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ABSTRACTS

(In this section of the Journal some of the more important articles on subjects of interest to clinical pathologists are selected for abstract, and these are classified into four sections: bacteriology; biochemistry; haematology; and morbid anatomy and histology.)

BACTERIOLOGY


The slow rate of growth of tubercle bacilli in the conventional fluid culture media has been overcome by the use of a synthetic basal medium to which is added 0-05% "tween 80" and 0-1 to 20% filtered sterile serum albumin (conveniently 0-25% bovine serum fraction V, prepared as a powder). "Tween 80" is a polyoxyethylene derivative of sorbitan mono-oleate, which is water-soluble and heat-stable. Inoculation of 5 ml. of this medium in 25-mm. test-tubes leads to rapid diffuse submersion growth in response to very small amounts of tubercle bacilli. It is believed that the "tween 80" acts as a wetting agent and that oleic acid is split off by a bacterial lipase to provide a readily available foodstuff; free oleic acid is, however, toxic, but this toxicity can be neutralized by the albumin. By adding 1-5% agar to this fluid medium and using 0-5% albumin, a solid medium is obtained that will give surface colonies from inocula in 1 to 2 weeks. Tubercle bacilli growing diffusely in the liquid medium retain their typical morphology and staining characteristics; they are viable for long periods and remain fully virulent. Such bacilli can be used for inoculation into experimental animals and into chick embryos, and they can produce, as well as react specifically with, immune sera. The medium can also be used for primary isolation of tubercle bacilli from pathological material.

[The use of water-soluble lipids is likely to revolutionize the techniques of culture of Myco. tuberculosis.] P. D'Arcy Hart.


A 20-year-old male was admitted to hospital with a 4 days' history of severe malaise, sore throat, productive cough, and vomiting; soreness of the eyes with a discharge had appeared 2 days before. On admission to hospital his temperature was 103° F., pulse rate 100, and respiration rate 30. He had (1) bilateral conjunctivitis with vesicles on the conjunctiva and a mucopurulent discharge; (2) ulceration of the nares and pustules on the upper lip; (3) discrete adherent white patches up to 1/2 inch in diameter on the inner sides of both cheeks and on the tonsils; and (4) numerous ronchi over both lungs. A throat swab showed "no haemolytic streptococci, no Corynebacterium diphtheriae, no Vincent's organisms"; the blood count was normal and the Wassermann and Kahn reactions negative. Two days later he developed (5) a purulent discharge and (6) vesicles (containing a pale yellow fluid free from cell lysis) on the base of the dorsum of the arms; after 2 days the vesicles had spread to the lower limbs and trunk. They varied in size and rapidly developed dark crusts. The temperature ranged from 102° to 104° F. and the fever did not respond to sulphamezathine, so 6 days after admission penicillin, 15,000 units intramuscularly every 3 hours, was given and the condition improved. The cornea remained clear; irritation with boric acid lotion and eye drops of 10%, "albucid" (sulphacetamide) every 2 hours were prescribed. A fortnight after admission the patient developed for 2 days slight consolidation at the right base with a pleuritic rub, cough, and viscid sputum. A throat swab at this time grew Staphylococcus aureus; biopsy of a vesicular lesion showed "slight vascular engorgement of the corium and a little oedema of the Malpighian cells"; blood culture was sterile. Three weeks after admission the eyes were clear, the skin lesions were only brown discoloured patches, and 10 days later the mouth was clear and the urethral discharge had ceased, but the prepuce was so densely adherent to the glans penis that circumcision was performed.

Henry Cohen.


Twenty-three cases of mild lymphocytic meningitis are reported; they probably formed about half those occurring in an epidemic among units served by a U.S. general hospital in Burma. The symptoms were: severe bilateral bursting frontal headache; "eye-ache" and pain on moving the eyes, fatigue, weakness, and nausea; vomiting; inconstant prodromal symptoms; fever (100° to 103° F.); sweating; conjunctival congestion; tremor; and neck rigidity, but not so marked as in bacterial meningitis. Reflexes, ocular muscles sensation, and mentality were normal, and there were no convulsions. Eight cases showed moderate lymphocytosis, the greatest shift being from 12% to 44%. There was no eosinophilia. Four patients while in hospital showed a probably significant heterophil antibody agglutination, and of 20 readmitted cases, seen 2 months after the onset, 13 gave agglutination titres of 1 in 7 to 1 in 224. Complement-fixation and virus neutralization tests for

J. clin. Path. (1947), 1, 47.
lymphocytic choriomeningitis, mumps, dengue, and three types of encephalitis were negative. The cerebrospinal fluid was abnormal in all cases. Cell counts varied from 0 to 490 per c.mm., lymphocytes predominating except in the case with the highest count. Protein varied from 29 to 70 mg per 100 ml. There was no relation between these findings and the severity of the symptoms, and in 4 cases the fluid was normal 4 weeks later. There was no evidence of spinal block, though manometric pressure determination could not be made.

The infection is regarded as being due to a virus, in the absence of bacterial, spirochaetal, or chemical factors, or of an associated disease likely to produce a reactive meningitis. The frequency of the heterophil reaction suggests infectious mononucleosis, some features of which were present. The test is, however, apparently non-specific, and a number of epidemic fevers in Japan give a positive Paul–Bunnell reaction. Poliomyelitis is unlikely, and tests for types of encephalitis were negative. The dengue group of diseases also appeared unlikely to be implicated. The absence of neurological dysfunction makes lymphocytic choriomeningitis again improbable. The disease is accordingly classed among the group of "bacterial meningoencephalitic and aseptic meningitis in only one-third of which have specific viruses been found. If any virus were isolated or identified it would probably fall into the dengue group."

W. A. Bourne.

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The consumption of pork products from a single wholesaler was held responsible for an outbreak of trichiniasis, involving 84 cases, occurring in New York in the early part of 1945. The values of the precipitin and intradermal tests as aids to diagnosis during the actual illness are considered. Fifty out of the 84 of the sufferers had eaten a sausage preparation called mettwurst. None of the pork products consumed had been subjected to the usual process of freezing for 20 days at 5° F.

