ASSOCIATION OF CLINICAL PATHOLOGISTS: 51st GENERAL MEETING

The fifty-first general meeting of the Association of Clinical Pathologists was held in London on October 1, 2, and 3, 1953, at the Westminster Hospital Medical School. For the first session on October 1 the chair was taken by Professor Matthew J. Stewart, C.B.E., and by Colonel L. R. S. Macfarlane, O.B.E. Professor R. Knox was chairman at the third session. Summaries of the scientific papers follow.

The second session was concluded by a film by Professor R. J. V. Pulvertaft and Dr. J. G. Humble on "Myelomatosis and Other Malignant Conditions of Bone."

Colitis Cystica Profunda

Dr. H. B. Goodall said that cystic enlargement of the mucous glands of the colon was rare. There were, however, two quite distinct types, the superficial, colitis cystica superficialis, as in pellagra, and the deep, colitis cystica profunda.

Colitis cystica profunda is characterized by the formation of mucous cysts in the submucosa associated with peculiar breaches in the muscularis mucosae. Involvement of the lymphoid follicles appears to be significant here. As these lymphoid aggregates are situated just deep to, or are intimately mingled with, the muscularis mucosae, abscess formation in the follicles may lead to breach of the muscularis mucosae, with the formation of penetrating "follicular" ulcers. Healing of these ulcers is accompanied by a downgrowth of epithelium resulting in the formation of deep, irregular, mucus-secreting glands. The accumulation of mucus in these crypts leads to the cystic change.

Colitis cystica profunda has been described in association with chronic bacillary dysentery, non-specific ulcerative colitis, tuberculous colitis, and carcinoma coli.

Dr. Goodall demonstrated operation material from two cases, the first patient having suffered from macrocytic anaemia and mucous diarrhoea followed by pelvi-rectal obstruction, the second from chronic ulcerative colitis with severe bleeding. In neither case were pathogenic organisms found.

A Naturally Occurring "Experiment" in Two Cases of Hypertension

Dr. G. J. Cunningham described two cases of clinically diagnosed malignant hypertension, together with the necropsy findings. Each case was found to possess aberrant renal vessels, one of which had become obstructed by a thrombus. The parts of the kidney supplied by this vessel showed mild hypertensive arteriosclerosis, while the remainder, supplied by patent vessels, contained necrotic lesions of both arterioles and glomeruli. On histological grounds the thrombus was considered to be mostly of recent formation, but some underlying atheroma had produced a measure of obstruction which was probably responsible for preventing severe lesions in the area supplied by it. The aberrant vessels were normal in appearance. The similarity of these findings to those of Byrom and Wilson in experimental hypertensive rats was emphasized.

Current Status of the Clinico-pathological Correlation of Naevi and Malignant Melanomas

Dr. Sophie Spitz and A. C. Allen said that they had analysed the clinical data of 934 patients with malignant melanomas. Of these, the histological slides of the primary lesions in 337 cases were available. Compared with their respective surface areas, there was a disproportionately greater incidence of primary melanocarcinomas on the soles of the feet, the mucosa of the female genitalia, and the head and neck region. The diagnosis of primary melanocarcinoma could not be made unequivocally in the absence of overlying junctional change. It is by the use of the criterion of the junctional change that multiple primary melanocarcinomas may be detected in the same individual. In this study 12 such instances (3.6%) were noted among 337 patients. The prognostic importance of the distinction of a second primary melanocarcinoma from a metastasis was emphasized.

Four instances of malignant blue naevi were observed in the files of the Memorial Hospital. The criteria for their histological differentiation from the benign cellular blue naevi were detailed. The slides of two additional cases from other institutions were submitted for opinion.

Five instances of melanocarcinomas of children were diagnosed; two of these were from other institutions. In each case it was possible to differentiate the histological pattern from that of the benign juvenile melanomas.

Lesions in adult life were not infrequently erroneously diagnosed malignant melanomas although they were actually benign juvenile melanomas that had persisted beyond puberty. Puberty was not necessarily the diagnostic demarcation. The superficial melanocarcinomas, as a group, have an appreciably
The Structural Features of Epiloia

Dr. L. Crome described structural abnormalities in epiloia which are found in the brain, skin, heart, kidney, lungs, bones, and, occasionally, other organs. The common lesions are tuberous sclerosis of the brain, adenoma sebaceum of the face, purkinjeoma (rhabdomyoma) of the heart, renal tumours, and phacoma of the retina. Incomplete forms of the disease are also seen, particularly among the relatives of the patients. Two cases of fibroelastosis of the heart were encountered in the present series, and another two cases had been previously recorded in the literature. (This association may prove to be more frequent if attention is paid to it in future studies.) Fibroelastosis has also been seen in association with other diseases and cannot therefore be regarded as a specific change occurring in only one disease.

