ASSOCIATION OF CLINICAL PATHOLOGISTS:  
56th GENERAL MEETING

The fifty-sixth general meeting of the Association was held at Cheltenham on April 5, 6, and 7, when a full programme of papers and demonstrations was arranged. Summaries of most of the papers follow.

Factors Affecting the Operation of the Haemolytic System in the Wassermann Reaction

P. N. COLEMAN (Northallerton) reviewed the various factors that control the operation of the haemolytic system in the Wassermann test. The photometric method for the complement titration described by Meyer, Eaton, and Heidelberger (1946) was well worth the extra trouble required. An equivalent increase in the accuracy of the haemolsin titration was not necessary. Times for haemolysis and the concentrations of the cell suspensions varied widely in the various methods. If one hour was allowed for haemolysis the exact time of reading was not critical because haemolysis would have proceeded virtually to completion. The use of concentrated cell suspensions reduced the number of tubes required for the full evaluation of reagent content and enabled "complete inhibition" to be reported as "positive"; sensitivity was adequate; reading of tests should be postponed until the cells had sedimented. With weak suspensions maximum sensitivity was obtained and tests could be read without delay; complete inhibition restricted to the first tube of a titration might indicate insufficient reagent to merit the description positive.

The idiosyncrasies of individual batches of sheep cells could sometimes introduce considerable variations into the Wassermann test. Commercially obtained formalized cells, though nearly always requiring less complement for haemolysis than fresh cells, gave more consistent results than cells obtained from unselected sheep at the abattoir. Complement preserved by Richardson's method was a very stable reagent which could be used to standardize the Wassermann test. It was used at a predetermined dose for the fixation stage, ignoring day-to-day variations of titre due to the vagaries of the cells.

REFERENCE

A Correlation of Estimations of Serum Mucoprotein, C-Reactive Protein, Anti-streptolysin O Titre, and the Sedimentation Rate

W. ALSOP, E. FINCH, and J. L. EMERY (Sheffield) reported that serological tests from a large number of children with acute rheumatism and other diseases showed that there was a close relationship between the C-reactive protein level and serum mucoprotein. The serum mucoprotein levels appeared to give no clinically useful guide for treatment, but in several cases a positive C-reactive protein test in the presence of a normal sedimentation rate anticipated a clinical relapse.

Rose-Waaler Test: Its Modifications and Clinical Significance

C. L. GREENBURY, A. G. S. HILL, R. SPALDING SMITH, and M. S. GOOD described their experience over two years with a modification of the Rose-Waaler test on a series of 700 patients which included 249 with rheumatoid arthritis. The test gave a positive result in 90% of all cases of rheumatoid arthritis, and in 93.5% of those with positive x-ray findings. In cases other than those of rheumatoid arthritis (with the exception of those given below) the positive rate was not higher than 3%. Subsequent follow-up is likely to show that the false positive rate is considerably lower. A few cases of rheumatoid arthritis are negative early in the disease, but for the most part even the earliest cases give good positive results. There was no relation between activity judged either clinically, by E.S.R., or by C-reactive protein, and a positive test.

The tests were performed in Salk trays, agglutination being judged by the pattern of sedimented cells. A high dose of sensitizing anti-red-cell serum was used. Most of the tests were done in duplicate using saline and 2.5% sheep serum as diluents for the test sera. When sheep serum was used as diluent titres were from two- to sixteen-fold higher than with saline, and a few sera were positive in serum but negative in saline. Sera producing an agglutination of sensitized cells in a dilution of 1:16 or higher were taken to be positive, provided that heterophile antibody was present in minimal quantity or had previously been absorbed.

It was found, in common with other workers, that serum from cases of "collagen disease" also gave positive results. Two further groups of patients were also found to produce positive results. The first, an at present ill-defined group of patients attending skin
clinics, and the second, patients with diffuse pulmonary fibrosis, finger clubbing, and arthralgia but no arthritis.

Use of the euglobulin fraction instead of the whole sera for the test did not improve the positive rate in cases of rheumatoid arthritis, nor could any excess of inhibitor be shown to be present in those cases of rheumatoid arthritis which gave negative tests.

It was concluded that the Rose-Waaler test at least, in the modification described, was a most useful and accurate aid to diagnosis.

