ABSTRACTS

This section of the ANNALS is published in collaboration with the two abstracting Journals, ABSTRACTS OF WORLD MEDICINE, and OPHTHALMIC LITERATURE, published by the British Medical Association.

The abstracts selected for this Journal are divided into the following sections: Acute Rheumatism; Chronic Articular Rheumatism (Rheumatoid Arthritis, Osteo-Arthritis, Spondylitis, Miscellaneous); Disk Syndrome; Gout; Pararheumatic (Collagen) Diseases; Non-Articular Rheumatism; General Pathology; ACTH, Cortisone, and other Steroids; Other General Subjects. At the end of each section is a list of titles of articles noted but not abstracted. Not all sections may be represented in any one issue.

The section "ACTH, Cortisone, and other Steroids" includes abstracts and titles of articles dealing with research into the scope and modus operandi of steroid therapy.

Acute Rheumatism


3 figs, 8 refs.

As part of a study of the aetiological relationship between rheumatic fever and Group-A beta-hemolytic streptococci, the prevalence of these organisms in the throats of school children in Miami, Florida, was investigated. The investigation was divided into two parts:

1) An intensive study of 333 children aged 6 to 9 years attending three different schools—representing a low-income white, a high-income white, and a mixed-income Negro population respectively—who were examined at monthly intervals from October, 1954, to May, 1955;

2) A concurrent survey carried out on 1,200 children of the same age group in 48 additional elementary schools throughout the same county area, one culture only being taken from each child and 150 being examined each month.

The intensive study revealed that 44.7 per cent. of a monthly average of 304.6 children examined harboured Group-A organisms at least once during the period of study. The percentage of children harbouring the organism decreased slightly with age, was higher for girls (44.4 per cent.) than for boys (38.3 per cent.), and was much higher in the Negro school (73.3 per cent.) than in the white schools (50.4 and 54.5 per cent.). Despite this last finding, however, the proportion of all cultures taken which yielded positive results was approximately the same in all three schools. Ten different typable strains of Group-A beta-hemolytic streptococci were isolated; Type 6 was the most common and occurred most frequently in March, April, and May. At no time were two different types isolated during the same period, though combinations of typable and non-typable organisms were encountered 4 times.

In the wider survey the average and monthly isolation rates of Group-A organisms were similar to those in the first group, and the same variations with age and sex were noted, suggesting that the findings in these respects in the intensive study were representative of the area as a whole. But although beta-haemolytic streptococci were recovered more commonly from Negroes (31 per cent.) than white children (22 per cent.), Group-A organisms were more frequent among the white (15 per cent.) than the Negro children (11.4 per cent.) in the second study.

The authors observed that although at one time the isolation rates of Group-A Type-6 organisms rose in two classes to 33 and 50 per cent. respectively, there was no noticeable alteration in the monthly absentee rate; the relationship between streptococcal isolation rates and respiratory illness is to be the subject of a further communication, as also are various serological and immunological observations and their relation to rheumatic fever and glomerulonephritis. The value of a duplicate plate technique in surveys of this kind is emphasized, cultures made on different media from pairs of swabs taken simultaneously in the present survey giving discrepant results in 40 per cent. of cases. D. M. Weir.


The experiment here reported from the University of Chile and Western Reserve University, Cleveland, Ohio, was designed to show whether or not the rapid elimination of haemolytic streptococci from patients suffering from acute rheumatism would materially affect the acute course or the late results of the disease. All patients (97) admitted to three hospitals in Santiago between June and September, 1956, with symptoms of rheumatic fever were included in the study. They were divided into two main groups, one comprising patients experiencing a first attack and one comprising those suffering a recurrence. Each main group was then subdivided into children and adults and each subgroup again
According to whether the illness had been present for more or less than 14 days before admission. All the patients were kept in hospital for 42 days and regular detailed observations were made to determine progress [for details of these the original paper should be consulted], and all received aspirin for 14 days to control acute symptoms. In addition, half the patients in each group, randomly selected (the treated group), received intensive penicillin therapy for 42 days, consisting in 500,000 units sodium penicillin 4-hourly for 10 days, 600,000 units procaine penicillin twice a day for the next 11 days, and 1·2 mega units benzathene penicillin on the 22nd day. At the end of the 42 days all patients received 1·2 mega units benzathene penicillin intramuscularly, this being repeated every 5 to 6 weeks for 10 to 14 months. At each subsequent visit the observations were repeated and at the end of 12 months the cardiac status was evaluated.

Detailed analyses of the results, which are discussed at length subgroup by subgroup, showed no significant difference in the acute course of the disease between patients receiving intensive penicillin therapy and those given no antibacterial therapy. However, at the end of 12 months, when those patients in whom there was evidence of antecedent cardiac valvular disease at the time of admission were excluded (27), comparison of the remaining patients showed that valvular disease of the heart was 2½ times more frequent in the control group than in the treated group. It is suggested that the disparity between the effects of penicillin therapy on the acute manifestation of active rheumatism and on the cardiac valvular lesions indicates that these two aspects of the disease may differ in pathogenesis, and that the valvular lesions may result from the presence and persistence of the haemolytic streptococci in the valves of the heart.

This paper was published simultaneously in Revista Médica de Chile.] C. Bruce Perry.


Of 1,693 children aged 1 to 16 years with acute rheumatism observed during the 7 years 1950-57, 36 (2·1 per cent.) were under 3 years old. Of these 36 (22 boys, 14 girls), three (9 per cent.) had a history of previous attacks compared with 748 (44 per cent.) in the whole series. It thus appears that acute rheumatism at this early age is not so uncommon as is generally supposed and that, contrary to experience in older children, it may affect boys predominantly.

Home conditions were satisfactory in all but one of these 36 cases. There was a family history in six cases (16·6 per cent.)—a low figure. All the patients were full-term infants with a satisfactory birth weight who had been breast-fed to the 5th or 6th month. The attacks usually followed catarrh of the upper respiratory tract, influenza, or influenza pneumonia. Five of the 36 developed pancarditis and nine died. Of ten whose primary attack occurred before the end of their second year, five died. The mortality among children under 2 years was 50 per cent., among those aged 2 to 3 17·4 per cent., and among those aged 3 to 7 11·5 per cent., whereas in the rest of the series (age 7 to 16) it was 0·8 per cent.

The commonest clinical picture of the disease in children under 3 years old was carditis with limb pains or polyarthritis. In no case were there symptoms of chorea.

L. Firman-Edwards.


In a previous paper from the New York Hospital-Cornell Medical Center (J. Amer. med. Ass., 1956, 160, 1457; Abstr. Wild Med., 1956, 20, 384) it was reported that, when 55 attacks of active rheumatic carditis of 3 days to 21 days' duration were treated with steroids for an average of only 7 days with early ambulation, there was no overt cardiac disease in most cases for an average follow-up period of 9 years, these results being in marked contrast to those obtained in 165 cases treated without steroids.

In the study herein reported a further 53 attacks of active rheumatic carditis in 46 patients (mostly children) were treated, after several days of initial observation and investigation, with various steroid hormones of the cortisone group, again for an average period of 7 days. The exact daily dose was determined by the circulating eosinophil count, the aim being to keep this below 10 per c.mm. The diagnostic criteria of active carditis were those of the American Heart Association, 26 of the attacks being presumably initial and 27 recurrent. The duration of the carditis before treatment was 4 to 21 days in 36 cases and 22 days to 4 months in seventeen. The clinical picture in most cases indicated severe disease. Improvement was generally rapid and impressive, particularly in those patients treated early in the disease, and progressive symptoms of carditis were terminated in 91 per cent. Five patients suffered a relapse soon after stopping treatment, but were re-treated with good response. Of 36 patients with initial attacks who were treated early, all but two recovered without overt cardiac damage. In the seventeen patients whose treatment was started late, progressive disease was prevented, although cardiac damage present at the onset of treatment was not reversed. Rebound phenomena without carditis were common on withdrawing steroid therapy (fourteen cases). The average daily dose of hydrocortisone was 320 mg. and of prednisone, prednisolone, and methylprednisolone 100 to 160 mg.