A Syndrome Associated with Intestinal Spirochaetosis

Dr. A. G. Shera said that this syndrome, hitherto unrecognized, consists of a persistent, relapsing diarrhoea. Usually chronic, rare acute cases have been encountered in children, with vomiting, pyrexia, and prostration. The diarrhoea tends to be of the early morning, explosive type with foetid, yellow stools, often blood-streaked.

Anorexia, indigestion, and intense flatulence, with lower abdominal pain and tenderness, are classical. Chronic cases lose weight. Some show nervous signs, namely, lassitude, undue sweating, and mental depression. Tympanites, with tenderness in the inguinal fossae, chiefly the left, are usual, and gingivitis or tonsillitis with Vincent infections are the rule, but may be missing in chronic cases, having disappeared.

The Vincent-fusiform infection passes the acid barrier of the stomach, assisted by hypochlorhydria in many cases and finally, with a vitamin-C deficiency leading to bruising of the bowel, produces one or more lesions of a finely granular proctitis or sigmoiditis, designated the "strawberry lesion," most often at the recto-sigmoid junction or a few inches above or below. In acute cases the whole bowel appears by sigmoidoscopy to be uniformly and intensely engorged. Diagnosis is by (1) faecal films stained by silver impregnation; (2) sigmoidoscopy and swabbing of the "strawberry lesions"; and (3) a vitamin-C saturation test.

Spirochaetes and fusiforms will be found, perhaps sparsely in (1), but in dense masses in (2), from which they have been cultured. Feeding guinea-pigs on a low vitamin-C diet mixed with Vincent gingivitis pus has produced caecal Vincent ulcers.

Such cases are designated as "primary spirochaetosis" in contrast to "secondary spirochaetosis" following dysentery, lambliasis, or neoplasms. These do not lack vitamin C.

Treatment is specific and effective and consists of giving "stovarsol" (oral) 0.25 g. twice daily for two 10-day courses together with vitamin C.
The incidence in the Eastbourne Hospital Group in the period January, 1945, to September, 1953 (inclusive), was 45 cases, i.e., approximately one case every two months.

Mode of Action of Staphylococcal Coagulase

Dr. E. S. Duthie said that staphylococci produce two kinds of coagulase, bound and free, which differ in their occurrence, mode of action, and antigen properties. Bound coagulase acts directly on the fibrinogen of certain animals and is responsible for the slide test. Free coagulase is liberated in the culture medium and clots any fibrinogen, provided that an activator (presumably a susceptible prothrombin) is present. This is the basis of the tube test for coagulase.

Bound coagulase is liberated in autolysis and its presence can be shown by an antibody inhibition test. Encouraging results have been obtained in the treatment of recurrent staphylococcal infection in man with a vaccine made from free coagulase, and it was now proposed to use this in combination with bound coagulase.

Laboratory Investigation of Poliomyelitis

Dr. G. L. Le Bouvier said that the new cultural and serological techniques for poliomyelitis research were being used to study the distribution of virus types isolated from paralytic patients in different parts of the country and the serological response of these patients. Eighteen of the strains isolated since 1946 have so far been typed and include nine of Type 1, four of Type 2, and five of Type 3. Three of the Type 2 strains were isolated this year from unrelated paralytic cases. No results of neutralization tests are yet available, but a number of sera have been examined in complement-fixation tests, using antigens of all three virus types. With a few of these, especially from infants, the antibody response appeared to be comparatively type-specific, but most patients' sera reacted with antigens of more than one type. The test, at any rate in its present form, will probably be of little routine diagnostic value, although it may well have its uses in virological and epidemiological research.

On the second day of the meeting the chairman at the first session was Dr. J. V. Dacie, at the second Dr. A. Durupt, and at the third Professor R. J. V. Pulvertaft, O.B.E. On the afternoon of October 2 a film on “Marrow Puncture” was shown by R. G. Macfarlane, and 11 demonstrations were on view. In the evening Professor Dorothy S. Russell gave the presidential address on “Further Advances in Pathology.”

