ABSTRACTS

Acute Rheumatism


The difficulty of maintaining continuous chemoprophylaxis with penicillin in children with a past history of rheumatic fever, together with certain theoretical considerations, led the authors to investigate the value of such prophylaxis compared with that of penicillin treatment given on clinical indication alone.

The study was carried out over a 6-year period on children who had at least one observed attack of rheumatic carditis and were attending the Cardiac Rheumatic Clinic of the New York Hospital, 110 of whom received continuous prophylaxis (Group 1) and 103 penicillin therapy for 10 days only when indicated by the onset of a respiratory infection or signs of faucial inflammation (Group 2). The selection of the groups was not made at random, children with recent carditis usually being given continuous prophylaxis, while transfers from one group to the other also occurred. Group 2 contained a higher proportion of older children (13 to 16 years) than Group 1.

The recurrence rate of rheumatic carditis was found to be 6-6 per 1,000 patient-months in Group 1 and 2-9 per 1,000 in Group 2. This difference was found to be due to the greater number of more susceptible children with recent attacks in Group 1. There was no significant difference between the recurrence rates in different age groups in either group. Altogether seventeen recurrences were observed in Group 1 (associated with chorea in seven cases and polyarthritis in nine) and eight in Group 2 (with chorea in three cases and polyarthritis in five). Spot throat cultures in Group 1 revealed the presence of \( \beta \)-haemolytic streptococci in nine of 98 children who had sore throats; none of these relapsed, whereas in throat swabs from ten children who relapsed no \( \beta \)-haemolytic streptococci were found. In Group 2, of 94 spot cultures from children with sore throats, \( \beta \)-haemolytic streptococci were isolated from fifteen, while of six throat cultures from patients with recurrences, \( \beta \)-haemolytic streptococci were isolated from five.

Although it is agreed that there has been a great decline in the incidence of rheumatic fever in recent years, the authors point out that this decline antedated the antibiotic era and has not been accelerated since. They conclude that for children under close medical supervision continuous oral penicillin prophylaxis has no advantage over adequate penicillin therapy as indicated. Indeed it remains possible that the recurrence rate in this trial would have been the same if no penicillin had been given at all.

[This is a challenging paper. Nevertheless, the authors' conclusions should not be accepted without fuller proof. The two groups were not comparable, and subclinical streptococcal infections were not looked for by estimation of the antistreptolysin-O titre. It is of interest that \( \beta \)-haemolytic streptococci were isolated from nine children receiving continuous prophylaxis, none of whom developed rheumatic fever, whereas of fifteen children in Group 2 from whom \( \beta \)-haemolytic streptococci were isolated, eight suffered a recurrence of their rheumatic carditis.]

John Lorber.


It has been claimed that in rheumatic fever the fasting serum level of lipoprotein streptolysin-S inhibitor is significantly lower than normal, even during the quiescent phase of the disease. This study reported from New York Medical College and Metropolitan Hospital, New York, was designed to determine whether rheumatic fever is associated with abnormalities in the serum lipid level which might be due to genetic or environmental factors. It was found that in rheumatic children under the age of 14 years in whom the disease had been quiescent for one year, the mean non-fasting lecithin-plasma level (2-76 mMol. per litre) was significantly lower than in their healthy siblings (3-15 mMol. per litre) living
under similar environmental conditions. The part played by constitution, heredity, and the disease in bringing about this difference is unknown [and its significance in aetiology is largely conjectural].

E. J. Holborow.


An investigation is reported from the University of Miami School of Medicine, Florida, of the antistreptolysin-O titre in serial blood samples obtained from 236 school children during the winter of 1954-55. Blood was drawn in all cases at the beginning and end of the study. Throat swabs were obtained as a routine each month and whenever β-haemolytic streptococci were cultured, blood samples were withdrawn more frequently. In 48 out of a total of 472 blood samples the antistreptolysin-O titre was 250 or higher. The lowest average initial and final titres were found in children from whom no streptococci or only Group-B organisms were isolated and the highest in those in Group-A organisms. Infection with streptococci of Groups C and G were accompanied by moderate increases in titre. A rising antistreptolysin-O titre in successive blood samples was observed in sixteen (29 per cent.) out of 55 children with typable Group-A strains, nine (27 per cent.) of 37 with non-typable Group-A strains, three (17 per cent.) of eighteen with Group-C organisms, and ten (9 per cent.) of 99 with negative throat swabs. Between 1953 and 1955 a general rise in antistreptolysin-O titre was observed among those children for whom data were available over the 2-year period. There were 57 incidents of Group-A streptococcal infection associated with a 2-tube rise in antistreptolysin-O titre, but none of the affected children developed rheumatic fever. The authors emphasize that the value of isolated and serial estimations of antistreptolysin-O titre is limited and requires careful assessment.

Allan St. J. Dixon.


The frequent occurrence of rheumatic heart disease in patients with an interatrial septal defect is well known, but the association of such disease with other cardiac anomalies has been less often mentioned. In this paper from the Medical College of South Carolina, Charleston, the authors report that among 36 patients operated on for patent ductus arteriosus and followed up for 2 to 7 years were six in whom cardiac murmurs were absent immediately following ligation of the ductus but became audible one to eight days postoperatively and thereafter persisted or in some cases progressed. After further study four of these six patients were thought to have definite and two to have probable but less certain rheumatic heart disease. Detailed case reports are presented.

The authors were impressed with this apparently frequent coincidence in their series and review some of the literature on the co-existence of rheumatic heart disease with various congenital heart lesions. They suggest that there may be an increased susceptibility to rheumatic carditis in all patients with congenital heart defects, and that this provides further evidence that the "post-pericardiotomy syndrome", occurring as it does sometimes after operations for congenital cardiac defect as well as after valvotomy for rheumatic valvular disease, may indeed as has been suggested be due to reactivation of the rheumatic fever. They therefore propose, as a practical implication of their study, that prophylaxis with antibiotics as a routine might be as desirable in congenital cardiac conditions as in rheumatic heart disease and that postoperative follow-up should be prolonged.

[To further this interesting speculation the authors will need to provide much fuller data in a larger series of patients. This relatively small study is unconvincing.]

Celia Oakley.


The incidence of rheumatic manifestations, of intercurrent respiratory infections, and of laboratory evidence of streptococcal infection was studied during a 3-year period at St. Joseph's Children's Heart Hospital, Rainhill, Liverpool. Most of the children were convalescent from rheumatic fever. For the first year no prophylactic treatment was given. During the second and third years phenoxyethylpenicillin (penicillin V) (60 mg. twice daily) and benzylpenicillin (penicillin G) (200,000 units twice daily) respectively were given. Throat swabs were cultured and blood was taken for estimation of the antistreptolysin-O (ASO) titre and erythrocyte sedimentation rate (E.S.R.) at fortnightly intervals. During the first year (control period) out of 38 children, three developed typical rheumatic fever and two less definite rheumatic fever. During the second year, one out of forty had typical and three less well-defined rheumatic fever. In the third and last year, only one case of typical rheumatic fever occurred among 39 children. The cases of chorea numbered three, two, and one respectively. Rheumatic carditis without other manifestations of rheumatic activity developed in one child during the second year and in one during the third. [Not a well-defined category: one child had a raised ASO titre and another erythema marginatum in addition to the cardiac signs, which consisted in heart failure in children with established valvular disease.]