It is suggested that when the duration of the disease is less than 3 weeks, short-term steroid therapy results in the termination rather than the suppression of the clinical signs and symptoms of active carditis, and that long-term hormone therapy is not required in such cases. Rebound phenomena (as opposed to relapse of the carditis) do not require further treatment.

The results obtained with treatment of such exceptionally short duration are remarkable.] John Lorber.
**ABSTRACTS**


The author reports from the National Institute of Cardiology, Mexico City, twelve cases of mitral valvular damage associated with a wide atrial septal defect (A.S.D.), eleven of which were confirmed at necropsy and one at operation. Since 40 per cent. of all patients admitted to the Institute have rheumatic heart disease and since A.S.D. is the second most common congenital abnormality seen there, the author expresses surprise that this combination of lesions has not been found more often; indeed, only once in 500 commissurotomies has it been discovered at operation, although the atrial septum is regularly explored.

The patients were eight females aged 14 to 71 years and four males aged 10 to 48 years. Rheumatic heart disease was usually predominant, and there was a definite history of rheumatic fever in five cases and a doubtful one in two; but the presence of A.S.D., while always apparent from auscultatory, fluoroscopic, and radiographic findings, was in three cases the more obvious lesion. Mitral valvular involvement was diagnosed in nine cases, tricuspid valvular disease in nine, and aortic incompetence in one; one patient had coarctation of the aorta. Cyanosis, due to pulmonary hypertension, was an important pointer to the possible diagnosis in five cases. Cardiac catheterization in two cases showed relatively high left atrial and pulmonary venous pressures. The disease progressed with increasing dyspnoea, haemoptysis occurring in six cases, and eventually nine patients died in congestive heart failure, one from renal failure due to therapeutic misadventure, and one immediately after operative closure of the A.S.D.; only one patient survives, in mild chronic failure.

Post-mortem examination showed that the heart was always large, weighing from 470 to 540 g. The most dilated cavity was the right atrium, followed in order of dilatation by the right and then the left ventricle, the latter being only slightly enlarged or even occasionally normal. In nine cases the septal defect measured between 15 and 60 mm. in diameter, but in the remaining three there was virtually a single atrium. Double mitral lesions, in which, however, stenosis predominated, were present in all cases. Tricuspid involvement was confirmed in seven cases and aortic damage in three; one case showed old pulmonary infarcts. Discussing this series, the authors stress that the co-existence of haemoptysis with severe chronic dyspnoea indicates venous capillary hypertension. They do not agree with the theory that A.S.D. is a protective mechanism against pulmonary hypertension in patients with mitral valvular disease. They accept Lutembacher's explanation for the atypical character of the diastolic murmur, but point out that their cases had other valvular lesions, differentiating them from true Lutembacher's syndrome. The radiological and cardiographic findings are also discussed.

R. S. Stevens.


**Chronic Articular Rheumatism**


A total of fourteen patients with rheumatoid arthritis or spondylitis received triamcinolone therapy over periods of 2 to 8 months. In this small series disturbing weight loss, progressive in some instances, occurred in ten cases. It is apparent that, in addition to the well-known side-effects of corticosteroids, new problems may occur with this steroid, including weight loss, headache, dizziness, and fatigue. Some of the new side-effects described may be sufficiently severe to preclude its use in long-term maintenance dosage. [Authors' summary.]


Two important features of rheumatoid arthritis are muscle weakness with wasting and the close relationship of the inception and course of the disease to psychological stress. As iproniazid has been reported to have a beneficial effect on both these features the authors have carried out a preliminary trial with this drug at the Charterhouse Rheumatism Clinic, London. Iproniazid inhibits mono-amine oxidase enzyme systems. Serotonin, histamine, and noradrenaline are all mono-amine substances and their breakdown is inhibited by iproniazid. It has also been shown in vitro that iproniazid diminishes the haemagglutination titre of the serum of patients with rheumatoid arthritis.

The drug was given to 26 ambulant out-patients with rheumatoid arthritis accompanied by muscle wasting and mental depression in a dose of 150 mg. a day in three divided doses, aspirin and the vitamin-B complex being also given. Eleven patients were unable to take the drug for longer than 2 weeks and showed symptoms of hyperexcitability of the nervous system, which passed off as soon as the drug was discontinued. The remaining fifteen cases were observed for periods of 2 months to one year. Any beneficial effect was noted within 10 days of taking the drug. Such effect consisted mainly in a great improvement in the depressive state accompanying the disease, and in some cases gain in weight and im-
proved functional capacity. There was, however, no
certain evidence of any effect of the drug on the disease
process itself, but its beneficial effect in relieving the
depression that so frequently accompanies rheumatoid
arthritis makes the drug a useful one in certain selected
cases. The average weight gain in eleven patients was
1 lb. 8 oz. (680 g.) per patient per month.

G. S. Crockett.

Effects of Simultaneous Short-Term Administration of
Corticotrophin and Cortisone Acetate in Patients with
Rheumatoid Arthritis. [In English.] KALLIOMAKI,
endocr. (Kbh.), 31, 49. 3 refs.
In studies carried out at the University Medical Clinic,
Turku, Finland, the authors compared the pharmacologic
effect of cortisone alone with that of cortisone
combined with corticotrophin (ACTH) in patients
with rheumatoid arthritis. Of the 21 patients studied, ten
(Group 1) were given 50 mg. cortisone daily, together
with 25 units ACTH intramuscularly for 10 days, while
the other eleven patients (Group 2) received 50 mg.
cortisone only.

Of the ten patients in Group 1, the joint symptoms were
improved in five and unchanged in five, while in Group 2
these symptoms were improved in four and unchanged in
seven. No other effects on the course of the disease were
observed. The erythrocyte sedimentation rate fell in
both groups and the lower rate was maintained for one
week after treatment in Group 1. The body weight of
patients in Group 2 increased for a day or two at the
beginning of treatment, but then returned to the basal
values by the 10th day; in Group 1 there was no change
in body weight. There was no significant change in the
serum sodium and glucose levels in either group but
the serum potassium level fell slightly in Group 2. No
effect on the blood pressure was noted. The eosinophil
count fell in both groups and remained low for more
than 3 days after cessation of therapy, and in this respect
also there was no significant difference between the
two groups. The authors conclude [nevertheless] that they
“feel justified in considering that . . . ACTH and corti-
sone acetate administered simultaneously yield effects
which are unlike those of cortisone acetate given alone”.

William Hughes.

Long-term Use of Prednisone and Prednisolone in Juvenile
Rheumatoid Arthritis: Report of Fifteen Cases.
97, 426. 22 refs.
At Los Angeles Orthopaedic Hospital prednisone and
prednisolone were given to fifteen patients with juvenile
rheumatoid arthritis, treatment lasting 8 to 24 months
(average 19 months). Ancillary measures, such as
physiotherapy and administration of aspirin, were con-
tinued, but no new methods of treatment were intro-
duced. Since the anti-rheumatic action of the two drugs
is similar they were used interchangeably in this study
and were given in full dosage (nine of the patients being
maintained on more than 10 mg. per day).