The Diagnosis and Treatment of Christmas Disease

Dr. J. R. O'Brien said that the diagnosis was established first by a clinical history identical with that of haemophilia.

Laboratory tests show, as in haemophilia, a long clotting time (but in some cases it may be normal), an abnormal prothrombin consumption, a delay in thrombin generation—even in those cases with a normal clotting time—and correction of the defect by normal plasma. The thromboplastin generation test will reveal whether the fault lies with the serum factors, amongst which is the Christmas factor, or the alumina-treated plasma fraction containing the antihaemophilic globulin. Once plasma from proven cases of haemophilia and Christmas disease is available, the fact that a tenth part of plasma from either disease will correct the plasma defect in the other enables the diagnosis to be made easily.

Treatment in general is that of haemophilia, except that any blood products transfused must contain Christmas factor and need not contain antihaemophilic globulin.

A single patient was intensively studied during five months, during which time he had a number of alarming haemorrhagic episodes for which he received stored bank blood, fresh plasma, reconstituted plasma, and serum. It was shown that the clotting time and prothrombin consumption were comparatively easily restored to normal, but that considerably more fluid was needed to restore the thromboplastin generation to normal. On several occasions bleeding continued when the first two tests were normal: but bleeding usually stopped when the thromboplastin generation was normal (the prothrombin consumption index was then usually less than 10%). All the fluids mentioned appeared equally effective and this man usually required 4 pints completely to correct his blood: the effect was maintained only for 24 to 48 hours.

Myelosis Involving the Granulocytic and Erythrocytic Systems

Drs. George Discombe and Kenneth H. Nickol said that uncontrolled hyperplasia of granulocytic precursors and erythroblasts, accompanied by release of primitive cells into the blood, was a rare phenomenon which had been described as leukaemia or erythroleukaemia. Hyperplasia, apparently confined to erythroblasts, was often regarded as a disease process sui generis and termed erythraemic myelosis.

Free use of blood transfusion has prolonged the life of patients with some of these syndromes, and allowed the pathological process to progress further, as illustrated by the following case: A man aged 72 was admitted with six months' history of increasing weakness, dyspnoea, and precordial pain on exertion: haemoglobin was 4.7 g. and 26,200 erythroblasts were present in each c.mm. of peripheral blood: the leucocyte count was 2,300 per c.mm. and there were 800 "blasts" per c.mm. The marrow showed erythroblastic hyperplasia with 71% erythroblasts; there were 0.5% myeloblasts, 9.5% progranulocytes, and 10% more mature granulocytes. A haemorrhagic state developed, and, though anaemia was controlled by transfusion, the patient died with cerebral haemorrhage seven weeks after admission. Erythroblasts and other "blasts" fell during the first five weeks, but
during the last two weeks of life the leucocytes rose to 10,000 per c.m.m., of which 1,500 were “blasts.” Marrow aspirated half an hour after death contained 13% myeloblasts, 31% progranulocytes, 24.5% neutrophil myelocytes, 10.5% more mature granulocytes, and 18% erythroblasts, a picture resembling acute granulocytic leukaemia.

It is suggested that acute granulocytic leukaemia sometimes has an erythroblastic onset, and that it may be impossible to differentiate between erythroblastic myelosis (should such an entity exist) and acute leukaemia, with an erythroblastic onset. Since nothing is known of the pathogenesis of these diseases, it may be desirable to group them together instead of subdividing them.

**The Distribution of the Sickle Cell Trait**

Dr. H. Lehmann said that when the sickle cell trait was discovered in American negroes it was thought to be a common negroid feature; however, the incidence of the gene is most variable in Africa. In Uganda it is about 20% in the Nilotic speaking tribes but almost nil in those speaking a language related to Hamitic, and it varies in those speaking Bantu. In the Bantus it is in inverse proportion to the degree to which they were in contact with the recent “Hamitic” invaders. All over negroid Africa the highest incidences are found in the north and east, they fall somewhat towards the west, and diminish towards the south; in South Africa itself the trait is virtually absent. Thus it might seem that the trait came from Asia, and indeed in contrast to the Semitic Arabs a Vedoid community of southern Arabia has been found to have a high sickle cell trait incidence without showing a similarly high frequency of the typically negroid Rhesus chromosome Rh±. In India again the Vedoids among the pre-Dravidians have a high sickle cell trait incidence, but Rh± is absent. These Indian Vedoids have a high frequency of the Australoid Rhesus chromosome Rh± but no sickle cells could be found in Australian aborigines. The Negritos of Asia do not show the trait. A last remnant of pure Negritos in the little Andamans was specially examined. In Europe some sickle cell trait carriers are found in Italy, and a few isolated pockets with a high incidence—each a few hundred strong—exist in Greece. Wherever the sickle cell trait is frequent there is malaria and a low social status involving close inbreeding.