Six children developed acute bronchitis during the first year, six during the second, and three during the third. Not all children considered to have active rheumatism had a raised E.S.R. Group-A β-haemolytic streptococci was found on only a single occasion (from a child taking benzyl-penicillin) and no child had typical tonsillitis. Two children showed a prolonged rise of the ASO titre during the control period in addition to those considered to have rheumatic fever, as did eight
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during each of the two treatment periods. Good blood penicillin levels were found with phenoxyethylpenicillin, but in spite of this the clinical results were poor. Higher and more sustained levels were obtained with the bigger dose of benzylpenicillin and the results were better, though the difference was not significant.

The frequency of high ASO titres in the absence of β-haemolytic streptococci on the throat swabs remains unexplained [but the throat swabs were not plated out fresh, but were taken to another hospital for that purpose.]

[This paper does not deal with the general management of children in the convalescent stage of rheumatic fever or during relapses. It does appear, however, that children are kept in hospital for very long periods and that steroid treatment is not used regularly.]

John Lorber.


Rheumatic heart disease in all its stages can be successfully treated on the same principles as other chronic allergo-infective diseases, such as tuberculosis and syphilis. Corticosteroid hormones in combination with antibiotics are the most potent therapeutic agents in such cases and are indicated also in the presence of cardiac failure, particularly in the young.

The therapy advocated often results in remissions and in prevention of recurrences and of progressive lesions of the cardiac valves. Therapeutic failures are due to already established irreversible rheumatic collagenosis and permanent sclerosis.

A. Orley.


In an attempt to determine the change which has taken place in the severity of rheumatic fever during recent years the clinical records were studied of the first 100 cases admitted in a first attack to the House of the Good Samaritan, Boston, during each of the years 1921-22, 1930-31, 1940-41, and 1950-51. All patients were under 20 years, the majority being under 10 years. There was a slight decrease in the incidence of carditis as judged by evidence of valvular disease, the incidence being 75 per cent. in 1921-22 and 60 per cent. in 1950-51. However, if the severity of the carditis was assessed in terms of cardiac enlargement there was a much more striking change. Of the 75 patients with carditis in 1921-22, 23 (30 per cent.) had marked cardiac enlargement while only fifteen (20 per cent.) had no enlargement of the heart. By contrast, in 1951-52, there was no cardiac enlargement in 28 (45 per cent.) and only in eight (14 per cent.) was it marked. Of the 100 patients admitted in 1921-22, 24 were dead within 5 years, whereas only three of those admitted in 1951-52 died within 5 years. The fall in the severity and mortality was gradual throughout the 40 years and was most marked towards the end of the 1930-39 decade, before the advent of penicillin. It is suggested that the most important factor responsible for the change was the considerable over-all improvement in the standards of living "of the poorer classes in urban areas". C. Bruce Perry.

Mimetic Features of Rheumatic-fever Recurrences.


In this paper from Irvington House and New York University College of Medicine an analysis is presented of the manifestations of recurrent attacks of rheumatic fever in 161 patients observed in at least one attack for whom accurate information about initial and subsequent attacks was available. In 61 patients, who had a total of 129 attacks, and there was no clinical evidence of carditis in the first attack and the heart remained normal subsequently. In ninety patients, with a total of 219 attacks, the heart was clinically involved in the initial attack; in subsequent attacks the valvular damage “remained the same, recrudesced, or became worse.” The remaining ten patients (thirty attacks) showed no cardiac involvement in the first attack but were found to have a significant diastolic murmur in recurrent attacks. It is suggested that in some cases at any rate the murmur may have been missed in the first attack. Non-cardiac manifestations of rheumatic fever were frequently repetitive in all patients. Joint involvement occurred in each of the 82 attacks in 39 patients, chorea alone in eight attacks in four patients, and carditis alone in twenty attacks in nine patients.

From their observations the authors consider that the major features of rheumatic fever tend to follow the same pattern in recurrent attacks and that this is particularly so in patients with valvular involvement. If the valvular involvement is not present in the first attack it is unlikely to develop in subsequent attacks. In the majority of cases in which permanent rheumatic heart disease develops valvular involvement is present in the first attack. Changes in the P-R interval in the absence of a significant murmur have not the same significance. It is suggested that if these observations are confirmed it might be possible to modify advice on the duration of prophylaxis in certain patients, since recurrent attacks of rheumatic fever are particularly dangerous in those likely to develop carditis.

C. Bruce Perry.


Chronic Articular Rheumatism
(Rheumatoid Arthritis)


In this paper from the University of Buffalo Medical School, New York, the authors report an uncontrolled trial of chloroquine phosphate in the treatment of 145 unselected patients with rheumatoid arthritis in varying degrees of activity. The usual dosage was 250 to 500 mg. daily, and the duration of the trial was 6 to 18 months. Side-effects occurred in 41 patients, the commonest being nausea, dyspepsia, headache, dizziness, pruritis, and dermatitis; in thirteen patients these reactions were severe enough for administration of chloroquine to be stopped. Corneal changes developed in two patients. Improvement was noted in only 35 (31 per cent.) patients. No correlation was observed between the response to the drug and sex, age, or duration of the disease.

J. A. Cosh.


In the first part of this paper from the Ospedale S. Giovanni Battista, Turin, the results of the Rose-Waaler test carried out on 3,050 occasions on 1,643 subjects, including patients with rheumatoid arthritis and various rheumatic and non-rheumatic diseases and healthy controls, are analysed in some detail. Sensitization of the erythrocytes was "reduced in intensity" in an attempt to increase specificity. With this modification agglutination at a dilution of 1:64 was regarded as a positive reaction.

Of 511 cases of rheumatoid arthritis, 63-9 per cent. gave a positive reaction to the test. Further analysis of these results showed that:

1. no patient under the age of 15 years gave a positive response, the highest percentage of positive responses being found in middle age regardless of the duration of the disease;
2. there was no significant difference in the behaviour of the response between the sexes;
3. the proportion of positive results and the height of the titre increased with the duration of the disease, very high titres being found in cases in which a positive response had been obtained early in the disease process;
4. there was a direct relationship between the intensity of the reaction and the severity of the radiological changes.

No clinical difference between cases giving positive and negative reactions could be detected, nor was any alteration attributable to treatment observed.