There was complete remission in three patients during
the period of observation (two of whom had had remis-
sions in the past) and some degree of improvement in
six others. The remaining six patients were either not
improved or became worse. However, twelve patients
reported subjective relief. Side-effects were numerous,
28 being encountered, but they were largely of a minor
nature and did not call for any modification in treatment.
Transitory diabetes mellitus was reported in one case.
There was some evidence that normal growth and in-
crease in weight were slowed down during treatment.
The author concludes that the findings provide no
evidence that these hormones alter the natural course of
the disease or retard progressive joint damage, but sub-
jective benefit was striking, while the minor side-effects,
which occurred did not present a serious problem.

B. E. W. Mace.

Studies of Adrenal Cortical Activity in Patients with
Rheumatoid Arthritis: the Diurnal Pattern and Twenty-
four Hour Levels of Urinary Total 17-Hydroxycortico-
steroids and 17-Ketosteroids. HILL, S. R., HOLLEY,
H. L., ULLOA, A., STARNES, W. R., HIBBITT, L. L.,
3 figs, bibl.
This paper from the University of Alabama reports a
comparative study of the diurnal pattern and 24-hour
excretion of urinary excretion of 17-hydroxycorticosteroids
(17-(OH)CS) and 17-ketosteroids (17-KS) in ambulatory
and hospitalized patients with rheumatoid arthritis and
control subjects. The mean rate of 17-(OH)CS excretion
(measured in 6-hour periods) in ten ambulatory normal
subjects was highest between 7 a.m. and 1 p.m. and lowest
between 1 p.m. to 7 p.m. This was also the case in eleven
hospitalized normal subjects and in ten hospitalized
patients with non-rheumatic chronic diseases. In con-
trast twelve hospitalized and eleven ambulatory patients
with rheumatoid arthritis showed little variation in the
rate of 17-(OH)CS excretion throughout the day and
night. The mean 24-hour excretion of 17-(OH)CS in the
two groups with rheumatoid arthritis was considerably
less than in the normal and non-rheumatic groups, though
it was considered to be within the normal range. The
constant diurnal pattern of 17-(OH)CS excretion found
in the patients with rheumatoid arthritis was not observed
with 17-KS, excretion of which decreased from morning
to evening in all groups. The mean 24-hour 17-KS
excretion was remarkably constant in all groups and fell,well within the normal range in the patients with rheu-
matoid arthritis.

The flattened diurnal pattern of 17-(OH)CS excretion
and the high ratio between total 17-KS and 17-(OH)CS
excretion in patients with rheumatoid arthritis as com-
pared with control subjects are of considerable interest.
The authors point out that speculation on a possible
cause and effect is unwarranted at this time, but that the
quantitative relationship of one hormone to another may
be as important as the absolute level of either hormone
alone.

Oswald Savage.

Several serological tests have been described in recent years as aids in the diagnosis of rheumatoid arthritis; all are based on the presence in the serum of a protein of high molecular weight, associated with the γ-globulin fraction and known as the "rheumatoid factor". In this study, carried out at the Veterans Administration Hospital, Birmingham, Alabama, the authors have compared three such tests, namely, the latex fixation test using whole serum as described by Singer and Plotz, the latex fixation test using the euglobulin fraction as described by Craig, Kerby, and Persons (*J. Lab. clin. Med.*, 1957, 49, 635), and the bentonite flocculation test of Bozicevich et al. (*Proc. Soc. exp. Biol. (N.Y.),* 1958, 97, 180; *Abstr. Wild Med.*, 1958, 24, 212). Each test was performed on the sera of:

1. 76 patients aged 19 to 72 years with a clinical diagnosis of rheumatoid arthritis (fulfilling the criteria of the American Rheumatism Association (A.R.A.), apart from the finding of a positive agglutination reaction);
2. Nine patients with "atypical rheumatoid arthritis", that is, with a disease clinically suggestive of rheumatoid arthritis but not fulfilling the criteria of the A.R.A.;
3. 71 patients with musculoskeletal disease other than rheumatoid arthritis, these being divided into eleven separate diagnostic categories.

The whole-serum latex-fixation method gave a positive result in 56 (74 per cent.) of the 76 patients with definite rheumatoid arthritis. A difference in the sex incidence was noted, 81 per cent. of the men but only 69 per cent. of the women giving a positive reaction, suggesting perhaps that a separate disease mimicking rheumatoid arthritis may occur in middle-aged women. None of the patients with atypical rheumatoid arthritis (Group 2) and only one in Group 3 (a patient with systemic lupus erythematosus) gave a positive result with this test.

The latex-fixation test using euglobulin gave a positive result in 86 per cent. of the 76 patients in Group 1, a negative result in all in Group 2, while in Group 3 only two patients (one with systemic lupus erythematosus and one with Sjögren's syndrome) showed a positive reaction. Lastly, with the bentonite flocculation test a positive result was obtained in 88 per cent. of cases in Group 1, in none in Group 2, and in only four cases (two of systemic lupus erythematosus and two of the "shoulder-hand syndrome") in Group 3.

The authors state that those patients with definite rheumatoid arthritis who showed no agglutinating activity by any of the three tests are being subjected to a latex-inhibition test which may reduce the size of this group. The significance of the reactions is discussed and the present results compared with those of other workers. It is of interest that in this series all three tests of agglutinating activity were negative in patients with osteoarthritis, ankylosing spondylitis, gout, Reiter's syndrome, Still's disease, scleroderma, "infectious arthritis", and rheumatic fever.


The authors, working in Lyon, France, observe that the peripheral neuritis which complicates rheumatoid arthritis is rare, though upwards of forty cases have been reported in the literature in 1933, and they have personally recognized three cases. It occurs most frequently in longstanding and severe cases of rheumatoid arthritis. The mean duration of the arthritis was 8 years and in only one case was it less than 1 year before neuritis set in. Previous treatment with hormones was mentioned in all except two cases. The dosage was often high and in some cases withdrawal was abrupt. Gold had also been used in the majority of cases. In one of their three personal cases, the neuritis which had been improving, relapsed after injections of copper. The neuritis is usually multiple and asymmetrical in distribution, and is a mixed neuritis with sensory, motor, and trophic effects. There is paralysis with pain and muscular atrophy in the distribution of the affected nerve. Involvement of a cranial nerve is rare, but such cases have been described. Vascular lesions of many kinds included cerebral and coronary thrombosis, purpura, and gangrene of the extremities. The prognosis was not good, a fatal issue being recorded in eighteen out of the forty cases recorded. Pure neural lesions, which included demyelination of the peripheral nerves and degeneration of the posterior columns, were recorded in only one case. In all cases the typical lesions of periarteritis nodosa were found. The distribution of lesions is widespread and the arteries of the peripheral nerves and the voluntary muscles are constantly affected. Discussing the pathogenesis, the authors point out that periarteritis nodosa occurs in other forms of collagenous disease, including malignant hypertension, Buerger's disease, and temporal arthritis. They consider that cortisone is an aetiological factor of importance. No particular line of treatment has yet been proved effective, and the authors advocate absolute rest, sedation, and the gradual withdrawal of steroid treatment. Prevention is more important and hormones should be given with care and withdrawal should never be abrupt.

William Hughes.


(Osteo-Arthritis)


(Spondylitis)


After a brief review of the literature concerning the hereditary factor in ankylosing spondylitis, the author reports an investigation of the incidence of ankylosing spondylitis and rheumatoid arthritis among the parents and siblings of seventy spondylitic patients attending Charing Cross Hospital, London. Among the 428 close relatives of the patients, sixteen with spondylitis were discovered. This incidence of roughly 1 in 27 among relatives of patients is far higher than previous estimates of the disease in the general population.