**Distribution of Abnormal Haemoglobins**

H. Lehmann (St. Bartholomew's Hospital, London) described the ethnological distribution of abnormal haemoglobins.

**Haemoglobin S.**—The distribution of the sickling gene is now fairly well known. A recent addition to knowledge was Aksoy's finding of a high sickling rate in the Eti-Turks, a small Arabic-speaking group in southern Turkey (Aksoy, 1955). A detailed study of the Eti-Turks (?) Hittites) jointly with Aksoy revealed also a high incidence of thalassaemia, and not surprisingly therefore of sickle cell-thalassaemia disease. It was remarkable how different the severity of this condition could be—often in the same family where the genes responsible were presumably identical. The thalassaemia gene, or a thalassaemia-like gene, has also been found in Africans in the Gold Coast. It can be extremely difficult to distinguish between a sickling homozygote and a person heterozygous for the genes for haemoglobins A and S who also carries a thalassaemia gene (Edington and Lehmann, 1955a and b).

The thalassaemia gene can suppress haemoglobin A formation to such an extent that no haemoglobin A can be demonstrated in the phenotype, though family studies will reveal the true genotype. It has been decided (Edington and Lehmann, 1956) to differentiate in the Gold Coast at least between "sickle cell disease" which comprises all conditions in which the sickling gene is involved and "sickle cell anaemia," reserving the latter term for the truly homozygous state.

**Haemoglobin C.**—Whereas haemoglobin S is distributed all over tropical Africa, haemoglobin C is restricted to West Africa. There the highest frequency was seen in the northern Gold Coast, being 28% in the Dagomba (Edington and Lehmann, 1956). In the southern Gold Coast the incidence is 10% (Edington, 1956). Further east in Western Nigeria it was found to be 7% in the Yoruba, but further east still in the racially related but more isolated Igalas east of the River Niger it was not found at all (Walters and Lehmann, 1956). It thus seems that haemoglobin C has arisen somewhere near the northern Gold Coast and that it is spreading southwards and eastwards.

...Never in the history of genetics, with the possible exception of Ford's melanism story in the moth, have geneticists and those with kindred interests been quite so close to having a ringside seat at the origin and dissemination of a 'new' gene (Neel, personal communication).

**Haemoglobin D.**—Up to recently this haemoglobin had been thought to be rare and to be present in a few families only. It has now been demonstrated at an incidence of 1% in Punjabs and in Gujeratis (Bird and Lehmann, 1956; Jacob, Lehmann, and Raper, 1956). One family has also been found in a survey of Turks (Aksoy and Lehmann, 1956). It is possible that haemoglobin D will fill the gap in the world distribution of haemoglobin variants between haemoglobin S in the west and haemoglobin E in the east.

**Haemoglobin E.**—This haemoglobin was found at an incidence of 13% in Siam, and was recently demonstrated at a similar frequency in Burmese (Chernoff, Minnich, and Chongcharoensuk, 1954; Na-Nakorn, Minnich, and Chernoff, 1956; Lehmann, Story, and Their, 1956). Near by in Indonesia and in the Veddas of Ceylon the incidence is about 4% (Lie-Injo Luan Eng, 1955; Graff, Ikin, Lehmann, Mournant, Parkin, and Wickremasinghe, 1954). Jointly with Bird haemoglobin E has now been found in Bengal, but so far it has not yet been reported in other Indian populations and this represents the first finding of the E variant in India. It is likely that haemoglobin E will be found to play in south-east Asia a part similar to that occupied by haemoglobin S in Africa.

**Haemoglobins G, H, and I.**—These have so far been found in single families only.

**Balanced Polymorphism.**—One of the most intriguing aspects of the distribution of the haemoglobin variants is the fact that they exist at high frequency, although many genes must be lost in each generation due to disease and death caused by the haemoglobinopathies (Neel, 1953). Allison (1954) brought forward evidence that the loss of the sickle cell gene by early death of sickling homozygotes was balanced by the greater fitness of sickling heterozygotes, who were less liable than normal homozygotes to become infected with malaria. This particular evidence could not be confirmed, but Allison's conclusions have been fully vindicated by Raper (1955). Raper found that, though there was no difference in the parasite rate between sicklers and non-sicklers, sicklers once infected showed a significantly lower density of *P. falciparum*. This applied only to children under the age of 2, i.e., before acquired immunity became established. As the severity of *P. falciparum* infection under the age of 2 largely determines the malarial death rate in an endemic area we have here the evidence supporting this first example of balanced polymorphism in man.