The results in numerous other pathological conditions are also reported (and are generally concordant with those of other authors). In a control of 628 subjects (which included cases of osteo-arthritis and periarthritis) false positive results were obtained in 0-63 per cent. High agglutinating titres were found in two out of 23 cases of pulmonary silicosis. In a group of 99 cases of wholly non-rheumatic disease only two positive reactions were obtained. Relatives of patients with rheumatoid arthritis gave a positive reaction in 27.3 per cent. of cases compared with 8 per cent. in a control group. Comparison of the Rose-Waaler test with the Hyland drop latex test showed correlation in 82.7 per cent. of cases. However, this latex procedure gave 14.5 per cent. false positive results compared with 0.77 per cent. with the Rose-Waaler test.

The second part of the paper deals with various investigations directed towards the elucidation of the nature of this phenomenon. Eradication of any one of the four portions of complement did not remove the agglutinating capacity of serum. No success was obtained in the determination of a precipitation reaction. The authors found no evidence of hypersensitivity or immunization to heterologous globulins. The agglutinating factor was found in joint fluid and in the interstitial fluid.

Harry Coke.


The author performed post-mortem brachial arteriography in thirty cases at Kivela Hospital, Helsinki, Finland; ten of the subjects had been treated for rheumatoid arthritis. The mean age of the group was 65 years and the control series was chosen from the same age group. The brachial artery was injected with a suspension containing 100 g. barium sulphate and 180 ml. water. The hand was pressed between two plates of plywood joined together with four bolts and nuts and then radiographed. Uniform narrowness and tortuosity of the digital arteries was seen in both rheumatoid subjects and controls and was considered to be due to arteriosclerosis. The changes seen only in cases of rheumatoid arthritis were:

1. local obliteration of the arterial trunks, particularly in the vicinity of the affected joint spaces;
2. local post-stenotic shuttle-like dilatations of the arteries;
3. hypervascularization and dilatation of arterioles close to bony erosions.

C. E. Quin.


At Kommunehospitalet, Copenhagen, the author found four cases of rheumatoid arthritis occurring in monozygotic twins. A concordant manifestation of the disease was found in only one set. That the twins were monozygotic was confirmed by clinical examination and by blood grouping. In the twins concordant for rheumatoid arthritis the disease started at the same age. In the other three sets the twins were discordant for rheumatoid arthritis after observation periods of 21, 30, and 5 years.
respective. When these four sets of twins are added to
46 recorded in the literature data are available regarding
fifty sets of monozygotic twins with rheumatoid arthritis
affecting one or both members. The disease was con-
cordant in eighteen and discordant in 32, so that the
discordance rate is 64 per cent. The author points out
that a discordance rate as high as this indicates the
existence of an exogenous factor. Information on these
fifty sets of twins was obtained from hospital departments
or hospitals for rheumatic diseases, from general hos-
pitals, from twins contacted by advertisements in the
newspapers, and by contacting twins whose names had
been obtained from parish registers. The discordance
rate was found to be highest in those twins attending
hospitals or for rheumatic diseases. A lower concor-
dance rate was found in twins attending general
hospitals and in twins who answered advertisements.
It is considered that the mode of collection must have
caused a selection mainly of concordant twins. This
view is supported by figures for eight sets of monozygotic
twins whose names had been obtained from parish
registers. In these twins the discordance rate was 100
per cent. These findings suggest that the role of hered-
ity in rheumatoid arthritis is negligible.

C. E. Quin.

Rheumatoid Arthritis: Current Therapy and Medical
92, 326. 12 refs.

Rheumatoid Arthritis: Present-Day Physical Therapy.

Rationale of the Physiatric Management of Arthritis.
53, 742. 2 refs.

Treatment of Rheumatoid Arthritis with Formaldehyde.
(Traitement de la polyarthrite chronique évolutive par
la formaldéhyde.) Yvanoff, J. (1960). Scalpel (Brux.),
113, 531. 8 figs, 13 refs.

Mode of Action of Phenylbutazone in Rheumatoid Ar-
thritis. (Über die Wirkung des Butazolidin bei der
primär chronischen Polyarthritis.) Winer, J. (1960).
Praxis, 49, 649. 1 fig., 7 refs.

Treatment of Rheumatoid Arthritis with Phenylbutazone
Observations of 980 Patients. (Leczence gościa stawo-
wego butazolidyny [na podstawie obserwacji 980
39 refs.

Chrysotherapy in Rheumatoid Arthritis. A Long-Term
Study of 435 Cases. (Chrysothérapie au cours de la
P.C.E.) Forestier, J., Certonciny, A., and Forestier,
F. (1960). Lille méd., 5, 247. 3 figs.

The Heart in Rheumatoid Arthritis. (Il cuore nell’
artrite reumatoide.) Scalabrin, R., and Curtarelli,
G. (1960). Reumatismo, 12, 1. 9 figs, 108 refs.

Subluxation of the Cervical Vertebrae in Rheumatoid
Arthritis. (Remarques sur la luxation des vertèbres
cervicales dans la polyarthrite rhumatoïde.) Coste, F.,

(Spondylitis)

Some Effects of Ankylosing Spondylitis on Pulmonary Gas
Exchange. Renzetti, A. D., Jr., Nicholas, W. E.,
Dutton, R. E., Jr., and Jivoff, L. (1960). New

Pulmonary function was studied in twelve male patients
with clinical and radiological evidence of ankylosing
spondylitis, but without lung or heart disease. It was
found that vital capacity and total lung capacity were
reduced but the maximum ventilatory capacity and the
index of intrapulmonary mixing remained normal.
Hyperventilation at rest and during and after exercise
was observed in most of the patients, and there was mild
arterial oxygen unsaturation in half of them. The per-
centage venous admixture was increased in five of the six
patients so studied. It is suggested that the hyper-
ventilation and the gas exchange defects might result
from relative over-expansion of the lower and under-
 expansion of the upper portions of the lung.

K. C. Robinson

Ankylosing Spondylitis in Two Families showing Involvement of Female Members Only. Grönvik Kornstad,
6, 59. 17 refs., 1 fig.

Rheumatoid Spondylitis with and without Arthritis
Med. intern. Fenn., 49, 17. 9 refs.

(Miscellaneous)

Clinical Picture of Rheumatic Thrombovasculitis. [In

The authors describe sixteen cases of rheumatic
thrombo-vasculitis occurring in eight male and eight
female patients ranging in age from 14 to 56 years,
several of whom had more than one attack. The vessels
involved were the cerebral arteries in thirteen cases, the
limb arteries in three, the pulmonary in three, the cardiac
in two, the renal in two, and the intestinal in one. Three
of the attacks took place during the first bout of acute
rheumatism, nine during subsequent attacks, and the
others during intervals between bouts. The outcome
was satisfactory in thirteen cases, but proved fatal in
three. Case histories of three of the patients are given,
including two of those who died and came to necropsy.
All the sixteen patients had cardiac lesions.