The family pattern of distribution of the spondylitides was influenced by a simple dominant gene with differing penetrance for males and females. Thus, among the 35 close relatives of nine female spondylitic patients, there were four cases of ankylosing spondylitis, which would seem to support a previous suggestion of greater penetrance in families with an affected mother or other female progenitor. In addition, six cases of rheumatoid arthritis were found among the 428 close relatives of the patients, an incidence of 1 in 71. The author notes that although this is twice or three times the estimated incidence of rheumatoid arthritis in the general population, the difference is not statistically significant. In one family the finding of the transmission of ankylosing spondylitis from grandfather to grandson through a rheumatoid mother strongly suggests a common genetic factor for the two diseases. **M. Wilkinson.**
(Miscellaneous)


The incidence of radiographic evidence of sacro-iliac joint disease in a series of 78 patients (76 men and two women) [ages not stated] who were treated at the London Hospital for Reiter’s disease was studied. All the patients had arthritis in one or more [unspecified] joints, with urethritis and sometimes conjunctivitis or iritis. In 46 cases the patient had had more than one attack. The criteria whereby the x-ray findings were assessed are stated [although the number of observers is not specified and the use of a “blindfold” technique is not mentioned].

The sacro-iliac joints were regarded as normal in 34 cases and abnormal in 35 (unilateral in six and bilateral in 29); there was doubtful evidence of sacro-iliitis in nine cases. Of the 35 patients with definite radiographic evidence of sacro-iliitis, sixteen complained of backache and twelve had iritis, the average duration of the disease in this group being 13 years. In contrast, of the 34 patients in whom no such evidence was found, only five complained of backache and three had iritis, while the average duration of their disease was 4-8 years. All the patients with sacro-iliitis who were examined had genital infection in the form of chronic prostatitis, and the authors discuss the strong but inconclusive evidence for the role of focal infection in the causation of this condition and others affecting the joints of the spine and pelvis.

The occurrence of iritis in association with rheumatic diseases, particularly ankylosing spondylitis, has frequently been reported. Of the twelve patients with iritis in the group with sacro-iliitis, nine had recurrent attacks, a point which the authors stress. All showed evidence of prostatitis. The difficulty of distinguishing patients with Reiter’s disease and sacro-iliitis from those with ankylosing spondylitis and iritis, and less commonly dysuria, are discussed.

J. Warwick Buckler.


Of the 53 patients with Reiter’s syndrome previously reported (Murray et al., J. Fac. Radiol. (Lond.), 1958, 9, 37; Abstr. Wld Med., 1958, 24, 238) the authors, working at the London Hospital, have compared the radiological findings in 25 with the corresponding findings in 81 cases of rheumatoid arthritis and 38 of ankylosing spondylitis. In all cases radiographs of the hands, feet, ankles (including the calcaneum), and pelvis were examined. Although the condition could not be differentiated radiologically in every case the following features were considered to be of value:

(1) In Reiter’s disease exuberant periosteal new bone formation on the plantar surface of the calcaneum was considered to be characteristic. (A critical re-examination of three patients with rheumatoid and two with ankylosing spondylitis showing this feature indicated that in these cases the initial diagnosis was beyond suspicion in only one, and in this one case it was thought that Reiter’s disease was present as well.) Of the patients with Reiter’s disease this sign was noted in 20 per cent. Similar, but less marked changes may be observed round the wrist. Destructive joint lesions are common in the feet, but rare in the hands. Sacro-iliitis occurred in 32 per cent. and became more common with increasing duration of the disease, but unlike the other lesions it was usually symmetrical. Generalized osteoporosis was not a customary feature in this disease.

(2) In the radiographs of patients with rheumatoid arthritis the usual findings were confirmed. Peripheral arthropathy was slightly more common in the hands than in the feet and was accompanied by generalized osteoporosis. Sacro-iliitis did occur in 12 per cent. of these cases, but was later in onset and always less severe than in the following group.

(3) Ankylosing spondylitis. Here the predominant and early involvement of the sacro-iliac joints, observed in all cases, was found to be associated with peripheral arthropathy in the feet in 24 per cent. and in the hands in only 11 per cent. of these patients.

In all three conditions, posterior erosions of the calcaneum were sometimes seen and periosteal new bone formation was common round the malleoli.

Useful tables of distribution of the lesions in these conditions are given. Attention is also drawn to the age distribution: thus ankylosing spondylitis is earlier in onset, on the whole, than is rheumatoid arthritis, while Reiter’s disease was found to occur in patients between the ages of 15 and 75, with its highest incidence in the fourth and fifth decades.

R. O. Murray.


The author reports eighty cases of post-dysenteric Reiter’s syndrome occurring in military personnel in Tunisia. The incidence of the syndrome followed closely the incidence of dysentery from June to December and affected mainly young men who had arrived recently from France. Urethritis, mostly abacterial in nature, was present in 80 per cent., eye involvement in 94 per cent., and arthritis in 96 per cent. of the cases observed. The arthritis affected mostly the lower limbs, especially the knees. In the more severe cases marked muscular wasting, particularly of the quadriceps femoris, became one of the most intractable features of the syndrome. In four cases there were transient quadriiceps femoris, with abnormal electrocardiographic findings. There was a well-marked increase in the α-globulin fraction of the serum proteins in no less than 94 per cent. of cases; a rise in the γ-globulin level was found in 60 per cent. of cases.

Aureomycin appeared to prevent later complications, such as ankylosing spondylitis, if given early; once the syndrome was well established, however, antibiotics proved ineffective.
Diacetylpicrocatechol given in combination with prednisone was found to be the most effective treatment of the established condition. 

G. W. Csonka.


The author, writing from the Georgetown University Medical Center, Washington, D.C., divides the activities of the hands into three general categories: “gripping”, “pinching”, and “tapping”. Cutting, for example, is a combination of the first two.

In early rheumatoid arthritis, the “spindle-shaped” appearance of the proximal interphalangeal joints may be obvious before any x-ray changes are seen. Later, the distal joints may become involved with narrowing of joint-spaces indicating cartilaginous destruction. Ulnar deviation is caused by the muscular pull of interossei and flexor muscles, in the presence of damaged metacarpophalangeal joints. There may also be ankylosis and resorption of epiphyseal bone.

In osteo-arthritis, the familiar Heberden node seen in middle-aged women may show only slight narrowing of the distal joint-space radiologically, and possibly slight lipping of the bone margin, but such nodes may become acutely inflamed without any additional changes on the x-ray film. Nodes may grow to a great size with evidence of cystic degeneration in the subchondral bone.

“Psoriatic arthritis” may, in its later stages, show severe rheumatoid deformities of the “opera-glass” type with chronic discoloration of the skin. Crimping deformities may be seen in gout and the well-known “punched-out” areas recognized on the films. Scleroderma may immobilize the hand by its contracting action. Similar restrictions may be seen in general calcinosis and one or two fingers may be affected in Dupuytren’s contracture; in all three conditions x rays will demonstrate unaffected joints. Current methods of treatment are useful in limiting deformities and should be vigorously pursued, but the tendency to neglect massage is unjustifiable. David Preiskel.


After giving a brief outline of the historical background of erythema nodosum, which was first described by Willan in 1798, the authors analyse seventy consecutive cases in order to establish the relative incidence of the three main causes—namely, tuberculosis, streptococcal infection, and sarcoidosis. The cases fell into six main groups:

1. Tuberculous—four cases—the oldest patient being aged 24 years;
2. Streptococcal—eight “proved” and seventeen “presumed” cases—the main criteria being a preceding tonsillitis and the finding of β-haemolytic streptococci;
3. Bilateral hilar-node syndrome without evidence of parenchymatous sarcoidosis—twenty cases, average age 32 years;
4. Erythema nodosum with pulmonary sarcoidosis—five cases, average age 42 years;
5. Middle-aged women with recurrent bronchitis—seven cases;
6. Miscellaneous and unknown—nine cases.