The incubation period varied between 2 and 35 days, but was usually between 5 and 17 days. Attention is drawn to the fact that in this, as in most of the large-scale outbreaks of this disease in recent years, there were no fatalities. The main symptoms were oedema of the eyelids, muscle pains, and fever. Gastro-enteritis, generally considered an early condition, was present in only 7 cases. Differential blood counts were carried out in 72 cases; in 64 eosinophils were found to exceed 10% of the total white cells, and in only 1 of the remaining 8 was the eosinophil count less than 5%. The eosinophil count is considered the most useful single laboratory test in the early diagnosis of trichiniasis, and if eosinophilia is not present the diagnosis should be doubted unless the infecting organisms are isolated.

The precipitin reaction was performed in 40 cases and gave a positive result in 33, with 5 doubtful positive reactions. The intradermal reaction with 1 in 10,000 dilution of trichinella antigen was performed in 38 of the 84 cases and gave a positive result in 15 in some after repeated tests. The earliest positive reaction was obtained on the sixth day of illness, but the best results were achieved after the end of the second week, which makes the test somewhat limited in its use. The authors question the generally accepted view that the skin test becomes positive before the precipitin test, as their results indicate the reverse. The advisability of using both tests in all doubtful cases is suggested. Muscle biopsies were not carried out because it was considered that the other available tests gave positive reactions earlier in the illness.

H. C. Maurice Williams.


It had been noted that sera from patients after smallpox vaccination which gave false positive Kahn reactions tended to become negative when exposed to ordinary room temperatures for several days. The author tested the sera of 59 syphilitic patients (92 sera and 219 tests) over a period of 2 to 6 months with the quantitative Kahn test; the sera were stored at +2° to +4° C. Of the 92 sera, 25 (27.7%) showed a moderate loss of titre; 10 (10.9%) showed a great and 57 (62.0%) maintained a constant titre. He also tested two groups of false positive sera. Group I consisted of 13 patients with smallpox, 15 with malaria, 5 with upper respiratory infections, 2 with scarlet fever, and 1 each with tuberculosis of bone, infectious mononucleosis, gonococcal arthritis, lymphogranuloma venereum, and a "general biologic reaction"; 109 sera were taken and 208 tests carried out; all showed a decrease of titre or became negative at various periods, usually within a month. Group II consisted of 1 patient with pinta whose serum maintained its titre for 3 months, and 5 with leprosy; 2 sera maintained and 4 lost titre. Illustrative cases with results of serum tests are given in seven tables. That the serum from the patient with pinta maintained its titre is not considered surprising, since the disease is due to a spirochaete; the reactions of the other sera are not so easily explained. The loss of titre in general may be due to non-specific antibody being more labile, or to an inhibitor, present in the serum, becoming activated: the difference in behaviour of syphilitic and non-syphilitic sera suggests that the two types of antibody are not the same.

T. E. Osmond.


In this comparison the in vitro activity of penicillin G and X (both pure crystalline) and of F and K (approximately 90% pure) has been tested against freshly isolated cultures of gonococci obtained from a large number of patients. The authors are doubtful whether the gonococcus is an appropriate organism for standard testing and consider that the meningococcus might be more suitable. The tests in a plate that pure crystalline penicillin is 7-3 times more efficient in vitro than is pure crystalline G against freshly isolated gonococci from 76 different patients, and that 90% pure penicillin is 3-3 times as efficient against the same organisms. Pure crystalline G and 90% pure K were also tested against gonococci from 40 different sources, and it was shown that the average in vivo efficacy of K was 1-3 times that of G.

[It will be appreciated that the fate of K in the body would discount its use as a practical therapeutic agent. The authors rightly urge that further clinical trials of crystalline penicillin X in gonorrhoea should be made as soon as possible. Their technique is ingenious and the paper should be read in the original by those who are interested.]

G. L. M. McElligott.
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BIOCHEMISTRY

Absorption and Excretion of Water. The Antidiuretic Hormone. Verney, E. B. (1946). Lancet, 2, 739. In the dog the peak of the diuresis which follows the ingestion of 250 ml. of water occurs after 50 minutes, but the absorption curve reaches the 250-ml. level at 35 minutes. Subtraction of the water-excretion curve from the absorption curve gives the water load curve, which represents the amount of water temporarily held in the tissues in excess of the optimal amount. The peak of the water-load curve occurs 15 minutes earlier than that of the excretion curve. There is therefore a delay of 15 minutes between the maximal stimulus to excretion and the maximal response of the kidney to the stimulus. The diuresis is inhibited by muscular exercise, emotional stress, or a rise in the osmotic pressure of the carotid arterial plasma.

The inhibitory effect of exercise is accompanied by an increase in the chloride, nitrogen, and pigment content of the urine. This inhibitory effect is only apparent and is really due to emotional stress, as emotional stress produced by mild faradism without exercise gives rise to a similar inhibition, which might be due to vasomotor changes, though the rise in chloride excretion is against such an interpretation. This hypothesis is disproved by the fact that the inhibitory response is unaltered by complete denervation of the kidneys. The argument that the inhibition may be due to release of adrenaline is disproved by the fact that the response is not altered by the removal of one adrenal gland and the denervation of the other. Moreover, occlusion of the renal artery, whether complete or partial, causes a different response, the inhibition of urinary flow rising suddenly as soon as the compression ceases. Lastly, direct measurement of renal blood flow during emotional stress demonstrates the independence of the response.