The authors state that the condition is much more
common than is realized and may often remain undiagnosed,
especially in the milder latent forms. Histologically
the lesions consist of lymphoid infiltration of the arterial
walls (granular leucocytes are also often found), with thickening of the walls and clot formation in the lumen. In one of the fatal cases thrombosis of the abdominal aorta with gangrene of the left leg is described. They suggest that this complication of rheumatism deserves further investigation.

L. Firman-Edwards.


The temporo-mandibular arthrosis described by Costen in 1934 may occur in later life in patients of either sex after removal of the molar teeth if there has been no satisfactory replacement, but this is really a secondary form. The primary condition typically occurs in women aged 15 to 30, usually in their early twenties. The author considers the symptoms to be due to a disturbance of joint function (with or without effusion, actual arthritis, and muscle spasm) which is secondary to a disturbance of bony growth of the mandible, skull, and/or maxilla, the amount or duration of growth of one part being out of relation to that of the other parts. In particular, growth in length and vertical height of the mandibular ramus may continue longer than the growth of adjoining structures; a corresponding inequality results if growth of the mandibular or maxillary alveolar elements or of the base of the skull ceases prematurely.

Clinically the diagnosis may be suspected if it is found that biting on a roll of cotton between the incisor teeth (that is, compressing the joint) increases the pain, while biting on the roll placed between the molar teeth (that is, "distracting" the joint) relieves the pain. The most popular method of treatment is to "raise the bite" by inserting a "platform" of acrylic resin between the occluding surfaces of the teeth, so relieving direct pressure on the joint. The author stresses that this interdental platform must not be too thick; its gradual removal, tooth by tooth round the mouth, may take up to 3 years. Injections of hydrocortisone into the joint help to allay inflammation and ease the pain. In no case has the author found it necessary to remove the articular disk or to divide the condylar neck. Post-mortem studies of 48 temporo-mandibular joints are described.

T. A. Clarke.

One Hundred Cases of Scapulo-humeral Periarthritis.


A short study of the clinical features and treatment of one hundred cases of scapulo-humeral periarthritis is presented. The incidence of this condition is high, constituting 15 per cent. of all cases of rheumatological disorders. It occurs twice as often in women as in men. It is unilateral in 71 per cent. of cases (right in 50 per cent., left in 21 per cent.) and bilateral in 29 per cent. Associated in one case in every three with osteo-arthritisic manifestations, scapulo-humeral periarthritis may be regarded as a "tendinous" form of degenerative rheumatism. The evolution varies greatly from one case to another.

In regard to treatment the corticosteroids by the oral route should be reserved for very painful cases and should be administered for short periods only. Hydrocortisone and the other injectable steroids may be introduced into the scapulo-humeral joint, but preferably into the subacromial bursa. Since 1944 the author has used progressively increasing doses of tuberculin administered subcutaneously at weekly intervals. The results have been good on the whole, with few failures (5 per cent.). Undesirable secondary effects are rare and not dangerous. The therapeutic effect is attributed to stimulation of the adrenal cortex as indicated by Thorn's test.—[From the author's summary.]


Gout


Zoxazolamine is rapidly absorbed and is eliminated from the body in approximately 6 hours. It acts by inhibiting the tubular reabsorption of urates. Over a period of 27 weeks it was given in the treatment of acute icteric, and chronic gout in eleven patients (nine male and two female). Pronounced uricosuric effects were obtained when a dose of 250 mg. was administered two to four times daily after meals and at bedtime. As regards diet, neither alcoholic nor purine foods were restricted in quantity. The daily intake of fluids ranged from 2 to 3 litres and when this was maintained it was not necessary to ensure that the urine was alkaline. There was some interference with the uricosuric action of the drug when salicylates were given concomitantly. On the other hand, phenylbutazone had an additive effect, as did probencid though to a lesser extent than phenylbutazone.

In ten cases the clinical condition was either controlled or improved, but in the remaining case a urinary infection supervened and the patient died from uraemia. A maintenance dosage of 250 mg. twice daily resulted in diminution in the size of topochaceous deposits. Dizziness and nausea were the only recorded side-effects and were usually mild. The onset of nausea could be prevented by giving zoxazolamine during a meal. In three patients with renal damage acute attacks of gout developed during the early stages of treatment; these exacerbations subsided promptly following administration of colchicine. In spite of the loss of uric acid in the urine, no uric-acid stones were observed. A. Garland.


At the National Institute of Arthritis and Metabolic Diseases, Bethesda, Maryland, 6-diazo-5-oxo-l-norleucine (DON) was administered to six patients with gout...
and to one patient with renal urate lithiasis in order to observe its effect on uric acid production. In three patients the drug suppressed the incorporation of glycine-1-14C into urinary uric acid. The absorption of glycine-1-14C from the intestine was unaffected by DON, this finding supporting the view that in the dosage used the drug acts primarily by suppression of purine synthesis.

Balance studies showed a reduction in serum urate levels and 24-hour urinary uric acid excretion in only two of the seven patients tested. The negative findings in the other five may have been due to the short duration of the balance studies and the presence of an expanded urate pool. The main toxic effects of the drug consisted in soreness of the mouth, sometimes with ulceration, and asymptomatic duodenal ulcers which healed promptly on medical treatment. No depression of the formed elements of the blood were seen. The high incidence of side-effects prevents the practical use of this particular compound in practice, but the possibility remains that more specific and less toxic inhibitors of purine biosynthesis may be found.

G. W. Csonka.

Results obtained by the Administration of Sulfoxypyridazoline (G 28 315) in 25 Cases of Gout. (Résultats obtenus par l'administration de sulfoxypyridazoline (G 28 315) chez vingt-cinq goutteux.) SERRE, H., SIMON, L., and CLAUSTRE, J. (1959). Montpellier méd., 56, 211. 7 figs, 10 refs.

The beneficial effect of salicylates and of probenecid in the treatment of chronic gout is well known. However, the effective dose of salicylates is close to the level of intolerance, and probenecid at times causes side-effects such as skin eruptions and gastric disturbance. Phenylbutazone is effective in acute gout, but its uricosuric effect is feeble.

In this paper from the University of Montpellier the authors describe the synthetic substance sulfoxypyridazoline (G 28 315), a derivative of phenylbutazone, which has been shown to be strongly uricosuric. It is a white crystalline substance and is available for therapeutic use in tablets of 50 and 100 mg. They have employed this drug since 1958, and here report their results in 25 cases of gout and in six control subjects. The following dosage schemes were tried, the daily amounts being given in four equal doses at 3-hourly intervals:

1. 400 mg. daily for 8 days followed by 600 mg. daily for the next 8 days;
2. 800 mg. daily for 8 days and then 1,200 mg. daily for 8 days;
3. 400 mg. daily for 5 days, 600 mg. daily for another 5 days, and 800 mg. daily for the last 5 days;
4. 800 mg. daily for periods ranging from 12 to 30 days.