Thus, of the seventy cases, 45-6 per cent. were of proven or presumptive streptococcal origin, 35-7 per cent. accompanied sarcoidosis, 13 per cent. were of mixed or unknown origin, and only 5-6 per cent. were tuberculous. The authors noted depression frequently in patients with disease of the sarcoid type. E. W. Prosser Thomas.


Reporting from the University of Barcelona the authors present, in Tables, the clinical findings in nineteen patients (one male) with subacute nodular migratory panniculitis, a new disease entity, the first fourteen cases of which they described in an earlier paper (Ann. Derm. Syph. (Paris), 1956, 84, 369). The diversity of the clinical and histological features of the entity may account for the difficulty in identifying it.

All the patients had nodules and plaques, which were limited to the lower part of the leg, but the age at the time of onset varied from 16 to 65 years. In the differential diagnosis nodular vasculitis and erythema induratum may have to be considered, but the situation of the nodules in nodular migratory panniculitis and their absence of ulceration are distinctive. It was noted that in eleven patients had acute tonsillitis before the onset of the condition. The histological findings are described (and illustrated in photomicrographs); the fundamental change was a capillaritis in the hypodermis, with the formation of a pseudo-foreign-body granuloma. Biopsy examination often enabled a definite diagnosis to be made. Treatment with potassium iodide caused some of the nodules to disappear.

[No information is given regarding the state of the circulation in the affected legs or whether or not there had been previous thrombophlebitis.] S. T. ANNING.


Conventional lumbar sympathectomy has been tried occasionally in the past for the relief of arthritic pain, but a poor impression has been obtained of its efficacy. On fourteen patients with pain due to arthritis in the lower limbs the present authors have performed a more extensive operation, removing the lumbar sympathetic trunk on the side of the painful joint from the crus to the pelvic brim and interrupting sympathetic fibres crossing from the opposite side by making “cross-hatch” cuts on to the periosteum of the 3rd and 4th lumbar vertebrae. This has necessitated mobilizing the vena cava and the aorta. Post-operative sweating patterns have shown patchy areas of anhidrosis on the contralateral thigh.
ABSTRACTS

suggesting that decussating fibres are in fact interrupted by this operation. In one additional case in which venous abnormalities prevented the removal of the upper lumbar trunk there was no relief of pain in the corresponding knee joint.

Brief case histories are given. Many of the patients were elderly; the oldest was 81 and the youngest 49 years old. Arthritic pain had usually been present for several years and steroid therapy had been tried without success. Intractable pain was [apparently] the only criterion for selection of the cases; vasomotor phenomena were not present. One patient had undergone obturator neurectomy and cordotomy with only temporary relief. There was no operative mortality or morbidity. All the patients reported relief of rest pain immediately on recovering from anaesthesia, with increasing mobility of the affected joint during the next 2 weeks. No relapse has occurred, the follow-up period ranging from 3 months to 3½ years. The authors believe that the operation interrupts pain fibres arising within the joints of the lower limb.

C. J. Longland.

Antimalarials in the Treatment of Sjögren’s Syndrome.


Since there is some evidence that Sjögren’s syndrome is a form of systemic lupus erythematosus, the author treated 25 patients with malarials. Two drugs were used: chloroquine sulphate and hydroxychloroquine sulphate (Plaquinil). Eight patients failed to improve (three of these had toxic reactions which necessitated withdrawal of the drug before it could take effect).

Of the remainder there was a variable degree of improvement, after 4 to 8 weeks of treatment.

The author considers that the results of this clinical investigation suggest that further trials of antimalarials in Sjögren’s syndrome “would be worth while”.

C. A. G. Cook.


At Rigshospitalet, Copenhagen, muscle action potential was studied by means of a three-channel electromyograph in 31 arthritic patients, most of whom had rheumatoid arthritis. At room temperature 138 potentials were recorded from the first dorsal interosseous muscle of the hand, the values being compared with those in ten healthy females, aged 19 to 22 years. In nineteen of the 31 patients there was a reduction in the duration of the potentials, which, the authors state, is characteristic of myositis and certain other forms of myopathy. In one instance the deviation from normal was as high as 35 per cent. The deviations were not attributable either to disuse atrophy or to a high intramuscular temperature, but serological tests appeared to show some relationship between the deviations and haemagglutination and streptococcal agglutination reactions. Electromyographic abnormalities were observed as early as one month after the onset of symptoms and before muscle atrophy had developed. They were not modified by gold or corticosteroid therapy.

In eleven patients the duration of action potentials was normal. Spontaneous activity was recorded in 18 cases, but the exact significance of this was difficult to determine. In one patient with ankylosing spondylitis the potentials obtained from the muscle in a state of relaxation resembled the fibrillation potentials associated with denervation.

It is of interest that in seventeen cases other muscles, such as the tibialis anticus, quadriceps extensor femoris, and opponens pollicis, were tested, and the responses were invariably normal.

A. Garland.

Effect of Myocardial Infarction on the Articular Disorder in Rheumatoid Arthritis. (Wpływ zawału mięśnia serca na dolegliwości stawowe w goścu pierwotnie przewlekłym.)


In the first of these two papers a clinical study is presented of five patients with rheumatoid arthritis quiescent for at least a year who were admitted to hospital after an attack of myocardial infarction of moderate severity. In three cases the inflammation of the joints flared up within 12 to 18 hours of the onset of cardiac pain, while in the other two joint pains developed in the 2nd and 4th weeks respectively. Phenylbutazone in doses of 0.6 g. daily was effective in controlling the joint pains, aspirin and other analgesics being less useful.

The second paper deals with the occurrence of polyarthritis in association with myocardial infarction in patients who had never previously suffered from joint disease. (The classic “shoulder-hand” syndrome is not included in the series.) During the 3-year period 1954-57, six such cases were seen. In one case the joint symptoms preceded the myocardial infarction by one day, in a second case they developed on the same day, and in others they appeared between the 4th and 6th weeks after the infarction. In all cases the pains in the joints disappeared, usually without any special treatment, though in some they lasted 6 to 7 months. In only one case were there objective clinical and radiological changes characteristic of rheumatoid arthritis; even in this case recovery was complete. The pathogenesis is obscure, possible factors suggested by the author including hormonal disturbances, "stress", and the products of tissue necrosis.

[The abstracter has recently treated a middle-aged woman who, after a severe attack of myocardial infarction, had an acute exacerbation of long-standing rheumatoid arthritis. The affected joints were very painful and the usual analgesics appeared to have little effect. Improvement in the joints began after 10 to 14 days, coinciding with the improvement in the cardiac condition.] A. J. Suchett-Kaye.


The relatively high incidence of gastro-intestinal side-effects with phenylbutazone led to a search for a
better tolerated derivative with similar pain-relieving activity. Such a derivative is hydroxyphenylbutazone (G.27202), which is identical with one of the two metabolites that can be isolated from the urine of patients receiving phenylbutazone, from which it differs in having a phenolic group in the para position of one benzene ring. It is readily absorbed from the gastro-intestinal tract, and with repeated daily oral administration the plasma level reaches a plateau after 3 days and thereafter remains constant. In a daily dosage of 800 mg, it causes significant retention of sodium and water in the body (as does an equivalent dose of phenylbutazone) but has no uricosuric effect. Animal experiments suggest that G.27202 has greater analgesic activity than phenylbutazone and less ulcerogenic effect.

The authors describe a clinical trial of G.27202 which was carried out at the Westminster Hospital, London. Of the 117 patients (52 male and 65 female) treated, 62 had rheumatoid arthritis, 25 ankylosing spondylitis, 26 osteo-arthritis, and four miscellaneous rheumatic conditions. The two drugs were given in equal doses (usually 100 mg, two, three, or four times daily with meals). All the patients received each drug for one to 3 weeks and were asked to state which (if either) was the more effective in relieving pain and stiffness. Records were also kept of side-effects due to the treatment and observations were made on fluid retention.