**Multiple Protection.**—The greater the number of factors which protect or might protect against malaria the more difficult will it be to demonstrate the protective action of sickle cell haemoglobin. Acquired immunity will protect sickler and non-sickler alike, hence Allison's conclusions cannot be disproved by an examination of the adult populations in endemic areas, as it has repeatedly been done. Colbourne and Edington (1956) had less clear-cut results in West Africa than Raper in East Africa; this they expected, because a simple comparison of sicklers and non-sicklers does
not take account of haemoglobin C present at high
frequency in West Africa, and possibly similarly pro-
tective against malaria. All attempts to discover
whether foetal haemoglobin had a protective effect in
infants (Allison, 1954; Lehmann, 1953) have so far
been frustrated by the simultaneous presence of other
protecting mechanisms, such as inherited maternal
immunity.

When Haldane (1949) pointed out that higher resis-
tance against malaria might be the advantage which
balanced the disadvantage of the thalassaemia gene in
affected populations, he also mentioned a possible ad-
antage enjoyed by thalassaemia heterozygotes on
diets deficient in iron. It is noteworthy that people
whose haemoglobin consists entirely of D or E (Bird
and Lehmann, 1956; Lehmann et al., 1956) have a
blood picture which resembles that of patients with
a compensated iron deficiency. There is a polycy-
aemia of more than 7 or even 8 million red cells per
c.mm.: the cells are hypochromic and very small.
Individuals should therefore be able to adapt them-
selves more easily to others to a diet deficient in iron,
or to loss of iron by chronic haemorrhages due to
hookworms.

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Haemoglobin C Disease

H. M. Rice (Nottingham) described the case of a
West Indian negro, 2 years, aged 38, who was found
on routine antenatal testing at the fifteenth week to
have a haemoglobin of 10.5 g. per 100 ml., with
numerous target cells in the blood film. Four weeks
later her haemoglobin was 8.7 g., and the film showed
a very high proportion of target cells, with some
hypochromia.

She was admitted to hospital for investigation, and
the relevant findings were:

Physical Examination.—Pregnancy normal for 20
weeks. Spleen + 2 fingerbreadths. Liver + 4 finger-
breadths.

Biochemistry.—Serum bilirubin 0.6 mg. per 100 ml.,
total serum protein 5.8 g. per 100 ml., thymol
turbidity 2, zinc sulphate turbidity 14 units, alkaline
phosphatase 5 K-A units.

Urine.—Albumin +. A few R.B.C.s, hyaline, and
granular casts. Sterile.

Haematology.—Hb 8.4 g. per 100 ml., P.C.V. 27%,
R.B.C.s 3.1 million per c.mm., M.C.V. 87 c.p.,
M.C.H.C. 31.1%, reticulocytes 2.2%, W.B.C.s normal
in type and distribution. Platelets normal. Red cells
showed anisocytosis and slight polychromasia. Target
cells 56%. Red cell fragility greatly decreased, begin-
ning at 0.40% and incomplete at 0.10% saline (control
0.50 to 0.35%). Coombs tests negative. Marrow
very active. Erythropoiesis mainly normoblastic, but
occasional megaloblasts present. Maturation arrest
at the myelocyte-metamyelocyte stage, M.E. ratio
1.3:1.

Haematological Examination of P. Family.—Blood
samples were taken from Mr. P., the son R. (aged
7), and the daughter Y. (aged 5).

Electrophoresis at pH 8.6 (veronal buffer, filter-
paper method) showed that Mrs. P. possessed only
haemoglobin C. Mr. P. only normal adult haemo-
globin (A), and both children a mixture of A and C.
Mrs. P. has, therefore, homozygous haemoglobin C
disease, and the children have haemoglobin C trait.

It has been stated that the incidence of haemoglobin C
trait is approximately 2.5%, and that haemoglobin C
disease should be found in approximately 1 in 6,000
of North American negroes. It would appear likely,
therefore, that other cases of haemoglobin C disease
may already be present in this country, and that we
must consider the haemoglobinopathies in all coloured
patients with anaemia.