At each dosage level the blood and urinary uric acid concentrations were determined.

The best results were obtained by the administration of 800 mg. daily, nothing being gained by using a higher dose. In the patients receiving this dosage the mean blood uric acid level, which before treatment was 5·73 mg. per 100 ml., fell during treatment to 3·36 mg. per 100 ml. The initial mean urinary uric acid excretion was 751 mg. in the 24 hours, but during treatment this increased to a mean of 1,175 mg. per 24 hours. No such uniform response followed in the controls tested. A comparison with probenecid was made in one case only, in which under treatment with probenecid (1 g. daily) the mean blood uric acid level was 3·25 mg. per 100 ml., but when treatment with G 28 315 was instituted in a dosage of 800 mg. daily the level fell after 15 days to 2 mg. per 100 ml. and the urinary uric acid excretion rose from 741 to 932 mg. per 24 hours.

The authors conclude that G 28 315 is a valuable uricosuric agent, and probably the most powerful. If every case the blood uric acid level was reduced to about 4 mg. per 100 ml. or less. Gastric intolerance was never observed, and no patient suffered any toxic effects on the kidneys, blood, or skin. The drug did in a few patients precipitate an attack of acute gout.

Kenneth Stone.


A study of the threshold for the perception of vibrations in gout and rheumatoid arthritis is reported in this paper from the University of Pittsburgh School of Medicine, Pennsylvania. Tests of perception were carried out with an electric vibrator, or biothesiometer, in which the rate of movement of a metal rod could be varied by increasing the input of the current. Oscillometric readings were also obtained. The patients with gout were taking 150 gr. (0·65 mg.) of colchicine and 1·5 "benemid" (probenecid) daily. The patients with rheumatoid arthritis were receiving steroids of the adrenocortical type, phenylbutazone, gold salts, and physiotherapy.

An increased threshold for vibratory-sense perception was observed in all cases. The reason for this was not clear but it is suggested that in cases of gout the phenomenon could be attributed to vitamin deficiency secondary to treatment with uricosuric agents, and that in patients with rheumatoid arthritis neuropathy and adrenocortical steroid therapy were associated with the decreased acuity of the vibratory sense. No significant difference was observed between controls and patients with gout or rheumatoid arthritis in the mean oscillometric index.

A. GARLAND.


This paper from the École Nationale de Médecine de Dijon presents an account of the histological features of cartilaginous lesions in gout. Extra-articular cartilage, such as that of the external ear, usually remains normal in gout, or is subject only to occasional and feeble infiltration by urates. In contrast, however, hyaline articular cartilage is characteristically involved: thus these lesions may show either scattered foci of necrosis in areas of

G. C. Garland.
uric acid deposition in the acute phase of an attack, or a variety of chronic changes as part of a “gouty arthropathy”. In discussing the mechanism of the cartilaginous changes in gout the exact nature of which is still obscure, the author suggests that the initial deposition of urates in this tissue may be the result of its avascularity, its richness in sodium, or its mucopolysaccharide content, while the mutilating destruction of the cartilage seen in gouty tophaceous and ankylosed joints appears to result from extensive dissecting fibrosis of articular and periarticular tissues as well as from the direct effect of urate deposits.

H. A. Sissons.


Pararheumatic (Collagen) Diseases


This complex study was carried out at the Rockefeller Institute, New York. Using extracts in normal saline of various animal and human organs as antigens the authors demonstrated complement fixation with sera from 33 out of 37 patients with systemic lupus erythematosus (S.L.E.), seven out of eleven patients with primary biliary cirrhosis, two out of three patients with Sjögren’s syndrome, and one patient with scleroderma. Positive results were also obtained with eight of 35 normal sera, but in low titre. Sixteen sera giving positive reactions with saline extracts were then tested against five preparations containing isolated calf thymus nuclei, an extract of such nuclei in phosphate buffer, isolated calf liver mitochondria, microsomes, and a soluble cellular fraction respectively. Ten of these sera, from patients with S.L.E., all reacted positively with all five cellular preparations. In the case of the mitochondria and microsomes it was possible to exclude contamination with soluble nuclear material as a cause of the positive reactions since complement-fixation tests using the supernatant from the last wash of these constituents as antigen gave a negative result in each case. Of the other six sera tested against the cell fractions four were from patients with biliary cirrhosis, one from a patient with discoid L.E., and one from a case of Sjögren’s syndrome. With these sera positive results were obtained against mitochondria and microsomes, but the results with the other preparations varied. However, the results with nuclear material always matched those with the soluble cellular fraction. In some cases control tests with ten normal sera gave low-titre (<1:16) positive results against mitochondrial and microsomal preparations only.

Further work with tissue extracts in various solvents and after treatment with certain enzymes suggested that a number of different cytoplasmic constituents were involved in these reactions, but that one of these constituents seemed to react only with S.L.E. sera. Electrophoresis of the test sera on starch medium and zone ultracentrifugation experiments showed that the antibody constituent of these reactions were γ globulins with a sedimentation constant of 7. (Some of the sera from patients with diseases other than S.L.E. contained additional active 19 S globulin.)

M. Wilkinson.


In the past ten years the authors have studied, with particular reference to cardiac involvement, sixty patients with systemic lupus erythematosus (S.L.E.) who were seen at the Hammersmith Hospital, the London Hospital, and the Canadian Red Cross Memorial Hospital, Taplow. Clinical details are given, and the non-cardiac manifestations, the serological, and haematological findings, as well as the post-mortem findings in the 27 patients who died, are described.

Of these latter endocarditis was found at necropsy in over half, the mitral valve being involved in ten cases, the aortic valve in four and the pulmonary and tricuspid valves each once. The valvular lesion was primary in thirteen cases and in two there was a secondary superimposed bacterial infection. The primary lesions, which were of a type previously reported in the literature, occur commonly at the base of the valve, particularly in the valve pocket, and numerous endothelial cells, Antischow myocytes, and inflammatory mononuclear cells are present, the disintegration of these resulting in the formation of haematoxylin bodies and eosinophilic fibrinoid material. The myocardial fibres were seldom involved, but in one patient there was patchy degeneration of some fibres, the nuclei of which lost definition and resembled the inclusion body of an L.E. cell. Myocardial fibrosis with associated vascular occlusion was present in two patients, but myocardial abnormalities were mostly interstitial and sometimes extensive. A common finding was a fibrinoid lattice with cellular infiltration, many of these cells undergoing degeneration to haematoxylin bodies. In some cases, the fibrinoid lattice appeared to have formed on collagenous strands proceeding from an oedematous area of connecitive tissue. The authors consider that the characteristic fibrinoid change derives mainly from clotting of fibrinogen in areas of gelatious exudate, but occasionally local cellular
infiltration occurs and the products of nuclear degeneration then contribute to the fibrinoid substance, which may thus differ in different diseases and even in different sites in the same organ. The pericardium was abnormal in twenty of the 27 patients coming to necropsy, the layers usually being obliterated. There was much fibrinoid change and many haematoxylin bodies.