Recent work has shown common immunological properties between the red cells of the newborn and of patients with sickle cell anaemia and of cases of thalassaemia major and also of some cases of the sickle cell trait and thalassaemia minor. The lethal tendency of a gene potentially causing sickle cell anaemia may thus be counteracted by its conferring a resistance to malaria similar to that found in early infancy.

**Serum Flocculation Tests and Sternal Puncture in the Diagnosis of Myelomatosis**

Dr. J. G. Humble and Professor N. F. MacLagan described the results found in myelomatosis using serum flocculation test and sternal puncture findings. The results in 18 cases were examined. Of these, 13 showed the abnormal cells in the marrow, 14 showed an increase in total serum globulin, 12 cases showed abnormal serum flocculation tests, and in nine of these the phenomenon of “dissociation” of these tests occurred. Using the serum colloidal gold, the thymol turbidity, the zinc sulphate, and the ammonium sulphate tests it was shown that any of these tests could be positive while the others were negative.

Taking the results together it was shown that one or other test was positive in 17 out of 18. The remaining case, with normal serum and sternal puncture findings, had a solitary tumour of the femur proved by biopsy and treated by irradiation. The patient was alive and well seven years later. The wide range of plasma cell types found in the marrow in this condition was demonstrated to show the difficulties met with in some cases.

**The Incidence and Significance of Iron-containing Granules in Human Red Cells**

This paper by Drs. A. S. Douglas and J. V. Dacie is published in full on page 307.

**A.C.T.H. and Adrenaline Tests in Burned Patients**

Dr. S. Sevitt said that the blood eosinopenia after burning was a reflection of adrenocortical hyperactivity. To determine whether acute adrenocortical failure had occurred after the eosinophils had returned, stimulation tests using A.C.T.H. (usually 25 mg.) or adrenaline (0.3 mg.) were performed on 21 patients recently severely burned. The tests were based on eosinophil counts made before injection and hourly thereafter for four or five hours.

Twelve of the 14 patients tested with A.C.T.H. gave normal eosinophil depression curves (maximum fall 60% to 87%) indicating normal stimulable reserves of the adrenal cortex. However, eosinopenia was not induced in a young girl tested on the fifth day, suggesting that adrenocortical failure was present. However, spontaneous eosinopenia developed a few days later, indicating that if failure had occurred earlier it was of short duration. She died 15 days after burning. In another child, several abnormal reactions within 10 days of burning were found, but on the sixteenth day the test was normal. She survived.

Since adrenaline produces eosinopenia indirectly, probably via the hypothalamus, its lack of eosinopenic effect in a patient reacting normally to A.C.T.H. is probably due to pituitary or hypothalamic disturbance. In nine of the 12 patients tested with adrenaline normal curves were found (maximum eosinophil fall 47 to 70%). Abnormal results were found in two children who had become confused and irrational. The A.C.T.H. tests were normal. When the children had recovered mentally, adrenaline tests were normal. Dr. Sevitt suggested that both the mental disturbance and the persistence of the circulating eosinophils after
adrenaline were due to similar cerebral changes affecting the cortex and the hypothalamus respectively.

The Passage of Bromide from Blood to Cerebrospinal Fluid in Tuberculous Meningitis

Drs. Honor Smith and G. Hunter said that in active tuberculous meningitis the passage of bromide from blood to cerebrospinal fluid was facilitated. They presented evidence to show that this degree of facilitation does not take place in other varieties of meningitis showing a comparable degree of disturbance in the cerebrospinal fluid. It was therefore suggested that this observed difference might form the basis of a diagnostic test in tuberculous meningitis.

On October 3 the chair was taken at the two sessions by Dr. C. P. Stewart and Dr. H. B. May respectively.