The Occurrence of Granulocytic Leukaemia in Cases
of Pernicious Anaemia

E. K. Blackburn (Sheffield) described three patients
with established pernicious anaemia who developed
granulocytic leukaemia some years after the diagnosis
of pernicious anaemia was made.

Possible causes of this very rare association were
discussed.

Observations on the Use of Intrinsic Factor-Vitamin
B12 Combination in the Treatment of Pernicious
Anæmia

D. Robertson Smith and W. M. Davidson (King's
College Hospital Medical School, London) said that
proved cases of pernicious anaemia had been treated
by oral administration of a preparation containing
7½ mg. vitamin B12 and 18 mg. intrinsic factor extract
per tablet ("bifactor," Organon). The results fell
into three groups.

(1) One case failed to respond but produced a com-
plete clinical and haematological remission with intra-
muscular vitamin B12.

(2) Two cases responded well and were maintained
for nearly a year, then relapsed with megaloblastic
bone marrows. One case recovered completely on
intramuscular vitamin B12 and the other is still under
investigation.

(3) The third group showed a satisfactory erythro-
opoietic response, but giant metamyelocytes in the bone
marrow and the neutrophil shift to the right in the
Ar negot count persist.ed for longer than after intra-
muscular injection of vitamin B12. Most cases
eventually developed abnormal blood pictures or mild
neurological signs despite maintained treatment.

It appears that the recommended oral dose of 15 μg.
vitamin B12 and 36 mg. intrinsic factor ("bifacton," 2
tablets per day) is insufficient to maintain a remis-
sion in pernicious anaemia, but it may be of value
in supplementing parenteral vitamin B12 therapy in
cases with subacute combined degeneration of the
cord.

Platelet 5-Hydroxytryptamine in Disorders of the
Blood
R. M. Hardisty and R. S. Stacey (St. Thomas's
Hospital Medical School, London) said that the vaso-
constrictor principle of the platelets ("serotonin")
had now been identified as 5-hydroxytryptamine
(HT). The object of the present investigation was
to determine whether the incidence of purpuric mani-
festations in various blood disorders was related either
to the concentration of HT in the platelets or to the
total HT content of whole blood.

The platelet HT concentration had been estimated,
and whole blood HT determined, in 83 patients with
various disorders of the blood and reticulo-endothelial
system, including leukaemias, polycythaemia vera,
lymphomas, pernicious anaemia, and simple iron-
deficiency anaemia, and in 15 patients not suffering
from disease of the blood.

The method had already been described (Hardisty
and Stacey, 1955).

Low mean platelet HT concentrations were found
in a high proportion of cases of all the haematological
disorders studied, and these resulted in low whole
blood HT level in many cases. Experiments on the
absorption of HT by platelets in vitro suggested that
these low platelet HT concentrations were attributable
to a defect of the platelets themselves. The mean
platelet HT concentration in these cases was unrelated
both to the blood platelet count and to the incidence
of abnormal bleeding.

All but two of the patients with purpuric mani-
festations had both thrombocytopenia and a whole
blood HT level below normal limits, but the incidence
of bleeding was less critically related to the whole
blood HT than to the platelet count.

It is concluded that the bleeding of thrombocyto-
penia cannot be attributed solely to HT deficiency,
and that there are no grounds for supposing that a
low platelet or whole blood HT concentration, in the
absence of thrombocytopenia, may be a cause of
abnormal bleeding.

Reference
130, 711.

Examination of the "Buffy Coat" from the
Haematocrit in Cases of Anaemia in Pregnancy
H. B. Goodall (Department of Pathology, Royal
Infirmary, and Queen's College, Dundee) said that
microscopic examination of the "buffy coat" was a
recognized haematological procedure. This technique,
controlled by marrow biopsy, has been applied to the
investigation of anaemia in pregnancy, and, by giving
a remarkably true reflection of the type of erythro-
poiesis in the marrow, has enabled the diagnosis of
"pernicious anaemia of pregnancy" to be made even
when the rest of the peripheral blood picture was not
characteristic.