The incidence of clinical cardiac manifestations is then discussed. Endocarditis is not recognized clinically so often as it is found at necropsy, since the organic murmurs are often soft and transient and the valvular lesion rarely results in significant obstruction or incompetence. The various murmurs elicited are described in detail, together with reproductions of illustrative electro- and phono-cardiograms. The aortic and mitral valves were found to be affected far more commonly than the valves of the right heart. Myocarditis was difficult to detect clinically because of its association with pericarditis, hypertension, and possible water retention as a result of corticosteroid therapy. In no case could heart failure be attributed solely to myocarditis. In the authors' experience pericarditis, a well-known complication of S.L.E., occurs in almost all patients at some stage of the disease. Of seven patients without necropsy evidence of pericarditis, five died exceptionally and suggestively early in the course of the disease. Pericarditis usually appears as an isolated or a recurrent attack and is frequently painless; no fewer than 52 patients showed electrocardiographic abnormalities consistent with acute or chronic pericarditis at some stage of the disease.

During the disease 26 patients developed a diastolic blood pressure of over 95 mm. Hg, which was attributed to renal disease in twenty cases. Corticosteroid therapy had been given to thirteen of these patients and occasionally aggravated the hypertension, but of the six patients with hypertension not due to renal disease four had received steroid therapy. Congestive heart failure developed in 22 patients, systemic hypertension being the main, but rarely the sole, cause; other contributory causes were pericarditis, fever, secondary infection, anaemia, and sodium and water retention. The response of the heart failure in these patients to sodium restriction, digitalis, and mersalyl was usually poor. In two cases an increase in the dosage of cortisone controlled the disease better and the heart failure improved, but generally the heart failure is made worse by administration of salt-retaining corticosteroids.

J. Warwick Buckler.


This paper from the National Institute of Allergy and Infectious Diseases, Bethesda, Maryland, describes another test for systemic lupus erythematosus (S.L.E.) depending on the affinity of L.E. serum for desoxyribonucleic acid (DNA). In this test, which is similar to the bentonite flocculation test for rheumatoid arthritis, bentonite particles are coated with DNA and bovine plasma albumin is added to prevent the particles from clumping. The addition of L.E. serum (not plasma) causes flocculation, but the reaction is more difficult to read than in the test for rheumatoid arthritis.

The DNA-bentonite flocculation reaction was positive in all of eight cases of active S.L.E. (in all of which the result of the L.E.-cell test was positive) and in two out of five cases of S.L.E. in remission (with a positive L.E.-cell reaction in four). The reaction was negative in 138 sera from patients without S.L.E. including six cases of rheumatoid arthritis with positive L.E.-cell reactions.

M. Wilkinson.


In studies carried out at the University of California School of Medicine, San Francisco, L.E. factor was measured by its ability to agglutinate sheep's erythrocytes treated with tannic acid and coated with a nucleoprotein extract from calf thymus. Rheumatoid factor was measured by the agglutination of cells coated with Cohn Fraction II of human plasma.

All sera from ten cases of systemic lupus erythematous agglutinated cells coated with nucleoprotein extract in titres up to 1:64,000, but only four of the sera agglutinated cells coated with Fraction II. All sera from ten patients with rheumatoid arthritis gave Fraction-II titres of 1:56,000 or higher, but none produced L.E.-cell agglutinated cells coated with nucleoprotein extract. Previous exposure of the treated cells to γ globulin inhibited Fraction-II haemagglutination, but not nucleoprotein-extract haemagglutination, whereas exposure of the treated cells to nucleoprotein extract inhibited nucleoprotein-extract haemagglutination but not Fraction-II haemagglutination. Deoxyribonucleic acid failed to inhibit nucleoprotein-extract haemagglutination. The formation of L.E. cells was inhibited by nucleoprotein extract, but not by γ globulin.

The authors consider that nucleoprotein-extract haemagglutination gives a quantitative measure of the serum factor responsible for L.E.-cell formation.

M. Wilkinson.


At the Hospital San Juan de Dios, Santiago, Chile, the authors treated sixteen patients with systemic lupus erythematosus (S.L.E.) with methylprednisolone, ten with triamcinolone, and twenty with dexamethasone. The number of new patients, not previously treated with corticosteroids, were eight, five, and seven respectively. Doses were varied according to symptoms and patients were transferred to and from the corticosteroids previously employed. While the conditions of the trials did not permit a precise comparison, no consistent...
superiority of any one of the newer corticosteroids emerged, and the considerable variation in patients’ response to individual drugs was confirmed. The authors conclude that prednisone and prednisolone have not been displaced in the treatment of S.L.E., but individual differences in response justify a trial of the various steroids available.

Allan St. J. Dixon.


In this study, undertaken at the Mayo Clinic to determine the value of testicular biopsy examination in the diagnosis of periarteritis nodosa, the authors have examined the records and histological sections of formalin-fixed blocks of the testes of 44 patients aged 11 to 71 (average 47) years seen at the Clinic during the period 1931-55, in thirty of whom the diagnosis of periarteritis nodosa was established or suspected. Abnormalities suggestive of the disease were found in 41 (93 per cent.) of these cases. Diagnostic arterial lesions were seen in 38 cases (86 per cent.), while less common changes included infarcts, degeneration or disappearance of the tubules, haemorrhage, and haematoma. Clinical abnormalities of the testis had been observed in only eight of the patients (18 per cent.), though the size had been recorded as subnormal in eleven (25 per cent.).

By sampling different sectors of the histological sections the authors made a rough estimate that positive diagnostic signs of periarteritis in a single testicular biopsy specimen could be expected in only about one in five male patients (22 per cent.). Testicular biopsy in the living patient is therefore recommended only when clinical findings suggestive of periarteritis are accompanied by testicular abnormalities and there are, moreover, no detectable cutaneous, subcutaneous, or muscular lesions. If biopsy is performed the specimen should include part of the tunica vasculosa as well as some of the underlying parenchyma.

A. Wynn Williams.


From the University of Colorado School of Medicine, Denver, the author describes one fatal case of periarteritis nodosa which followed cortisone therapy and a further case in which, however, the patient recovered on withdrawal of therapy; the lesions in the former case were confirmed histologically. In a review of the literature he has found 36 reported cases of arteritis occurring in rheumatoid arthritic patients treated with steroids. The three cardinal symptoms are progressive neuropathy, widespread multiple involvement of the organs, and constitutional reaction.