Comparison of the inhibitory response to emotional stress with that due to the intravenous injection of adrenaline and of posterior pituitary extracts shows significant differences. Adrenaline produces a sudden fall in urinary excretion and an almost equally sudden recovery, a response unlike that of emotional stress. On the other hand, a suitable dose of posterior pituitary extract produces a response identical with that of emotional stress. There is a latent period (absent in experiments with adrenaline) followed not only by a decrease in urinary excretion but by an increase in urinary chloride and nitrogen. The return to normal is more gradual than after adrenaline injection. Exact similarity between the responses to emotional stress and to injection of posterior pituitary extract does not prove a causal identity. The proof is found in the fact that the polyuria which follows removal of the posterior pituitary subsides after a week. Thereafter emotional stress fails to elicit the typical response, which, however, occurs as usual after the injection of posterior pituitary extract.

Increased activity of the sympathetic nervous system must accompany the inhibitory effect of the posterior pituitary. The action of adrenaline is not specific, tyramine being as effective. It is probable that increase of cerebral blood flow is the common factor preventing release of the antidiuretic substances. It seems, therefore, that low sympathetic tone associated with noxious stimuli is favourable to the prolonged secretion of antidiuretic hormone. The prolonged secretion of this substance caused by such mild disturbances of the central nervous system that it becomes important to determine whether the secretion is varying continuously under the control of some factor in the animal's internal environment the maintenance of which within a narrow physiological range is important for the animal's welfare. It seems probable that this factor is the osmotic pressure of the carotid plasma, as shown by the finding that the injection of hypertonic solutions into the carotid artery causes an inhibition of urinary flow, the magnitude of the response varying with the tonicity of the solution at constant rate and period of injection and with the period of injection at constant volume and tonicity. This effect disappears after removal of the posterior pituitary but can be mimicked by the injections of posterior pituitary extract. It can be produced by the injection either of sodium chloride or of iso-osmotic dextrose, and is therefore dependent on the osmotic pressure and not specifically the substance. Comparison with the effects of posterior pituitary injections demonstrates that increase in blood chloride of 8 mg. per 100 ml. causes the pituitary to secrete 1 μU. per second. There can be little doubt that the secretion of the posterior pituitary is a hormone in the true sense, its liberation being continuously governed by the contemporary concentration of chloride and possibly of other osmotically active substances in the arterial plasma. The control is presumably effected by osmoreceptors connected by nervous paths with the pituitary.

[This important paper should be read in full.]
Raymond Greene.


The author believes that the clinical features of acute inflammation are due to the liberation of "biochemical substances" from injured cells. In this paper he summarizes his extensive work on this subject and describes the five substances he has so far isolated from inflammatory exudates.

Leukotaxine increases capillary permeability, so that plasma proteins, dyes, colloids, and bacteria readily escape into and are concentrated in the injured area. The author has isolated this in a relatively pure form; it seems chemically not to be a histamine-like substance, as postulated by Lewis, but a relatively simple poly-saccharide. It is positively chemotactic to polymorphonuclears, but does not induce general leucocytosis. Leukotaxine is abundant in the rabbit's succus entericus, and may be found in such fluids as the contents of ovarian cysts.

L.P.F., a leucocytosis-promoting factor contained in inflammatory exudates, causes leucocytosis and hyperplasia of narrow granulocytes and megakaryocytes. The author has also isolated this substance, which appears to be a pseudoglobulin and not present in normal serum.

Necrosin is associated with the euglobulin fraction of inflammatory exudates but not of normal serum. Intradermal injection of necrosin causes an intense inflammatory reaction followed by superficial necrosis; the lymphatics are occluded by fibrin, and blood vessels may be thrombosed. Intravenous injection of necrosin produces necrosis of the liver, pleural effusion, intestinal haemorrhages, or renal changes. Necrosis is lethal to mice.

Pyrexin is another factor in the euglobulin fraction of inflammatory exudates which induces fever when injected intravenously into mice. Pure necrosin is not pyrogenic. Injection of the whole euglobulin fraction of inflammatory exudates causes leucopenia as well as necrosis and pyrexia. Vomiting, diarrhoea, and "general apathy" may also occur. The leucopenia seems to be
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due to “a trapping of the leucocytes in lungs, liver, and spleen.” It is ascribed to a specific leucopenic factor.

[This paper gives little idea of the stimulating qualities of Menkin’s book, The Dynamics of Inflammation. The author’s postulate, that the effects he describes in this paper are due to definite chemical entities constantly present as such in inflammatory exudates, may not gain general acceptance until much confirmatory evidence is available.] Martin Hynes.


Urinary phosphatase was determined by the hydrolysis of monophenyl phosphate and the estimation of liberated phenol by the diazo method of Theis and Benedict, which is unaffected by uric acid. The daily excretion of phosphatases in the urine of 50 males and 25 females without genito-urinary disease was estimated. Alkaliphosphate excretion was low and irregular and showed no significant variation with age or sex. The average daily acid-phosphatase excretion in females is about 50 units, irrespective of age. The male acid-phosphatase excretion level is similar in childhood, but rises sharply at puberty above that of females, reaching a maximum at 350 units between 30 and 40 years and returning to the prepubertal level in old age. The normal rate of haemolysis will explain female urinary excretion of acid phosphatase, but the acid-phosphatase excretion increase in the male during the reproductive period is usually assumed to come from the prostate. Samples collected over 24 hours from 3 men by suprapubic cystotomy suggest, however, that part of the excess acid phosphatase is excreted through the kidneys. No alteration in phosphatase excretion was found in disease of the prostate or in nephritis.

E. F. McCarthy.


Urine samples collected every 24 hours for 11 days from 1 diabetic and 5 healthy persons were examined for nicotinamide methachloride by Coulson, Ellinger, and Holden’s method (Biochem. J., 1944, 38, 150). The subjects were given oral doses of 100 mg. of nicotinamide after the third and ninth urine collection, and of 1 g. of methionine every 12 hours on the seventh to eleventh day. The methionine did not affect the methachloride excretion rate, but when the dosage of nicotinamide was prolonged so as to deplete the body stores of “methyl-donators,” added methionine increased the urinary response. The effect was demonstrated by experiments on groups of 5, 8 (3 pellagrins), and 8 (3 pellagrins) mental patients, whose 24-hour urine samples were collected for 14 days. The patients received either oral or subcutaneous doses of nicotinamide after the third to the thirteenth urine collection and oral doses of 1 g. of methionine every 12 hours on the ninth, tenth, and eleventh days of the test. The effect of methionine was greater after a daily intake of 500 mg. of nicotinamide than after one of 100 mg.