During this investigation it was also found that
erthropagocytosis was not uncommon in the blood
of pregnant, parturient, and puerperal patients. The
possibility that the ingested red cells are foetal had
in one case been confirmed by differential agglutina-
tion, but in other instances the phenomenon may
merely indicate a haemolytic process affecting the
maternal erythrocytes.

Vacuolation in the Cytoplasm of Lymphocytes
J. N. Cumings (The National Hospital, Queen
Square, London) said that in an examination of nine
cases of a variety of cerebral lipidoses vacuoles were
found in the cytoplasm of the lymphocytes in four
cases of amaurotic family idiocy in greater numbers
than in any controls. Two other cases of amaurotic
family idiocy also showed a few vacuoles. The con-
tral cases were from a wide range of diseases and
included epilepsy.

No evidence was found to indicate the nature of
the contents of the vacuoles.

Two Cases of Tetrachloromethane Poisoning in
Industry: Pathological and Legal Aspects
G. A. Dunlop (Worksop) said that tetrachloro-
methane was a toxic liquid, volatile, with properties
resembling chloroform. The toxic action of the
vapour falls mainly on the liver parenchyma and the
bronchial mucosa. Special precautions should be
taken by those who use it—viz., forced draught
ventilation, extra intake of calcium, and abstinence
from alcohol. Storage should be in sealed, steel
containers.

Poisoning with this substance is not scheduled under
the Compensation Acts, and claims for compensation
must be made under "accident" and not under
"process."

The Clinical Histories in Cases of Sudden Death in
Infants Reported to the Coroner
J. L. Emery and E. M. Crawley (Sheffield).—In a
series of 50 infants referred to the Coroner as sudden
unexpected death, the history as obtained by the
Coroner was consistent with histories obtained after
the child had been buried in only five instances.

The histories obtained by the Coroner's Officer were
substantially inconsistent with both morbid anatomical
findings and later histories in 33 of the cases.

The follow-up histories indicated some abnormality
in all infants before death, and, in the majority, symp-
toms of over two days' duration.

It is suggested that the inadequate histories are due
to the psychic trauma of the unexpected death to the
mother, together with the fear produced by the police and the Coroner's investigations.

The procedures connected with these "sudden deaths in infancy" would appear to need revision.

**Staphylococcal Infections in Hospital**

H. C. M. WALTON (Swansea) said that during the past year four kinds of staphylococcal infection had been encountered in patients in hospitals for other conditions: (1) gastro-enteritis, (2) infection of operation wounds, (3) pneumonia following cortisone or A.C.T.H. therapy, and (4) skin sepsis.

In the largest outbreak of gastro-enteritis, 60 out of 100 patients at risk were affected after eating frozen chicken imported from France. *Staphylococcus aureus* was isolated from a sample of the chicken. Besides the usual precautions for the prevention of food-poisoning, it is important to stress that food should be at room temperature for the shortest possible time. When food is not in the refrigerator where germs cannot multiply, it should be undergoing the process of cooking, which kills them.

In operation wounds, serious infections have been encountered either where sulphasuxidine has been used before a bowel resection or where antibiotics are used for peritonitis after operation.

The difficulty here has been that the clinicians use a broad spectrum antibiotic, usually one of the tetacyclines. A staphylococcus, often insensitive to these, is only found loculated in the peritoneal cavity at necroscopy.

One of the effects of cortisone and A.C.T.H. therapy is to reduce immunity to infection. One patient under treatment with A.C.T.H. for thrombocytopenic purpura developed acute pneumonia and died within 24 hours. Another patient receiving cortisone for an allergic eczema developed furunculosis and subsequently staphylococcal pneumonia.

Skin sepsis, usually in the form of furunculosis, occurs most frequently on the buttocks of heavy or helpless patients, but it may occur on any part of the body which is slightly damp or excoriated.

The spread of infection is usually successfully prevented by (1) a disinfectant hand-cream (1% hibitane) on the hands of nurses and affected patients; (2) 0.5% hibitane in spirit on the buttocks of all bed patients (recently silicone vasogen barrier cream has been used, and appears valuable and saves much of the nurses' time); (3) disinfection of bed-pans by boiling or disinfectant. The local spread of boils can usually be prevented by painting the neighbouring skin with 1% copper sulphate (in children 1% gentian violet is useful) or ultra-violet light.

