found to be 8.8 mg./day, significantly lower than that of 52 normal men (11.6 mg./day), the age distribution for these groups being very similar. Twenty-eight men with active gastric ulcers had a mean output of 7.8 mg./day; 40 men who had undergone partial gastrectomy for duodenal ulcer some 10 to 15 years previously showed a mean output of 7.8 mg./day; the mean for 29 men with duodenal ulcers in a quiescent phase was again 7.8 mg./day. For these three groups the mean age was slightly higher than that of the controls and the active
duodenal ulcer group. Very little difference was found in the excretion of 17-ketosteroids between the control and duodenal ulcer groups. The excretion of 17-ketosteroids in the gastric ulcer and post-gastrectomy groups was slightly lower than in the control group.

In the active ulcer group a definite correlation was noted between 17-HCS excretion and the volume of urine (D.U. r = 0.52; G.U. r = 0.49). A similar correlation was found for the post-gastrectomy group (r = 0.54). This finding was not observed in the controls (r = 0.11) and the quiescent ulcer group (r = 0.23).

The excretion of 17-HCS was estimated before, and six months after, partial gastrectomy for peptic ulceration, in 18 men. In 13 of these the post-operative excretion was less than the pre-operative level, the mean falling from 9.9 to 6.9 mg./day. A similar observation for 17-ketosteroid excretion was noted in 23 out of 28 cases, the mean falling from 11.4 to 8.3 mg./day. This fall was not observed after vagotomy and gastroenterostomy (23 cases) when there was very little difference in the pre- and post-operative levels.

**Experience with the Estimation of Serum Protein-bound Iodine**

D. R. C. Willcox and W. G. King (Bethlem Royal and the Maudsley Hospital, London) gave an account of the use and control of a method of estimation of serum protein-bound iodine (P.B.I.) slightly modified from that of Grossman and Grossman (1955). The results over a period of five years were summarized and their clinical significance discussed.

Precautions against contamination and the advantages of universal containers for the ashing stage were described. The effect of various ashing temperatures and of subsequent complete solution of the ash was shown. The use of standards carried throughout the whole procedure was considered essential. Recovery experiments estimated 95–98% of thyroxine added to serum precipitates. In routine use consistency of results was further checked by repeating one estimation from the previous batch on each occasion. The S.D. of the differences between such repeated estimations is 0.44 μg. per 100 ml.

In considering the results of some 2,000 duplicate estimations, 51 normal subjects gave a range and mean in close agreement with those originally described. It was shown that the distribution of values in euthyroid psychiatric and in euthyroid general hospital patients differs little from the normal, although there is a very small overlap with the hypothyroid and hyperthyroid groups, which are clearly separated from the normals. The general stability of thyroid function was demonstrated in serial studies, but some exceptions were quoted. The relationship to adrenocortical function and to mood or psychiatric diagnosis was considered. The results from 60 carcinomatosis patients submitted to hypophysectomy were also discussed.

**Reference**