Some Observations on the Pituitary-Plasma Ascorbic Acid Relationship

Drs. J. Harkness and C. Donovan said that they had confirmed the work of Stewart, Horn, and Robson (Biochem. J., 1953, 53, 254), in which it was shown that an injection of A.C.T.H. causes in the next four hours an increase in the plasma total ascorbic acid, plus an increased proportion of "reduced ascorbic acid" in this total. Cortisone caused no change in the total level but also produced an increased proportion of "reduced ascorbic acid." A portion of the ascorbic acid is present in plasma in the oxidized form—dehydroascorbic acid. They suggested that the changes in the plasma ascorbic acid levels could be used as a test for pituitary function.

Using a constant stimulus to the pituitary, the ascorbic acid test indicates differences in individual responses. The degree of response in some psychotics was lower than in normal controls. Using a constant group of subjects, the ascorbic acid test indicates differences in the response to a variety of stimuli. Changes similar to those produced by A.C.T.H. were caused by electric convulsive therapy, emotional stress, oral sodium salicylate, or butazolidin. Insulin coma causes an unusual and complicated response pattern.

The Inadequacy of the Thiosulphate Clearance as a Measure of Glomerular Filtration Rate

Drs. J. E. Craik and A. P. Kenny reported comparisons of the thiosulphate and inulin clearances in man in 63 pathological cases. Patients were given sodium p-aminohippurate (P.A.H.), inulin, and sodium thiosulphate simultaneously by continuous intravenous infusion. Renal plasma flow (P.A.H. clearance at low plasma concentrations), maximal tubular excretory capacity or TmpAH (P.A.H. excretion at high plasma concentrations), and glomerular filtration rate (inulin clearance) were estimated in the usual way; the thiosulphate—inulin clearance ratio (T/I) was calculated during both low and high P.A.H. periods.

When plasma P.A.H. is low the T/I (percentage) is 123 ± 2.76. With high plasma P.A.H. T/I falls to 98 ± 2.21 (corrected). This indicates that thiosulphate is actively excreted by the renal tubules and that excretion is blocked at maximum P.A.H. levels. Tubular thiosulphate excretion becomes maximal at plasma thiosulphate concentrations of 16 mg.%. At about 16 mg.% the clearance of thiosulphate is close to that of inulin; T/I is not affected by variations in filtration rate or renal blood flow, but it varies directly with TmpAH, thus emphasizing the importance of tubular excretion.

During high P.A.H. periods in cases of severe renal damage with TmpAH below 20 mg./min. T/I falls to 87; with TmpAH of 20-40 the ratio is 91. In each group the difference from the ideal of 100 is statistically significant, thus indicating active tubular reabsorption of thiosulphate.

The estimation of plasma thiosulphate is unsatisfactory. Only the "indirect" method is sufficiently sensitive, but with high P.A.H. levels it gives falsely high results. The "blank" readings are relatively high, equivalent to 2–3 mg.%.

When cases are grouped according to pathological lesions no significant variation in T/I is found except in myxoedema. In this condition T/I at high P.A.H. levels is 113, which is 15 above the mean, or 2.2 times the standard error. In three cases examined before and after treatment the T/I fell from 109 to 101. This may indicate that in myxoedema tubular reabsorption of thiosulphate is inhibited.

Post-operative Retention of Salt and Water

Dr. A. A. G. Lewis, in conjunction with Mr. L. P. Lequesne, spoke on post-operative retention of salt and water. A study of 21 cases submitted to major operations and given a fixed intake of water and electrolytes before and after operation showed that three distinct changes occur. For 24 to 48 hours after operation there is a diminished excretion of water, the result of antidiuretic hormone being released. This is due to the emotional disturbance associated with the operation, probably accentuated by morphine and anaesthesia. Urine specific gravity and sodium concentration are high. One case was studied in which this retention lasted for three days with signs of water intoxication, which disappeared when the diuresis occurred on the third day. Sodium retention occurred in two phases, often separated by an increased sodium excretion. The first, on the day of operation, is probably mainly due to haemodynamic factors, though associated with an increased excretion of potassium evidently marking the onset of increased adrenocortical activity. The second phase usually begins on the third day after operation. This could be considerably reduced by ensuring a reasonable potassium intake throughout. In some cases, particularly when no potassium was given, continuous post-operative sodium and water retention could be observed resulting from the fusion of these three phenomena.
The Fallacies of the Test Meal

Dr. Avery Jones said that it was generally agreed that fractional test meals were of limited value in the diagnosis and management of gastric diseases. Previously, too much has been expected from gastric analysis, mainly because of a failure to appreciate how complex is the physiology of acid secretion and how many variables can be introduced by technique during the tests. The standard form of reporting a fractional test meal is often misinterpreted; the shaded area on many test meal reports corresponds to the findings in 80% of Bennett and Ryle’s original series on healthy subjects, but the remaining 20% with hyperchlorhydria or achlorhydria were all subjects who were perfectly free from symptoms. Follow-up studies on patients with high readings have not shown any correlation with dyspepsia, unless there was an increased volume of secretion. A high acid curve may be due to rapid emptying of the stomach or to hypersecretion. Although this has long been recognized, the recent physiological studies by Hunt at Guy’s Hospital have clearly differentiated the relative roles of these two factors.