The lessons to be learned are:

(1) That broad spectrum antibiotics should be used for the shortest possible time to tide the patient over an acute phase.

(2) At present it takes not less than 24 hours to give a bacteriological report with antibiotic sensitivities. As soon as a report can be given within a few hours much unnecessary antibiotic therapy will be avoided.

(3) Much more work must be done both on the most effective ways of eliminating staphylococcus from hospitals and also of determining which types of staphylococci are really dangerous.

**Puerperal Fever**

J. D. ALLAN GRAY (Central Middlesex Hospital) described the spread of Group A haemolytic streptococci among the staff and patients of a maternity unit. It began among the pupil midwives with a succession of sore throats which did not yield sulphonamides, penicillin, holidays, or tonsillectomy. In spite of strenuous efforts the organism spread among 55 of the staff and 57 of the patients. The vast majority of both staff and patients showed either no evidence of infection or at most only a trivial illness. Two infants unfortunately died: one was thought to have had a cerebral injury and the other developed his fatal illness after his discharge from hospital. While a combination of penicillin and streptomycin was required to eliminate the streptococci from the staff, penicillin alone was sufficient to eliminate them from the patients. The marked difference between the staff and the patients in the difficulty with which the streptococci could be eradicated was eventually shown to be due to the presence of penicillinase-producing staphylococci in the noses of the majority of the staff.

The administrative actions to combat the outbreak were outlined and suggestions made for preventing or at least limiting a similar outbreak in the future.

**Intrapartum Pyrexia**

R. F. JENNISON (Manchester) described a retrospective study of the causes of perinatal death which showed a relatively high incidence of pneumonia and an apparent association with maternal pyrexia during labour. A study was made, therefore, of the bacteria in high vaginal swabs taken on two occasions during labour from all mothers with pyrexia and from a control group. The most common pathogenic micro-organisms isolated in each group were the same—namely, *Bact. coli*, non-haemolytic streptococci, both aerobic and microaerophilic, and *Strep. faecalis*, but the proportion of patients with these organisms was much higher in the pyrexial group than in the other. This increased bacterial content in patients with pyrexia was associated with the length of time that the membranes had been ruptured before the swabs were taken and even more to the length of time that the pyrexia had been present. Half of the patients with pyrexia were treated with antibiotics, and the numbers of pathogenic bacteria were decreased by half as compared with the untreated group. During the trial period of four months, five instances of pneumonia in stillbirths or neonatal deaths occurred in the group with untreated pyrexia, whereas none occurred in the other two groups. In three of these infants the organisms isolated and seen in the lungs of the infant were similar to those already iso-
lated from the vagina. All the pneumonias occurred in infants whose mothers had temperatures in the higher range and for longer than 48 hours or whose membranes had been ruptured for a similar period. Although the number of deaths from infection in this series was small, it suggested that patients whose temperatures were above 99.4° F. for more than 48 hours or whose membranes had been ruptured for a similar period should be considered as possibly infected, with consequently a risk to the foetus.

Recent Advances in the Technique of Muscle Biopsy

A. L. WOOLF (Smethwick) said that Coërs (1953) had shown that the likelihood of a muscle biopsy specimen containing nerve endings was greatly increased if the specimen was taken from the region of the motor point. If muscles in which the fibres run parallel with the surface and unattached to the fascia are taken and the motor point for each fasciculus determined on the exposed muscle, nerve endings are almost always found. By means of the techniques of vital staining with methylene blue and Couteaux’s modification of Koelle’s histochemical method for acetyl cholinesterase, applied to human muscle for the first time by Coërs (1952, 1953a and b), the nerve endings can be demonstrated much more completely than hitherto. In this way one can, in slow degeneration, show swellings of sub-terminal nerve fibres and terminal expansions, together with early delicate and later better formed sprouts from surviving neurons. In convalescent acute degeneration and chronic progressive degeneration affecting only a proportion of neurons, functionally effective collateral sprouting with a raised terminal innervation ratio results. Subneural apparatuses may consist of single large units in chronic degeneration. They are less sharply outlined and paler than the massues de croissance of regeneration. Sprouting more proximally, especially from diseased neurons, may result in very delicate non-myelinated fibres, apparently not insulated from one another. This may conceivably result in a spread of impulses from neuron to neuron, giving rise to spontaneous movement of groups of muscle fibres as in fasciculation. Healthy neurons sprout in myopathies and are particularly vigorous, especially in dystrophia myotonica.