The saturation test described by Ellinger, Benesch, and Hardwick (Lancet, 1945, II, 2, 197) would be affected by a depletion of the body reserves of “methyl-donators,” and the following modified test is recommended. Twenty-four-hour urine samples are collected for 18 days and the urinary nicotinamide methachloride is estimated. Doses of nicotinamide (100 mg.) are administered subcutaneously after the third and twelfth, orally after the sixth, and rectally after the ninth urine collection, and the percentage of ingested nicotinamide excreted during each 24- and 72-hour period after dosing is calculated. The results obtained for 6 physically fit and 3 pellagrin mental patients are discussed. The urinary response to nicotinamide administered rectally was slightly less than to that given orally, showing that nicotinamide can be absorbed from the lower intestine.

J. E. Page.


The author used the Beckman pH meter and Rakoff’s vaginal electrodes to study vaginal pH in 52 pregnant and 15 non-pregnant women. This report differs from previous ones in that the author has determined the pH in different sites of the vagina—namely, anterior fornix, posterior fornix, and left and right lateral walls, the averages for these being 4.26, 4.37, 4.34, and 4.46 respectively. In non-pregnant women the average was 4.34, while in pregnancy the figure was 4.38. The over-all pH average in apparently normal vaginas varies between 3.27 and 4.99.

C. W. Kimbell.


The rate of absorption of penicillin injected subcutaneously into thigh or arm can be considerably slowed by exerting light pressure with a rubber tourniquet proximal to the site of injection. Results comparable to those obtained with oil-beeswax preparations can thus be achieved. The penicillin concentrations in the blood were estimated by the capillary-tube method of Fleming and by another method devised in St. Mary’s Hospital, London, with phenol-red as an indicator of the growth of staphylococci. Trials showed that the tourniquet should be applied for times varying from 1 hour after injections of 10,000 units to 5 hours after 100,000 units. With this method of administration the number of injections can be reduced to three of 75,000 units in 24 hours or to five of 100,000 units in 48 hours without letting the penicillin level fall below the lowest effective one.

Geoffrey McComas.


A micro-method is described for the estimation of penicillin in serum: it is a modification of previous methods described by Fleming and by Dr. J. Fielding. The medium used consists of serum (human, horse, sheep, or ox) 2 ml., 10% glucose solution 2 ml., water 6 ml., and phenol red, saturated solution, 0.25 ml. This can be sterilized either by steaming in bulk or by boiling for a few minutes. A suitable quantity of the medium is inoculated with the test organism (5 ml. of a 24-hour broth culture to 1 ml. medium): the authors use a haemolytic streptococcus, which produces acid more quickly than staphylococcus. Serial dilutions of the serum to be tested (25-ml volumes) are made in the inoculated medium on the surface of a paraffined slide. Glass capillaries made from soda glass, not from hard
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Urinary 17-ketosteroids can be divided into alpha and beta fractions, the alpha produced by the adrenal cortex and testes, the beta by adrenal cortex only. The authors report cases of adenocortical carcinoma with markedly elevated total 17-ketosteroids in which differentiation into alpha and beta fractions was of value. The first case was in a woman of 31 years with menstrual disturbances, gain in weight, hypertrichosis, and a mass in the right upper quadrant of the abdomen. Total urinary 17-ketosteroids amounted to 75 mg. per day (alpha 19.7, beta 55.3). (Normal for adult women: total 2.7 to 8.1; 5 to 15% alpha.) With the right suprarenal removed, 10 days after operation total 17-ketosteroids measured 3.8 mg. per day. The patient was well one year after operation. The second case was in a 2-year-old girl with pubic hair and a large clitoris. Excretory urograms showed a right adrenal tumour depressing the right kidney. Urinary 17-ketosteroids measured 78.5 mg. per day (alpha 15.7, beta 62.3). (Normal for a child aged 4 to 7 years: average of 1.3 mg. per day.) An adrenal cortical adenoma undergoing carcinomatous change was removed from the right side. Ten days after operation 17-ketosteroids measured 0.9 mg. per day. The child was well 6 months after operation, but there was only slight retrogression of pubic hair. The third case was in a man of 43 with an inoperable carcinomatous mass in the left adrenal region and no hormonal symptoms; 17-ketosteroids amounted to 86 mg. per day (alpha 36.6, beta 49.4). (Normal for adult man: 3.4 to 15 mg. per day.) The amount fell with radiotherapy, which produced clinical improvement, but rose again with re-growth of the tumour. The patient was discharged as unfit for further treatment.

D. H. Patey.


Bull spermatozoa lose respiratory activity and motility when kept under aerobic conditions in egg-yolk medium. This inhibition is due to hydrogen peroxide, which is formed by enzymic action for some dialysable constituent of the egg yolk. The chemical behaviour of this constituent during attempts at its isolation suggested that it is an amino-acid. L-Tryptophane, L-tyrosine, and L-phenylalanine can replace egg-yolk medium and in the presence of living spermatzoa give rise to hydrogen peroxide. Only these three amino-acids of the many tested had this property. Such specificity of an L-amino-acid-oxidase is unusual. The adverse effects of hydrogen peroxide on sperm respiration and motility are produced with concentrations that are chemically undetectable, but appreciable since the effect is abolished by the addition of catalase.

[The finding will be useful in arranging optimal conditions for the storage and transport of sperm for artificial insemination, but probably has no physiological importance. Judgment on this will await more detailed description of the aerobic conditions needed for the enzymic activity.]