The author’s first case occurred in a female patient aged 51 with a history of rheumatoid arthritis for 34 years, during which she had received 25 to 75 mg. cortisone daily, together with supplements of other steroids, gold and salicylates. Burning and sensations of tingling developed in the hands, followed by wrist and foot drop. Progress was intermittent, but by the end of 6 months there was generalized paralysis and areflexia. Purpuric skin eruptions appeared, followed by gangrene, first of the rheumatic nodules in the hands and later involving the nail cuticle. The gangrene spread to include the finger tips and around the ankles. Patches of viable tissue in the midst of gangrenous areas suggested disseminated arterial lesions. At necropsy a necrotizing arteritis, indistinguishable from periarteritis nodosa, was found to be widespread in the viscera and particularly in the vasa nervorum of the vagus nerves.

The second case was seen in a 39-year-old woman with rheumatoid arthritis who had been treated for over 5 years with corticosteroids. She suffered from weakness and hypo-algesia of the extremities and showed loss of reflexes, cyanosis, and impending gangrene of the fingers and toes. The cortisone was withdrawn under cover of a week’s treatment with ACTH (corticotrophin). A week later the punctate gangrenous lesions and the peripheral cyanosis had disappeared, the neuropathy showed some improvement, and the rheumatoid nodules also cleared up. Observation for a year has revealed no return of these signs and symptoms.

The author discusses the mechanism of arteritis in such cases and comes to the conclusion that it is a sensitization phenomenon related to the tuberculin and Herxheimer reactions.

William Hughes.


The authors of this paper from Harvard Medical School and the Peter Bent Brigham and the Robert Breck Brigham Hospitals, Boston, describe five cases of scleroderma (progressive systemic sclerosis) in which acute renal failure caused death. Because the cases were selected no conclusions could be drawn concerning the incidence of renal involvement in scleroderma, but this is known to be present in the majority of cases examined post mortem. The classical skin changes of scleroderma were present in all five cases. The acute form of renal disease was characterized by rapidly advancing ureaemia with, in some cases, hypertension, and death within a month. In one case there was evidence of preceding renal damage. Pathologically, the chief features were intimal proliferation of the small intralobular vessels, fibrinoid necrosis of the afferent arterioles and sometimes of the glomerular loops, and focal cortical infarction. In the more chronic form obliteration of the glomeruli and interstitial fibrosis occurred. These features were sometimes seen in the absence of hypertension. It is pointed out that lesions resembling those seen in other collagen diseases have also been described in cases of progressive systemic sclerosis. The authors emphasize the rapidly fatal outcome in the acute form of the disease, which appears to be little if at all affected by any currently available treatment.

G. L. Asherson.

Cardiac involvement in scleroderma was first described in detail by Weiss and others in 1943 (*Arch. intern. Med.*, 71, 749), although a single case had earlier been reported by Heine in 1926 (*Viechows Arch. path. Anat.*, 262, 251). In the present communication the author describes her investigations in fifteen cases (including four at necropsy), all the patients having cardiac symptoms of varying degree, including dyspnoea, tachycardia, precordial pain, and arrhythmia (extra systoles or gallop rhythm). Radiography revealed moderate enlargement of the heart to the left in seven cases, and unfolding of the aortic arch in ten; electrocardiographic changes present in fourteen cases consisted in low voltage in eleven, left-axis deviation in seven, right-axis deviation in four, and abnormalities of the T wave in thirteen. Pathological examination of the heart muscle in the four fatal cases revealed myocardial involvement by the sclerodermal process. The coronary arteries were intact, but the smaller vessels showed fibrinoid infiltration and narrowing of the lumen, and the muscle fibres adjacent to the patches of cardiosclerosis were hypertrophied. All layers of the heart were involved, and there was slight pericardial exudate. Mitral stenosis was present in all four cases, while there were lesions of the aortic valve in two cases and of the tricuspid valve in three.

The condition is sometimes mistaken for rheumatism and in five of the author's cases this was the first diagnosis. Subjective symptoms are often absent in the early stages. Treatment is unsatisfactory, but the prolonged administration of steroid hormones is insisted upon.

*L. Firman-Edwards.*


General Pathology


It has been reported by Golton and others (Canad. med. Ass. J., 1957, 77, 1098; *Abstracts. Wild Med.*, 1958, 23, 454) that certain polysaccharides can be used in place of *g*-globulin to "sensitize" latex particles in the latex fixation test of Plotz and Singer. The present authors, working at Yale University School of Medicine, described a modified latex fixation test agglutination in which heparin is used as the heterologous sensitizing agent and which they applied to ninety sera specially selected as likely to give false positive reactions by reason of having a high *g*-globulin content (over 20 per cent. of total protein) as determined by paper electrophoresis. The heparin-latex test gave 52 per cent. positive results as against 20 per cent. in the standard test, which gave 6.4 per cent. false positive results in a series of 313 unselected control sera. The authors conclude that the heparin-latex method offers no improvement in routine tests for rheumatoid arthritis.

[The investigation was undertaken on account of the fact that the definition of "rheumatoid factor" adopted by the Arthritis and Rheumatism Foundation "implies the obligatory presence of an 'outside' *g*-globulin in serological reactions in which the rheumatoid factor participates". It is difficult, however, to determine the source of this obligation in the official definition.]

Harry Coke.


The author reports the results of an electrophoretic study of the serum glycoproteins in 120 rheumatic patients and 33 healthy control subjects. In the controls, glycoproteins were present in all plasma protein fractions, the highest content being in the *a*-globulins. In patients with active rheumatism the glycoprotein content in both the *a*- and *a*-globulin fractions was higher than in the controls, but in the albumin and *b* and *y*-globulin frac-
Precipitin Reaction between Rheumatoid Factors and Gamma Globulin: Studies by Double Diffusion in Agar. 


From New York University College of Medicine the author reports a study of the nature of the precipitin reaction which occurs between "aggregated" human \( \gamma \) globulin (Cohn Fraction II in 1 per cent. solution heated to 63° C. for 10 minutes) and sera showing agglutination to a titre of 1:1,024 or greater in the Rose-Waaler Test. Strongly positive agglutinating sera from 22 cases of rheumatoid arthritis, one case of sarcoidosis and one of "hyperglobulinaemic purpura" all gave precipitin lines on testing by the Oudin double gel diffusion technique. Separate precipitation lines between a rheumatoid arthritis serum and antisera to 7 S and 19 S \( \gamma \) globulin were demonstrated by immunoelectrophoresis, whereas the aggregated human \( \gamma \) globulin produced only a single precipitation line corresponding to the 19 S molecule [\( \beta \) beta-2-M].