References


Pituitary Necrosis in Raised Intracranial Pressure

LIONEL WOLMAN (Royal Infirmary, Sheffield) said that, among 270 patients dying with a tentorial pressure cone resulting from a unilateral space-occupying lesion, 12 cases with recent necrosis of the anterior lobe of the pituitary were found.

The necrosis due to infarct ranged in extent from a small solitary area to as many as five discrete areas occupying most of the pars glandularis, but separated from each other and from the capsule by a zone of intact tissue.

The age of the infarcts histologically assessed could be correlated with the probable duration of tentorial coning.

The commonly associated herniations and displacements found in these cases were noted, the most frequent being herniation of the hippocampal uncus through the incisura, herniation of the frontal lobe beneath the falx, and herniation of the gyrus rectus into the prechiasmatic recess with tilting of the optic chiasma.

The blood supply to the anterior lobe passing down the hypophysial stalk was considered to be impaired by mechanical factors resulting from the distortion of the optic chiasma, hypothalamus, and infundibulum. The mechanism whereby these infarcts occur appears to be quite distinct, and separated this group from necrosis of the pituitary occurring post-partum and from various other causes.

Salivary Tumours: A Clinical and Pathological Study

J. M. CAMERON and A. DICK (Glasgow) reported that in a series of 88 cases of salivary tumours classified into five main subgroups attention was focused mainly on the pleomorphic adenoma or the so-called mixed tumours. It was shown that the parotid gland was the most frequent site, followed by the submandibular and sublingual glands in that order; that they first occurred between the third and fifth decades but that no age was exempt, and that their growth was extremely slow. There was apparently a slight prevalence among females and recurrence in about 30% whatever the treatment. Support was given to the theory already put forward that the cartilage-like material in many of these tumours was in fact no true cartilage but represented a myxochondroid substance developed by degeneration from epithelium and stroma. It was of interest to note that occurrence of pleomorphic adenoma in father, son, and daughter of one particular family: this fact has seldom if ever been recorded before. Death in eight of the 14 cases of carcinoma was attributed to malignant salivary tumours. Adenolymphoma occupying 10% of the tumours was shown to appear in the sixth decade and an unusual bilateral case was reported. Also there appeared to be a high incidence in this series of blood group A amongst patients with such tumours.

Acute Uraemic Renal Failure after Head Injury and Surgical Operation

W. H. TAYLOR and J. V. O. REID (Radcliffe Infirmary, Oxford) described how acute renal failure, as defined by a blood urea concentration greater than 100 mg./100 ml. with a urinary urea concentration of less than 2.0 g./100 ml., developed after surgical operation or head injury in 25 patients who were examined at necropsy. Fifteen patients showed post-mortem histological evidence of acute tubular necrosis.
In three of the earliest cases casts were seen to be produced by haemorrhages from capillaries into tubules. These haemorrhages may be important in the process of cast formation. Of the 10 patients without acute tubular necrosis, one had normal kidneys and nine showed only hydropic changes in the tubules. In at least four of these cases the duration of acute renal failure exceeded 48 hours and should have been sufficient for acute tubular necrosis to have become manifest.

Previously described clinical features of acute renal failure were not consistently present in either the tubular necrotic or non-necrotic groups. Oliguria (less than 300 ml. of urine per day) occurred in 11 patients. The urinary chloride ratio was greater than 4:1 in all patients except three with acute tubular necrosis, so that unregulated tubular loss of chloride with a plasma:urine chloride ratio of approximately 2:1 was not a characteristic feature. The specific gravity of the urine was fixed between 1008 and 1014 in only about one quarter of the cases.

It is concluded that after head injury and surgical operation acute renal uraemic failure may be present in the absence of histological tubular necrosis, and that when there is tubular necrosis its characteristic clinical features may be absent, thus causing diagnostic confusion.