P. C. Williams.


This is a review of the dinitrobenzene assay of sex hormones and its applications in physiological, biochemical, bacteriological, and clinical research. The author's method for the assay of sex hormones in urine and blood is given in detail. The method has also been worked out for the assay of androgenic hormones in blood.

M. B. Klein.

HAEMATOLOGY


In some 92% of cases of erythroblastosis foetalis the mother is Rh-negative—that is, all her cells are not agglutinated by the anti-Rh (anti-D) serum and her serum contains anti-D agglutinins or blocking antibodies. In about 8% of cases of erythroblastosis foetalis the mother is Rh-positive; in these cases the factor responsible is one of the other Rh antigens, such as Hr[c] or in some cases the ordinary A and B antigens or possibly other rare blood group factors. When A or B are responsible "tests of the affected infant's saliva or the deceased infant's organs should reveal the infant to belong to the non-secretor type." "The demonstration of specific increase in anti-A or anti-B agglutinins is contributory evidence." [These two statements are difficult to reconcile, since it has been shown by Smith that iso-immune responses to A and B during pregnancy only occur when the infant is a "secretor." ] The statistical proof of the part played by A and B in causing occasional cases of erythroblastosis foetalis is given in the following table:

<table>
<thead>
<tr>
<th>Matings</th>
<th>Compatible %</th>
<th>Incompatible %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random</td>
<td>65</td>
<td>35</td>
</tr>
<tr>
<td>215 Rh-negative mothers*</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td>28 Rh-positive mothers*</td>
<td>50</td>
<td>50</td>
</tr>
</tbody>
</table>

*Mothers of erythroblastotic infants.

In this table incompatible matings are defined as those in which the father's blood contains A or B and the mother's serum contains corresponding anti-A or
anti-B agglutinins. The higher value for incompatible matings in the Rh-positive mothers indicates that iso-immunization by the A or B factors can explain at least some of the exceptional cases. That incompatible matings of this kind also sometimes cause early foetal death is suggested by the following figures:

<table>
<thead>
<tr>
<th>Matings</th>
<th>Compatible</th>
<th>Incompatible</th>
</tr>
</thead>
<tbody>
<tr>
<td>115 with 2 or more miscarriages</td>
<td>46%</td>
<td>54%</td>
</tr>
<tr>
<td>43 with 2 miscarriages or stillbirths</td>
<td>44%</td>
<td>56%</td>
</tr>
</tbody>
</table>

"These figures are highly suggestive and probably significant." Obviously the statistical proof cannot be expected to be so convincing as in the case of the connexion between the Rh factor and erythroblastosis foetalis, since there are certainly many causes of abortion and stillbirth besides iso-immunization to A and B. Further support for the view that immunization against A and B occasionally causes foetal death is provided by the observation that the proportion of A children in matings between A fathers and O mothers is slightly smaller than that produced by matings between O fathers and A mothers. Erythroblastosis foetalis occurs very rarely in the first-born; however, transfusion of Rh-negative women at any time before pregnancy tends to increase this occurrence, especially in its more severe form.

Erythroblastosis Foetalis in the First-born of Rh-negative Women

<table>
<thead>
<tr>
<th>Transfusion History</th>
<th>Previously Transfused</th>
<th>Never Transfused</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severity of disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Severe</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Foetal deaths</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>9</td>
</tr>
</tbody>
</table>

All persons giving transfusions of blood should be aware of this most serious risk. [This paper is a summary of information previously published, but it is worth reading even by those who are already familiar with Levine's contributions. Only a few points in it can be referred to in this abstract.]

P. L. Mollison.


At present two different preparations of blood-group-specific substances are available commercially in the U.S.A.: (1) the A specific substance isolated from hog stomach, and (2) the AB specific substance isolated from horse stomach. Both are chemically free from protein, and neither will sensitize guinea-pigs. These purified preparations are of practical use:

1. In neutralizing the anti-A and anti-B iso-antibodies of blood of group O. There is now abundant evidence that anti-A and anti-B agglutinins in group O blood frequently cause some degree of destruction of the recipient's erythrocytes when the latter are of group A or B; occasionally the degree of destruction is sufficient to cause severe or even fatal reactions, a danger that can be avoided by the addition to the blood of small amounts of AB substance to reduce the strength of the antibodies to a harmless level.

2. In suppressing anti-A and anti-B iso-agglutinins in anti-Rh sera. In making Rh tests, sera obtained from human beings who have been sensitized by pregnancy or transfusion are most frequently used. These of course often contain anti-A or anti-B agglutinins, which must be removed or neutralized before the sera can be used to test AB cells. Complete suppression of the anti-A and anti-B agglutinins can be effected by quite small amounts of the purified group-specific substance.

3. In production of potent grouping sera. As little as 0·1 mg. of blood-group-specific substance injected intravenously into human beings will often produce a tenfold to one-hundred-fold increase in the original iso-agglutinin titre. At the same time the avidity of the sera is increased (a minority show a small or negligible response).

P. L. Mollison.


In an effort to correlate the laboratory findings with the clinical condition of the babies at birth, the authors studied the antibody titre of 179 Rh-negative expectant mothers. The maternal sera were examined for complete and incomplete antibodies. The investigations were carried out in 1944–5, and the latter type of antibody was detected by its blocking activity with Rh\textsubscript{0} (cDe/cde or cDe/cDe) cells and not by the Race-Coombs test.