G.27202 was considered the more effective by 15 per cent. of the patients and phenylbutazone by 32 per cent.; 29 per cent. considered that the drugs were equally effective and 24 per cent. that neither was effective. Of the 89 patients who were helped by both drugs, 34 considered them to be equally effective, eighteen preferred G.27202, and 37 preferred phenylbutazone. Of this last group, fourteen patients were given G.27202 in increasing doses until an effect equivalent to that of phenylbutazone was produced. The effective dose ratio of G.27202 to phenylbutazone was 2 : 1 in five cases, 5 : 3 in one, and 3 : 2 in eight. Many of the patients who preferred G.27202 were intolerant of phenylbutazone.

Of the 117 patients in the trial, 25 developed symptoms of gastric intolerance with phenylbutazone, which in twenty cases were so severe as to necessitate discontinuation of treatment. The corresponding figures for G.27202 were ten and four respectively. Evidence of fluid retention was found in three cases with phenylbutazone and five with G.27202. One patient developed pyrexia and an urticarial rash while taking G.27202 and two patients complained of giddiness and headache with both drugs. There was no evidence of leucopenia in any case. G.27202 was administered in doses of 300 to 400 mg, daily to fourteen patients for periods of 3 to 12 months without evidence of intolerance.

The authors emphasize that although these drugs relieve the pain of chronic rheumatism, they have no significant anti-inflammatory effect on swollen joints. They conclude that, in general, G.27202 has less pain-relieving activity than phenylbutazone, but is decidedly less liable to cause gastro-intestinal disturbance; it may therefore play a useful part in cases in which phenylbutazone is poorly tolerated. Further modification of the phenylbutazone molecule may produce less toxic and more useful compounds for the treatment of chronic rheumatic disorders.

P. T. Main


Results of Treatment with Phenylbutazone Calcium in Association with Prednisone in Rheumatology. (Resultados obtidos com o emprego da fenilbutazona cálcico associado a prednisona em reumatologia.) NEBÓ, F., SPILSBORGHS, G., and PAULO, S. (1959). Rev. Ass. med. bras., 5, 164. 6 figs, 8 refs.


Disk Syndrome


Gout


The modern treatment of gout depends on increasing the loss of urates from the body by giving drugs which depress renal tubular reabsorption of filtered urate. The phenylbutazone derivative sulphinpyrazone ("anaturan"; "G-28315") is such a drug. In this paper from Mount Sinai Hospital, New York, and the National Heart Institute, Bethesda, Maryland, the authors report their experiences with the clinical use of sulphinpyrazone in 44 patients with gout, of whom 42 were in the tophaceous stage, twelve had extensive deposits of urate, and eight had persistent pain and stiffness between attacks.

In 29 patients, the initial mean urate excretion per 24 hours was 509 mg., 25 of them showing a daily excretion of less than 600 mg. After they had been treated with sulphinpyrazone in a dosage of 400 mg. per day, the mean daily excretion rose to 839 mg., being over
600 mg. in 25 cases. In forty patients with an initial serum urate level over 7 (mean 10·7) mg. per 100 ml., this level fell to a mean of 7 mg. per 100 ml., 22 patients showing values below this. With the dosage of 400 mg. daily, however, only seven out of forty patients achieved normal serum urate levels (below 6 mg. per 100 ml.) and in some “resistant” patients the serum urate level fell further following an increase of the dosage to 600 or 800 mg. per day. Reduction in the size of visible tophi occurred in all but four of twenty patients followed up for over 7 months. Side-effects, mostly mild, occurred on eighteen occasions in twelve patients; these included dyspepsia and gastro-intestinal upset (five cases), renal colic and/or calculus (eight), and a flare-up of acute gouty arthritis (five). Insufficient time has elapsed to assess any long-term hazards. A combination of sulphinpyrazone and zoxasolamine had a synergistic action in one patient. Four illustrative case histories are presented to show that some patients were tolerant of sulphinpyrazone but intolerant of other uricosuric drugs and vice versa. The authors conclude that sulphinpyrazone is a useful addition to the several uricosuric drugs at present available. *Allan St. J. Dixon.*


**Pararheumatic (Collagen) Diseases**


A combination of “quinacrine” (mepacrine), hydroxychloroquine, and chloroquine was given to 45 patients with chronic discoid lupus erythematosus (L.E.) and three with subacute systemic L.E. seen at Boston City Hospital and in private practice between October, 1956, and January, 1958. The drugs were given in a tablet containing 25 mg. quinacrine, 50 mg. hydroxychloroquine, and 65 mg. chloroquine. A dosage of one tablet morning and evening was adequate in twenty patients, but thirteen required three tablets, six required four, and two required six tablets daily [sic]. Only one patient (with subacute systemic L.E.) required eight tablets a day before the response was adequate. There was complete clearing of the lesions in nineteen cases of chronic discoid L.E. and in one of subacute systemic disease, while the clearing was almost complete in nine further cases of chronic discoid L.E. Partial clearing (50 per cent. of the lesions completely healed) was obtained in sixteen cases of discoid L.E. and in two cases of the subacute systemic form. Generally, improvement became evident 2 to 4 weeks after the start of treatment. The authors point out that assessment of the value of treatment was based on objective improvement in the inflammation; the scars in L.E. cannot change. Of the twenty patients with complete clearing, thirteen relapsed but a remission was obtained and maintained with smaller doses than those given initially. Apart from minor gastro-intestinal disturbances in four cases, reactions severe enough to necessitate cessation of treatment occurred in six cases only—namely, skin reactions in three and an abnormal cephalin flocculation titre in three, in one of which there was associated blond dis-coloration of the hair. In one patient with psoriasis as well as chronic L.E., the psoriasis appeared to become worse with this treatment regimen. It is concluded that this combination of antimalarial drugs may be more effective than any one of the drugs given alone, but that quinacrine, “because of its tendency to produce skin reactions is the drug most likely to be displaced, in part or altogether, by either or both of the others”.

E. W. Prosser Thomas.


An investigation of the part played by splenectomy in the management of acquired haemolytic anaemia is reported in this paper from the Hematology Research Laboratory, University of Texas, Galveston. The authors describe in detail three cases of systemic lupus erythematosus in which steroid therapy did not result in any improvement in an associated acquired haemolytic anaemia, but satisfactory remission followed splenectomy. The rationale of the operation is discussed. Contrary to the findings of others splenectomy did not have any ill-effects on the course of the primary disease.

R. B. Thompson.


The authors report from the Royal Melbourne Hospital, Victoria, Australia, the findings in fourteen patients with lupoid hepatitis, this term being used to describe the condition in which patients with chronic hepatitis and cirrhosis also show a positive result in the lupus erythematosus (L.E.) cell test; nine of the ten female patients and two of the four males were below the age of 40. In five cases the initial illness resembled acute infective hepatitis, while two patients had chronic nutritional hepatitis due to alcoholism; in the remaining seven the jaundice developed insidiously and without apparent cause.
The hepatitis was unusually severe and progressive, with recurrent exacerbations of jaundice and sometimes episodes of hepatic failure. The liver and spleen were enlarged. Liver function tests were "profoundly disturbed", and the erythrocyte sedimentation rate (Westergren) was increased. The serum γ-globulin level was usually above 2 g per 100 ml., a finding in itself suggestive of an immunological disorder. The plasma oxalacetic glutamic transaminase level was raised in eight out of nine patients tested, indicating the presence of liver-cell necrosis. Other systemic manifestations included joint pains (seven), rashes (four), renal lesions (three), ulcerative colitis (three), pleural effusion (two), and haemolytic anaemia, lymphadenopathy, myocarditis, and thrombocytopenia in one case each. The L.E. cell test usually gave a weakly positive result; in eight cases the test result was positive only once, but in the remaining six it was positive on several occasions, and in one case repeatedly. The auto-immune complement-fixation reaction was positive in nine out of ten patients tested. Of eleven patients treated with cortisone, four responded immediately, one had a moderate remission, four showed slight and sometimes transient improvement, but two showed no improvement. Liver biopsy was performed in twelve cases and necropsy in the eight fatal cases; the liver invariably showed both macroscopically and microscopically the characteristic appearances of active chronic hepatitis.