Further Simplifications of Tubeless Gastric Analysis

JOHN HARKNESS (Taunton).—Segal has recommended (Segal et al., Gastroenterology, 1955, 28, 402) an azure A-cation exchange resin compound in which the quininium of the present tubeless gastric analysis is replaced by a dye which eventually colours the urine. This new compound still suffers the disadvantages of interference by drugs and food, and the need for an injection of histamine to verify achlorhydria.

The speaker proposed that a more reliable test could be obtained by estimating the overnight urinary excretion of quinine following an oral dose of 500 mg. quinine carbonate suspended in weak alcohol or water. Food and drugs do not affect the result. Although histamine is not given, it is claimed that this technique will detect the false achlorhydrias missed by the standard intubation alcohol-histamine fractional test meal. A satisfactory test can be carried out by a patient in his own home. Achlorhydrics excrete 0–100 μg. quinine overnight (further experience may increase the upper limit slightly); subjects with free hydrochloric acid in the gastric juice excrete 320–30,000 μg. in eight hours.

Cryoglobulinaemia: A Clinical-pathological Account of Two Cases

H. E. Hutchison (Glasgow) gave a brief clinical and pathological description of two cases in which abnormality of plasma protein was thought to have been concerned in the development of a haemorrhagic state.

The first patient was a man aged 74 years who first noticed bluish swollen areas on the backs of the fingers, on the tip of the nose, and along the ear margins following his attendance at a football match in the snow.

One month later he was admitted to hospital with a more severe attack. The skin changes improved over the next few days, but he precipitated a recurrence by putting his hands into cold water. Gangrene developed and he began to weaken. Excessive susceptibility to cold was further suggested when similar changes appeared on the scalp when his bed was moved under an open window during ward cleaning, and was confirmed by clinical experiment. No abnormality in the blood cytology or coagulation mechanism could be detected. On chemical estimation the plasma albumin and globulin were normal and no precipitate was detected on chilling the serum; the E.S.R. was normal and the fibrinogen 500 mg.%. At necropsy no evidence of disease of the haemopoietic system was discovered.

The second patient was a man aged 60 years who 20 years previously had an attack of unilateral haematuria, which remained unexplained even after surgical exploration of the kidney. Haematuria recurred once 10 years later. About this time he began to suffer attacks of unconsciousness. Among results of investigations were rather flat sugar-tolerance curves, and these led some two years later to surgical exploration of the pancreas to exclude the possibility of an islet-cell tumour. One year before his death he developed signs of congestive cardiac failure. At this time the E.C.G. findings showed no evidence of coronary artery disease, but they did so a few months later, the rapidity with which the changes developed being noteworthy. At this time purpura was first noticed, and then only on the hands and arms. Gross cryoglobulinaemia was present, amounting to 40% of the total globulin and found in the α fraction on electrophoresis. Narrow examination revealed early infiltration by a lymphoid reticulum. No sensitivity to cold could be demonstrated by experimental chilling of the skin. The patient died at home some six weeks later, and necropsy was not carried out.

Experiments with Membrane Filters

L. R. S. MacFarlane (Royal Army Medical College, Millbank).—The method described by Goetz and Tsumeishi, writing in the Journal of American Waterworks in 1951, for growing coliform and other organisms on a molecular membrane after filtration has been applied to various other organisms with a view to more rapid diagnosis.

A modification of the method was described, the membrane filter being laid direct on a moist solid medium after filtration. Liquid media and filter pad had been dispensed with.

Of a large variety of organisms tested, many grew well by this method, but none surpassed recognized laboratory methods for speed, although some did with regard to selectivity.
In the field of epidemiological medicine, however, there seems a very great use for this method.

The routine examination of pooled urines for carriers of the enteric group, and of kitchen waste waters for the same purpose, and also of pooled throat swabs to detect carriers can be carried out expeditiously by this method.

Large fluid quantities can be put through and large numbers of plates saved. For example, 500 throat swabs can be emulsified and put through in batches of 10: a positive batch can be re-examined by normal methods, only 50 swabs now needing to be examined. The same applies to pooled urines.

Large amounts of kitchen waste waters can be examined at one session, and one is certain of examining the whole specimen.

The method appears to be time-saving and economical, and could also be applied to rectal or Moore's swabs if swarming organisms could be eradicated.