The 179 pregnancies are divided into four groups: group 1, normal Rh-negative children; group 2, normal Rh-positive children; group 3, "subclinical" haemolytic disease of the newborn; group 4, severe haemolytic disease of the newborn. In group 1 (61 cases), only 9 showed isolated complete anti-Rh antibodies, probably carried over from previous pregnancies. Group 2 (78 cases) showed no ante-partum antibody production, but a small titre of either complete or incomplete antibody might appear post partum, reaching a maximum usually in the second week. There was no significant difference between primiparous and multiparous women. Group 3 (17 cases) showed production of antibodies in the last 12 weeks of pregnancy. Ante partum, in this group, there appeared to be a predominance of blocking antibody, but the amount of this fell after delivery. Of the 17 mothers, 3 were primiparous and 14 multiparous—a significant difference. In group 4 (20 cases) antibodies were always demonstrated ante partum and usually the amounts of the two varieties (complete and incomplete) varied inversely; in no case did they rise or fall together. Most commonly the complete antibodies diminished as pregnancy advanced and the incomplete antibodies increased.
ABSTRACTS

In 4 cases stillborn children were delivered, and in 3 of these complete antibodies were demonstrated in the maternal serum. On the other hand, in only 3 of 12 infants born alive were blocking antibodies not demonstrated in the mother's blood. The authors point out that this contradicts Wiener's view that the incomplete antibody is of more serious import, and discuss the possibility that the incomplete antibody acts as a protective substance for the foetal red cells. The antibody titres in group 4 rose to a maximum about the second week post partum and then declined. 

A. J. Buller.


A method is described of substitution transfusion given immediately after birth in the sub-icteric stage of haemolytic disease of the newborn to prevent subsequent damage to the liver and brain. Hepatic damage in cases of icterus gravis by excessive red-cell haemolysis and a reactive liver haemopoiesis has been recognized. If this is to be avoided the end-products of haemolysis must be removed or their formation prevented. This may be done by withdrawal of the infant's Rh-positive cells and their replacement by harmless Rh-negative cells. Withdrawal and replacement should be carried out simultaneously. The technique is as follows: (1) Isotonic saline or pooled plasma is infused into an arm vein. (2) Blood (50 to 60 ml.) is withdrawn by syringe from the longitudinal sinus. (3) Rh-negative blood of a compatible group replaces the plasma or saline infusion. (4) When an estimated substitution of 80% has been accomplished the needle is removed from the fontanelle. The estimate is based on the infant's weight, counting the total blood volume at 10%. (5) The infusion is continued until 75 to 100 ml. of Rh-negative blood has been given in excess of the amount recovered, 10 ml. of 10% calcium gluconate being injected into the vein to counteract the citrate in the blood or plasma. The procedure takes from 1/2 to 1½ hours. Alternatively blood may be withdrawn from a very small branch of the radial artery at the wrist. It is difficult to obtain enough blood from superficial veins. (Withdrawal of blood from the longitudinal sinus is not without its dangers in a jaundiced baby.)

Details of cases in which the prognosis was considered grave are given. Seven patients recovered and 2 died, both of whom might have recovered if treatment could have been started in the first 24 hours of life. Emphasis on anaemia as the indication for treatment is an error; the protection of the liver is the primary indication. About 30% of cases of haemolytic disease show liver damage and 10% kernicterus; until these changes can be accurately forecast, substitution transfusion should be used in all cases. If cases are to be selected the following are the most helpful criteria: (1) multiparity with a history of erythroblastosis in previous pregnancies; (2) serological studies; (3) during delivery, the presence of icteric amniotic fluid; (4) an excessively large, pale placenta; (5) excess of nucleated red cells in the blood in the cord. With such indications preparation should be made in advance and substitution therapy instituted as soon as the baby is born.

A. G. Watkins.


Miller, in association with other workers, has previously shown that myelokentric acid and lymphokentric acid are present in varying amounts in the urine of patients with acute and chronic leukaemia, Hodgkin's disease, and lymphosarcoma. He has suggested that these substances are of fundamental importance in the abnormal processes of blood-cell production in the leukaeasias, since they may constitute a balance mechanism in normal blood-cell proliferation and maturation. Lymphokentric acid is thought to bring

Five patients with Addisonian pernicious anaemia were given rapidly repeated blood transfusions until the erythrocyte counts and haemoglobin values in three were within normal limits. The symptoms attributable to the diminished oxygen-carrying capacity of the blood were relieved, but not such complaints as anorexia, apathy, and other digestive disturbances; these disappeared with liver extract. This sequence is typical of the nutritional deficiency disorders and indicates that blood transfusion does not relieve the fundamental defect in pernicious anaemia.

Injection of liver extract into the patients with normal blood counts following transfusion failed to cause any reticulocytosis, thus showing that this phenomenon occurs only when the stimulus of anoxia is exerted on the bone marrow. After transfusion but before the administration of liver the "bone marrow megaloblasts characteristic of pernicious anaemia" disappeared. The authors believe that a "maturation arrest" due to nutritional deficiency exists in pernicious anaemia. That haemolysis may be a factor of importance in the causation of anaemia they do not, however, attempt to deny.

[From the context it seems probable that the authors mean by the word "megaloblast" the most primitive nucleated red blood cell and not a series of abnormal elements. It is in this latter sense that most haematologists now employ the term, and as it is customary to regard the bone marrow in pernicious anaemia as dysplastic, the "maturation arrest" hypothesis becomes untenable.]

R. Bodley Scott.


The authors have studied by Hahn's technique the rate at which small doses of radioactive iron injected intravenously are used for haemoglobin synthesis. In healthy adult men utilization is almost complete 75 days after injection; normal dogs, however, used only 35 to 70% of the injected isotope. In iron-deficient patients and dogs there was complete utilization in 5 to 6 days. In hypoplastic anaemia less than 4% of the injected isotope was used; in pernicious anaemia in relapse utilization was insignificant until red-cell formation became active as a result of giving liver; it was then greatly accelerated and eventually became complete. In haemolytic anaemia the percentage of an injected dose of radioactive iron in the peripheral blood varied greatly from time to time.

The authors seek to explain some of these results on the hypothesis that iron recently stored, whether derived from absorption from the alimentary tract, from injection, or from breakdown of haemoglobin, is retained in a form mobilized more easily than iron which has been stored for longer periods. It is thus used selectively for current needs. They point out that as radioactive iron is not used completely for haemoglobin synthesis it is unsafe to use as a measure of absorption the proportion of an oral dose appearing in the blood, as has been done in the past.