The incidence of histological lesions in the liver was assessed in a further nineteen patients with systemic lupus erythematosus. In nine of these the liver was enlarged, while minor liver changes were found in eleven patients, but in most cases were insufficient to give rise to clinical or biochemical manifestation. Typical chronic hepatitis was present in two of these patients.

In discussion the authors state that lupoid hepatitis differs from classic systemic lupus erythematosus in that hepatic disease is the initial and dominant feature throughout, but overlapping features in both groups suggest a similar pathogenesis, possibly mediated through abnormal immunological responsiveness with auto-destruction (autoclasia) of host tissues. It is suggested that a closer study of cases of lupoid hepatitis "may provide clues as to why active chronic hepatitis pursues its relentless course". J. Warwick Buckler.


In this study reported from the Hospital Salvador (University of Chile), Santiago, the clinical and laboratory findings in 100 patients with disseminated lupus erythematosus treated with corticoïdes were compared with those in 25 "untreated" patients seen before 1950. The groups were similar in regard to age at onset, and severity and mode of presentation of the disease. Between 1950 and 1955 cortisone, and from 1955 onwards prednisolone, were the drugs most frequently employed. The initial dose was 200 to 500 mg. per day of cortisone or its equivalent, while the maintenance dose ranged from 6-25 to 175 mg. per day. (Chloroquin and isohaemotherapy were also given in a number of cases.) Treatment was continued as long as practicable, this period being less than one year in 52 cases, 1 to 2 years in 26, and 2 to 7 years in 22. Patients showing only fixed discoid lesions were observed without treatment, but all others with evidence of disease activity, that is, rash, fever, fall of hair, blood changes, and a positive result in the L.E.-cell test, were treated in the hope of preventing the development of irreversible changes, such as nephrosis.

Of the 100 treated cases, 55 developed some degree of Cushing's syndrome; dyspepsia occurred in 27, but was controlled by changes of diet or dose or by alkalis; three patients suffered from peptic ulcer, which was fatal in two; hypertension developed in 22 patients, but could usually be controlled with hypotensive drugs; heart failure was a complication in twelve patients, in three of whom treatment had to be stopped; ten patients developed epilepsy, which in four cases was related to steroid treatment and responded to reduction of the dosage or withdrawal; six patients suffered from meningitis or miliary tuberculosis, demonstrated at necropsy in five. Only one patient developed uncontrollable pyogenic infection attributable to the corticosteroids. Adverse crises were not observed. Osteoporosis and pathological fractures occurred, but the exact incidence was not known since these complications had not been systematically looked for. In the few patients who became pregnant the doses of corticosteroids were reduced and no ill effects on the mother or foetus were seen. Of the 25 untreated patients, 21 died, the mean survival period being 11.8 months from onset of disease; the other four were not traced, but were presumed to be dead. In contrast, the over-all mortality in the treated group was 50 per cent. and the mean survival time 30.9 months from onset among those who died. Comparison of various groups showed that survival was related to the promptitude and adequacy of treatment.

The authors re-affirm the especially bad outlook in this disease for patients with the nephrotic syndrome or nitrogen retention, or in cases with severe onset. They stress the need for constant supervision, both in hospital and after discharge, and for measures to ensure prompt readmission and treatment for complications. They conclude that in conjunction with general medical care, the advent of corticosteroids has considerably improved the prognosis in disseminated lupus erythematosus. A. St. J. Dixon.


In a previous study of the results of all forms of treatment of diffuse progressive scleroderma, the author and colleagues found that extensive sympathectomy resulted in palliation in about 88 per cent. of patients. In an
ABSTRACTS

The author considers that "there is a very close relation between Raynaud's disease and scleroderma of the acrosclerotic type to the point of possibly being the same disease with different degrees of involvement".

J. McLean Baird.


Two cases of scleroderma associated with cystic changes in the lungs and pulmonary adenomatosis are described [from Whittington Hospital, London]. In Case 1 the adenomatosis was possibly malignant, in Case 2 it was unequivocally so with metastases to pleura and diaphragm.

The appearances of cystic fibrosis of the lungs found in association with scleroderma are discussed. It is considered that these changes show no essential difference from those found in honeycomb lung and that the pulmonary fibrosis of scleroderma is similar to other pulmonary fibrosis or granulomata in being the antecedent of honeycomb lung.

The relation of "tumourlets" and pulmonary adenomatosis to carcinoma and the pathogenesis of hyperplastic respiratory epithelium are discussed. The hypothesis is put forward that the hyperplastic epithelial changes are in some way related to impaired respiratory function associated with increased pulmonary fibrosis.—[Author's summary.]


Nine patients with generalized scleroderma were studied at necropsy with special reference to cardiac and renal lesions. Seven had myocardial fibrosis, which was attributable to scleroderma in four. Only two of the patients without other causes of heart failure and with myocardial fibrosis exhibited congestive heart failure. In one of these the heart failure was a prominent clinical feature, while in the other it appeared to contribute to the death caused primarily by carcinomatosis.

Renal lesions of significance were observed in three of the patients, each dying of uraemia. The renal lesions of scleroderma form a characteristic picture, with multiple arterial occlusions and cortical infarcts. Hypercellularity of glomeruli with fibrinoid necrosis of the basement membranes of the glomerular tuft is occasionally observed. The vascular lesions are impossible to distinguish from those of primary hypertension, but taken with the presence of multiple cortical infarcts and glomerular changes like those seen in lupus erythematosus they form a complex that appears to be specific for the kidney of scleroderma.—[Authors' summary.]


The author describes, from the Department of Pathology, University of Melbourne, the renal lesions in...
three cases of scleroderma occurring in females aged 36, 46, and 69 years respectively. All three patients died of renal failure between 1 and 2 years from the onset of the disease. He has also collected and tabulated the relevant details of 34 similar cases reported in the literature.

The significant renal lesion is a mucoid and loose fibrous swelling of the walls of the intralobular arteries without inflammatory reaction, the arterial lumen being narrowed or obliterated. This interference with the blood flow leads to focal cortical infarcts. The appearances of the renal lesion and the clinical course of the disease are almost identical with those described in malignant hypertension. The administration of adrenal corticosteroids is not recommended in the treatment of scleroderma, since in a number of reported cases of this disorder these drugs have appeared to accelerate the progress of the hypertension or even to determine its appearance. A. W. H. Foxell.


This paper records the results of a study at the Mayo Clinic of the pulmonary function of 22 (nine male and thirteen female) patients aged between 28 and 75 years with scleroderma. The first symptoms of the disease had occurred 4 months to 15 years (average 3:3) before this examination. The chief complaint referable to the lungs was exertional dyspnoea in fifteen cases and cough in three; in two patients there was also emphysema which, however, was probably unrelated. Radiography of the chest showed no significant amount of fibrosis in eight cases, slight localized fibrosis in two, moderate generalized fibrosis in two, and severe generalized fibrosis in ten; this was usually most prominent in the lower half or two-thirds of the lung fields. The severity of pulmonary fibrosis was not always proportional to the degree of sclerodermatous involvement of the skin.