By the Ouchterlony technique a reaction of identity was obtained by employing antisera to three different proteins produced in a number of different animal species. A number of experiments in which the Ouchterlony principle was employed were described, the results of which, in the author’s opinion, indicate that both the 7 S and the 19 S \( \gamma \) globulins take part in the rheumatoid precipitin reaction. Identity of reaction by fusion of the precipitation lines was shown between both 7 S and 19 S \( \gamma \) globulins and rheumatoid sera, together with the two additional pathological sera mentioned. The immunological relationship was further studied by a new modification of the Ouchterlony diffusion method and compared with other known antigen-antibody reactions. Three of the 24 sera showed two precipitin lines on reaction with aggregated human \( \gamma \) globulin, and it is considered that "these findings appear to confirm the existence of at least two rheumatoid factors, one of which reacts with human and rabbit \( \gamma \) globulins, and one of which reacts primarily with human \( \gamma \) globulin".

[Knowledge of the antigenic constitution of the aggregated human \( \gamma \) globulin might be interesting here in view of the known possibility of six different proteins constituting \( \gamma \) globulins (Heremans) and the multiplication of antigens obtained in some proteins by heat (Shultze).]

Harry Coke.


ACTH, Cortisone, and Other Steroids

Experiments were carried out at Glasgow Royal Infirmary designed to determine the relative persistence of certain steroids in the joint cavity following intra-articular injection. Specimens of synovial fluid were obtained from fifty joints (49 knees and one elbow) at intervals after the injection and were then examined chromatographically for the presence of steroid.

In the first experiment prednisolone trimethylacetate was injected into eight joints and hydrocortisone acetate into eight, the sixteen joints being aspirated completely after 24 hours and the fluid examined. Prednisolone was identified in the fluid from all eight joints into which this was injected, but hydrocortisone was not recovered from any of the joints injected with this steroid. In a further experiment prednisolone was injected into 12 joints, which were aspirated at longer intervals. Prednisolone was present in the fluid up to 6 days after injection of 50 mg. As an extension of this, sixteen further joints were injected and the fluid examined 7 days later; prednisolone was not usually present when the original dose was below 50 mg.

Finally, five joints were aspirated 10 or 14 days after injection of 60 to 100 mg. prednisolone. Of three joints aspirated 10 days after injection, two contained steroid; there was no steroid in the fluid from two joints aspirated after 14 days. The steroid was detected in an elbow joint after 14 days, although the dose had been only 25 mg.

The rapid disappearance of hydrocortisone from the joint cavity confirms the findings of previous workers. Prednisolone detected in joint fluid was usually the free alcohol, and it is presumably this form which exerts an anti-inflammatory local action, the relatively insoluble trimethylacetate acting merely as a local application. B. E. W. Mace.


Ten patients, previously adrenalectomized for Cushing’s syndrome, who have subsequently developed evidence of a disturbance of the pituitary gland, have been studied. All of these patients were very deeply pigmented. In eight cases a tumour of the pituitary gland was demonstrable either by roentgenologic examination or by such evidence plus restricted visual fields. In two cases, markedly elevated levels of ACTH were found in association with deep pigmentation, but no tumour of the pituitary was demonstrable. In five of the ten patients it was possible to demonstrate a level of plasma-ACTH above that usually observed in Addisonian patients, or in other patients in whom a bilateral adrenalectomy has been carried out. All five patients who did not have raised levels of plasma-ACTH, but who were deeply pigmented and who did have evidence of pituitary tumours following adrenalectomy for Cushing’s syndrome, had received irradiation to the pituitary gland before the first plasma was obtained for ACTH assay. The average time from adrenalectomy to the appearance of the pituitary tumour was 3 years (range 1-8 years) and, as noted above, pituitary histological examination in two cases was reported to show cells of a “chromophobe type”.—[From the authors’ summary.]


The rapid screening test for adrenocortical insufficiency described in this paper from Providence Hospital, Detroit, depends on the changes in the concentration of sodium in the urine 4 hours after an injection of 25 units ACTH (corticotrophin), a reduction of 50 per cent. or more in this concentration being indicative of sodium retention and thus of a responsive adrenal cortex. Several illustrative cases are described. The authors conclude that although the test does not necessarily reflect the over-all integrity of the complex functions of the adrenal cortex it does measure changes in mineralo-corticoid activity, probably of the 11-17-oxysteroids, and point out that it is mainly this mineralo-cortico defi- ciency which produces the serious clinical problems of adrenial insufficiency.

A. Gordon Beckett.


Other General Subjects

In this communication from the Institute of Medical Chemistry, University of Berne, the authors discuss the observed fact that the administration of 1 to 1.5 g. acetylsalicylic acid (aspirin) in man produces a marked increase in the urinary excretion of the hormonal catecholamines adrenaline and noradrenaline and of their precursors, such as hydroxytyramine (dopamine). The total amount of catechol excreted in the urine is also significantly increased. The maximum increase usually
The authors suggest that the increased blood levels of adrenaline and noradrenaline stimulates the anterior lobe of the hypophysis in its secretion of the adrenal cortical hormone ACTH (corticotrophin), this in turn causing secretion by the adrenal glands of therapeutically valuable steroids, the suggested chain of reaction being: acetylsalicylic acid → adrenaline-noradrenaline → ACTH → cortisone.


The effects of rubefacients on the semi-transparent cheek pouch of the Syrian hamster were assessed directly at Stanford University School of Medicine, San Francisco, by micromanipulatory methods, transillumination, and motion-picture recording with 16-mm. colour film. Dial with urethane provided anaesthesia, while the materials tested included esters of nicotine acid (ethyl, methyl, n-hexyl, and tetrahydrofurfuryl) in concentrations of 0.1 to 100 per cent. in mammalian Ringer’s solution, essential oils (mustard, wintergreen, clove, capsicum, turpentine, and camphor), and histamine. Occasionally vasoconstrictive agents—adrenaline, noradrenaline, electric current, or cold Ringer’s solution—were used beforehand to induce a standard vessel size if the arterioles were found to be in maximum dilatation.

With all groups of materials a maximal and comparable degree of vasodilatation was achieved regardless of concentration, suggesting an all-or-none response. There was simultaneous vasodilatation beyond the site of contact of the stimulant, indicating that the vasodilatation produced by rubefacients is mediated by a conducting mechanism with nerve-like properties acting upon smooth muscle units to give the all-or-nothing response. The only differences noted between the various agents were in latent period and duration of response. In a few cases an unexplained vasoconstriction was obtained with the agents used. The participating vessels included the arterioles, the precapillary sphincters, and the large venules, all of which contain smooth muscle. Capillaries participated only by passive dilatation due to increased blood flow. Local anaesthesia was found to abolish the effects noted above. In 100 per cent. concentration, all the materials tried produced the classic signs of inflammation. The authors feel that the results suggest that rubefacients act through local perivascular transmission of the vasodilator impulse. Allene Scott.