R. Bodley Scott.


The ability of normal plasma to accelerate the coagulation of haemophilic blood has long been recognized. This effect has been shown to be unrelated to any of the formed elements of the blood. This paper records the fractionation of haemophilic plasma by the Physical Chemistry Department of the Harvard Medical School and subsequent testing of the fractions for anti-haemophilic activity in comparison with those of normal plasma. Both plasmas were similar in detectable protein content, Tiselius diagrams, and fibrinogen and prothrombin content. Normal plasma and normal fractions I, II, III, and IV-1 contain a substance capable of accelerating clotting of haemophilic blood. This substance is absent from haemophilic plasma and its fractions. The fractions mentioned contain most of the globulins and the fibrinogen.

Further efforts (article XXXIII, p. 876) have been made to determine the protein fractions of normal plasma which have the power of accelerating the clotting of haemophilic blood. After removal of fibrinogen from Fraction I by heat, the residual solution retains diminished its anti-haemophilic power.

R. Bodley Scott.

MORBID ANATOMY AND HISTOLOGY


A careful study at 1,460 consecutive necropsies disclosed that in 139 (9.5%) adenomas were present in the colon or rectum. In 80 cases the tumour was single, in 59 multiple. There was a steady increase in the incidence after the age of 30, the incidence reaching a maximum in the eighth decade, when 25.8% of the males and 20.5% of the females were affected. The author found that he could not classify the tumours on their macroscopic or microscopical appearances. There was no recognizable difference from the adenomatous of familial adenomatosis coli. Different cross-sections of the same tumour showed varying microscopical appearances. The tumours were prone to trauma and infection, inflammation, ulcers, small abscesses, and haemato-
mata, haemosiderin being found in them at times. Evidence of previous or present colitis was found in only one case in association with an adenoma, and so the author considers colitis an unlikely exciting agent and believes the tumours to be true neoplasms.

It was noted that adenoma was commonest in the sigmoid colon, as was carcinoma. Early carcinomatous change was found in 10 of the 139 adenomata. This might occur in any part of the tumour—stalk, base, or periphery. In one case 2, and in another 3, adenomata showed early carcinomatous degeneration. Three of the 10 also had manifest carcinoma associated with the malignant adenoma. In the 1,460 necropsies 20 manifest or obvious carcinomata of the colon were found, and 13 of these had either benign adenoma or adenoma with malignant transition associated with them. Two cases in which a very early carcinoma appeared to be arising from the mucous membrane were also seen, both of which were unassociated with either adenoma or manifest carcinoma elsewhere in the colon. Thus a significant association between adenoma and carcinoma is shown, and the conclusion is drawn that, while some carcinomata arise directly from the mucous membrane, the majority arise in adenomata.

[This valuable article would repay study in the original.]

N. Tanner.


The author describes fully, with illustrations, a series of cases of bone lesions culled largely from his own observations. He describes a bone tumour in a young girl which, though radiologically diagnosed as a sarcoma, proved to be syphilitic. Here the onset 7 weeks after a blow at the site had suggested to the author the possibility of an infective lesion and caused him to advise against amputation. Another sarcoma-like tumour in the humerus of a child was accompanied by an apparently typical secondary deposit in the lungs. This precluded surgery, and sulphathiazole administration was advised. In 2 years, restitution of the bone to normal was complete and the “secondaries” had vanished. The author suggests that this may have been a manifestation of reticulo-endotheliosis. A case of sarcoma in the femur of a young man showed seemingly good response to radiotherapy, but there was local recurrence within a year, and later, after amputation, skeletal metastasis. The author suggests that surgery, to be successful, should follow closely on radiotherapy. A further case of bone disintegration occurred at the lower end of the femur in a boy, aged 14, who was suffering from paralytic deformities. This showed gradual spontaneous consolidation and recovery. The lesion is considered, for reasons based upon the radiological appearance, to have been probably a neurotrophic joint condition allied to Charcot’s disease.

That biopsy may prove misleading, and should not in the face of contrary radiological evidence be given too much weight, is the moral drawn from 2 further cases of sarcoma. Biopsy material was reported to be inflammatory, but both cases developed secondary deposits. Two cases of osteoclastoma are described. The author states that radiotherapy may cure, but immobilization in plaster during the active stages is important. The first patient did well. The second was poorly immobilized, did not respond to treatment, and had eventually to undergo amputation for secondary haemorrhage. The patient is now otherwise well. Failure to give due weight to the radiograph by the surgeon in the case of a man of 58 with a swelling at the knee-joint resulted in amputation. The lesion proved to be a Baker’s cyst. The radiograph showed typical osteo-arthritis changes only. The rapid onset of secondaries after diagnosis of a bone sarcoma in another case described suggests the hopelessness of surgical intervention, but against this is quoted Speed’s case in which, after amputation of a sarcoma, secondaries in the lung became shrunken and hard in outline, and remained unchanged 10 years later.

The author concludes that clinical and radiological evidence must be carefully correlated, that biopsy may be misleading, and that too hasty recourse to surgery may be ill-advised. He makes a plea for more emphasis on clinical radiology and less upon physics during the training of students.

A. M. Rackow.


The authors report their study of 922 cases of testicular tumours collected at the Army Institute of Pathology (U.S.A.) between October, 1940, and May, 1946. Most of these occurred in men of military age, 18 to 38 years, although men up to 50 years of age were also included. The distribution of the tumours was: 35% seminomatous, 35% teratocarcinoma (malignant teratoma), 19% embryonal carcinoma (including choriocarcinoma), 4% adult teratoma, and 3% miscellaneous tumours. The incidence (corrected for army population in each age group) of teratocarcinoma was practically constant throughout the age groups, being approximately 1 per 100,000 men, whereas the incidence of seminoma rose with age. Structurally the most homogeneous tumours were the seminomata, although a small number of cases showed anaplasia and were difficult to differentiate from embryonal carcinoma. The authors believe that seminoma does not arise from spermatogonia but from primordial germ cells; they suggest that this tumour should be called “germinoma.” It is emphasized that seminomata differ both structurally and biologically from embryonal carcinomata. The common varieties of the latter type of tumour are those which show glandular and papillary structures (adenocarcinoma and papillary adenocarcinoma), and those which resemble trophoblastic elements, usually cytotrophoblastic and occasionally syncytiotrophoblastic components of chorionic carcinomata.