Achlorhydria is a term frequently misinterpreted. In clinical practice it implies a gastric juice with a pH greater than 3.5, but at this level there is still about one-third of a milli-equivalent of hydrochloric acid per litre. Patients with histamine-fast achlorhydria may be studied further by 24-hour pH curves, those with primary anaemias giving a pH of 4.5 or higher, whereas those with ulcer dyspepsia showing free acid (i.e., pH less than 3) for many hours throughout the day.

An important indication for a test meal is in problem, undiagnosed cases with symptoms referable to the upper abdomen and in whom radiological reports have been negative. Evidence of unsuspected carcinoma may sometimes be found. The presence of acid does not exclude carcinoma, and indeed it is found in at least one-third of patients with gastric carcinoma, but gross blood-staining and an increase between free and total acid are commonly found.

There is very little to be gained from the routine use of test meals in peptic ulcer.

Renal Response to Massive Alkali Loading in the Human Subject

Dr. P. H. Sanderson reported on the effect of administering up to 140 g. of sodium bicarbonate to patients with peptic ulcer. Although “chemical alkalosis” develops, such doses are well tolerated and renal damage does not occur: sodium is retained. It seems probable that renal damage when described in association with alkalosis is usually due to dehydration from vomiting, with consequent renal ischaemia, rather than to the alkalosis itself.

The Colorimetric Determination of Serum Cholinesterase

Dr. B. W. Meade said that the method described by de la Huerga, Yesinick, and Popper (1952) had been compared to the Warburg manometric technique; they correlated well ($r=0.81$), in 25 cases including a number of values below normal. The colorimetric method was found to be easily reproducible and to be satisfactory for routine use. The observed range of values in 60 normal persons was 140–385 $\mu$mol. of acetylcholine bromide hydrolysed by 1 ml. serum in one hour. There was no significant difference between the means of the values found in men and women.

The mean of levels obtained in eight patients adjudged thyrotoxic, having a basal metabolic rate greater than 115% and/or a positive radioiodine test, differed from that of 10 patients in whom these tests were normal ($P<0.1<0.5$), but the overlap of results was so great as to render the test of little value as a diagnostic aid. There was no significant correlation between the B.M.R. and the serum cholinesterase level.

Liver Function Tests in Rheumatoid Arthritis

Dr. P. W. Darby reported liver function tests carried out in 50 cases of rheumatoid arthritis and 45 hospital patients. These, rather than healthy subjects, were used for the control group so that the incidence of false positive results of the type reported by Kramer (1950) in non-hepatic disease could be determined.

The following tests were carried out: serum bilirubin and urine urobilinogen estimations, the bromsulphalein test (Mateer, Baltz, Marion, and MacMillan 1943), estimation of total urine coproporphyrin (Schwartz, Hawkinson, Cohen, and Watson, 1947; Schwartz, Hawkinson, Sieve, and Watson, 1951), and five flocculation tests — thymol turbidity, the serum colloidal gold reaction, thermal flocculation, zinc sulphate, and ammonium sulphate turbidity tests. Serum bilirubin and urine urobilinogen estimations gave normal results. With the bromsulphalein test 23% of the rheumatoid group and 4.5% of the control group were abnormal. Urine coproporphyrin output was abnormal in 31% and 5% of the test and control groups respectively. One or more of the flocculation tests was abnormal in 73% of the rheumatoid group and 40% of the control group. Statistical analysis of the bromsulphalein and coproporphyrin tests showed that the difference between the rheumatoid and control groups was highly significant.

The positive flocculation tests represented changes in serum proteins which might or might not be due to liver disease. The results with bromsulphalein and coproporphyrin, however, showed that in rheumatoid arthritis a degree of liver damage exists which is significantly greater than that in other causes of chronic ill-health.

References