Choriocarcinoma (chorion-epithelioma) is regarded as a variety of embryonal carcinoma rather than a separate entity, because chorionic structures were observed also in predominantly embryonal carcinomata and because gynaecomatia and related endocrine changes were associated as often with embryonal carcinomata (or teratocarcinomata) as with chorionic carcinomata. Under the term teratocarcinoma the authors include all tumours which contain differentiated teratoid structures and foci of histologically malignant growth. Most of such tumours examined were mixtures of teratoma, embryonal carcinomata, and/or chorionic carcinomata. Teratocarcinoma may be considered as arising from the teratoid differentiation of embryonal carcinoma. Teratoma without histologically malignant elements should not be termed benign, because they often produce metastases. The metastases of seminomata consisted usually of the same type of cell as the primary growth, but occasionally the metastases showed the characteristics of embryonal carcinoma or teratocarcinoma.
The metastases of embryonal carcinomata were likewise similar to the primary growth, but in some cases the metastases had the structure of chorionic carcinoma, although there was no evidence of this in the primary growth. With teratocarcinomata 40% of the metastases consisted of embryonal or chorionic carcinoma and 60% of teratoid structures. The immediate prognosis is bad in embryonal and chorionic carcinomata and poor in teratocarcinomata and adult teratomata. In seminomata, in comparison with the other tumours of the testis, the immediate prognosis is good. G. Popjak.


Following up the work of Randall, who in 1941 described the finding of small macroscopic calcareous deposits on the surface of the renal pyramid in 20% of 1,100 pairs of kidneys, the author investigated microscopic calcareous deposits in the substance of the renal papilla. The diameter of these deposits is at least five or six times that of a normal tubular cell. He found them in all of 170 kidneys examined. Some of these organs were apparently healthy and some were diseased; all were removed from bodies more than 9 years of age at the time of death. Discussion of these findings concerns the possibility that these microscopic deposits may form the nidus for the formation of Randall's plaques, and so perhaps for renal calculi in certain circumstances.


A study of the cytology of conjunctival scrapings, exudates, and follicular expressions may, in combination with the bacteriological report, be of great assistance in making a correct diagnosis in cases of conjunctival disease. The staining method recommended is by Giemsa, 1 drop of stock solution in 1 ml. of distilled water, applied for 1 hour after fixing in absolute methyl alcohol. Excess stain is removed by washing in two changes of 95% alcohol. A polymorphonuclear leucocyte reaction is found in most cases of acute and chronic conjunctivitis, the outstanding exception being diplobacillary infection. An eosinophil reaction is characteristic of all allergic inflammation and is found in hay-fever conjunctivitis and in various drug cosmetic allergies as well as in spring catarrh. Mild eosinophilia is found in ocular pemphigus but not in phlyctenular conjunctivitis. There is also a basophil reaction in allergic inflammations of the conjunctiva, parallel with the eosinophilia, but this is not specific because it may also occur in such non-allergic inflammations as trachoma. Mononuclear cells, chiefly lymphocytes, are found in exudates from epidemic kerato-conjunctivitis and acute follicular conjunctivitis. There is a similar reaction to the typical virus infection, such as that due to herpes or molluscum contagiosum. Plasma cells are found in the exudates of trachoma. Keratinization of epithelial cells is found in vitamin A deficiency and also in kerato-conjunctivitis sicca. The author is unable to confirm previous observations that trachoma can be diagnosed from conjunctival cytology at an early stage, but states that the cytology of expressed trachoma follicles is characteristic. The predominant cell is the lymphoblast, which shows degenerative changes, and there are many macrophages (Leber cells). This typical appearance is due to the necrotizing action of trachoma toxins.

A. G. Cross.


This well-documented paper records experiments made on rabbits and post-mortem observations on 28 cases of human thyrotoxicosis. Histologically there is a basic similarity. In the severe cases there is generalized atrophy of the hepatic parenchyma with gross cytoplasmic deprivation (glycogenolysis); in the more extreme cases there is also necrosis, generally central and most obvious in the subcapsular zone. Intoxication of low intensity and short duration produces lesser parenchymatous lesions of reversible degree. If of longer duration, or repeated, the intoxication is followed by fibrosis, both primary (portal in situation) and secondary (in relation to the necrosis).

A. C. Lendrum.


Five fatal cases of Wernicke's encephalopathy were studied histologically. All the subjects were said to have been chronic alcoholics, though there is no reference to the amount of alcohol, its nature (except in one case), or the duration of alcoholism. Naked-eye examination of the brain showed cortical atrophy in 4 of the cases and small haemorrhage in the brain-stem in 2. Microscopic examination revealed histological changes confined largely though not entirely to the periventricular grey matter of the midbrain and pons—throughout the hypothalamus, mammillary bodies, medial aspect of the thalamus, inferior colliculi, and to some extent in the floor of the fourth ventricle. In the affected areas the capillaries showed proliferation of endothelial cells and the perivascular spaces were enlarged. There were areas of old and fresh haemorrhages, perivascular and of different sizes. Focal areas of parenchymal necrosis varied from one to several millimetres in diameter. Within the areas of haemorrhage and necrosis, focal neuronal degeneration was present in all cases. In the affected areas astrocytes showed proliferation and degeneration, and to some extent transformation. Oligodendroglia was swollen, with multiplication of cells. It is considered that underlying the histological changes there is a deficiency of nutritional factors, the chief of which is thiamine. It is considered that thiamine lack interferes with carbohydrate metabolism, with resulting anoxia of the tissues.

Hugh Garland.