Pulmonary function tests showed that total lung capacity was usually reduced in the presence of radiological fibrosis. Vital capacity was reduced in all the patients, with or without radiological signs, in no case exceeding 63 per cent. of normal. Residual volume was reduced only in those with severe pulmonary fibrosis. Arterial blood oxygen saturation was reduced in one of the patients with emphysema and in two with severe generalized fibrosis. Hypoxaemia after exercise occurred in most of the patients with generalized pulmonary fibrosis. G. Loewi.


Because of the conflicting views about the classification of acrosclerosis and its relation to diffuse scleroderma the authors, from the Warsaw Medical School, present an analysis of 45 cases of diffuse scleroderma, 33 of which were of acroscleroderma type. Of these 33 cases, only five were in men, and one of them was atypical. In all but three of the cases, there were simultaneous features of both so-called acrosclerosis and "diffuse" scleroderma, which made distinction between the two diseases impossible and led to the conclusion that acrosclerosis is a variety of diffuse scleroderma preceded or accompanied by Raynaud's phenomenon.

Sensory chronaxy is regarded as very important for prognosis, successive distinct and increasing prolongations being an indication of rapid development of the disease, whereas diminution is a favourable symptom. The pathogenesis of scleroderma is thought to be probably connected with damage to higher autonomic nervous centres, including those exerting vasomotor control. E. W. Prosser Thomas.


The results of prolonged administration of potassium para-aminobenzoate in the treatment of 72 patients with scleroderma are reported in this paper from the Temple University Medical Center, Philadelphia. The drug was given in capsules or in a solution to a total daily dosage of 12 g. in adults and 1 g. per 10 lb. (4-5 kg.) body weight in children. There was marked improvement in 24 out of sixty patients treated for more than 3 months. The skin gradually became soft and freely movable over the subcutaneous structures. At the same time, the patient gained weight and began to experience a sense of well-being. In 34 patients the improvement was moderate, and in two "none to slight".

The author states that potassium para-aminobenzoate is less likely to give rise to anorexia or nausea than the crystalline acid or the sodium salt. Treatment is interrupted if anorexia or nausea supervenes, because hyperglycaemia may develop when the drug is taken during a period of inadequate food intake. The mode of action of para-aminobenzoate in scleroderma is not known, but it is suggested that the drug increases the amount of tissue oxygen. The activity of mono-amino oxidase is enhanced thereby and regression of fibrosis ensues.

In addition to administration of para-aminobenzoate, various forms of physiotherapy were found to be of value. For example, dynamic traction splints helped to minimize contractures of the fingers and deep-breathing exercises promoted expansion of the chest in cases of relative rigidity of the thoracic cage. Finally, "urecholine" was effective in patients complaining of dysphagia, a 5- or 10-mg. tablet being crushed and swallowed 30 minutes before meals. A. Garland.


Among seventeen cases of polymyositis and dermatomyositis seen in a 2½-year period at the Wadsworth Hospital, Veterans Administration Center, Los Angeles, there were eight in which various rheumatic and arthritic symptoms occurred. Certain features were found helpful in differentiating these eight cases from rheumatoid arthritis. Muscle weakness was prominent, particularly around the pelvic and shoulder girdles; the arthritis was
mild and did not produce either deformities or radiological changes; difficulty in swallowing was frequent; and the findings of increased serum transaminase activity and electromyographic changes were notable. However, the sheep cell agglutination test frequently gave positive results in these cases.

In most cases prolonged treatment with adrenal steroids produced significant relief from the rheumatic symptoms and improvement in muscular strength.

Oswald Savage.


General Pathology


At the University Medical Clinic, Freiburg, the results of the latex fixation test and the Rose-Waaler haemagglutination reaction were compared in 257 patients with a variety of rheumatic disorders, in fifty patients with non-rheumatic diseases, and in thirty healthy subjects. The results of the two tests were generally in agreement, discordant results being most often due to a false positive reaction to the haemagglutination test. Neutralization of the rheumatoid factor with γ globulin produced a similar fall of titre in both tests. In progressive rheumatoid arthritis (68 cases) the latex fixation test gave 84-3 per cent. and the haemagglutination test 83-7 per cent. positive results. On the other hand in chronic polyarthritis with a cyclic course both tests usually gave a negative result, and this condition is therefore thought to represent a separate disease entity from rheumatoid arthritis. In the other rheumatic and non-rheumatic diseases positive results were very rare, and the group of healthy subjects gave entirely negative results. The latex-fixation test is preferred by the authors to the haemagglutination reaction as it is a simpler procedure, is more easily reproducible, and gives rise to fewer doubtful results.

G. W. Csonka.

Latex-Fixation Test and the Agglutination Reaction with Sensitized Sheep Erythrocytes in the Demonstration of Characteristic Serum Changes in Rheumatoid Arthritis. (Der Latex-Test und die Agglutination mit sensibilisierten Schaf-Erythrozyten am Kältepräzipitat im Rahmen der für die primär-chronische Polyarthritis charakteristischen Serumveränderungen.) HARFER, F. (1959). Z. Rheumaforsch., 18, 150. 4 figs, 18 refs. Serum from 256 patients (77 with rheumatoid arthritis, 105 with other rheumatic disorders, and 74 with non-rheumatic diseases) was examined by the latex-fixation test, the Rose-Waaler haemagglutination reaction, streptococal L-agglutination and O-agglutination reactions, and the antistreptolysin reaction. The latex test has the merit of simplicity and gave positive results in 90 per cent. of cases of rheumatoid arthritis, which was a much higher proportion than was obtained with any of the other tests used. In the cases of other types of rheumatic disease and of non-rheumatic disease, the proportion of positive reactions was very low with all tests except the antistreptolysin reaction, which was positive in four (25 per cent.) of sixteen cases of atypical...
chronic polyarthritis, in 22 (46 per cent.) of 48 cases of non-articular rheumatism, and in thirteen (17 per cent.) of the 74 cases of non-rheumatic disease, compared with sixteen (21 per cent.) of the 77 cases of rheumatoid arthritis.

G. W. Csonka.


In a combined study carried out at five centres in and near Chicago, an attempt was made to demonstrate clear-cut serological differences between rheumatoid arthritis (35 cases) and systemic lupus erythematosus (28 cases), and further to evaluate a group of seventeen cases of rheumatoid arthritis in which L.E. cells were present in the peripheral blood. Two variations of the sensitized sheep-cell agglutination test were used. In the euglobulin method of Ziff the euglobulin fraction of the serum protein is separated by dialysis against an acid buffer at 4° C.; an initial dilution of 1 : 14 is tested and a titre of 1 : 28 is considered positive. In the cold precipitation method of Svertz the globulin is precipitated from the serum by adding fourteen volumes of cold distilled water and allowing it to stand for 48 hours at 4° C.; the initial dilution is 1 : 4 and a titre of 1 : 16 is considered positive.

The euglobulin test was highly sensitive for rheumatoid arthritis (71 per cent. positive), but the result was also positive in 54 per cent. of cases of systemic lupus erythematosus. The cold precipitation test, though less specific for rheumatoid arthritis, gave a positive result in only four cases (14 per cent.) of lupus erythematosus. In the patients with rheumatoid arthritis and L.E. cells both tests gave a higher proportion of positive results, and in higher titre, than in the group with rheumatoid arthritis and a negative L.E.-cell reaction. The authors suggest that both tests be performed when diagnostic problems involving these diseases arise.

Oswald Savage.


Biopsy specimens of synovial membrane from joints of rabbits, cats, and man were examined histochemically and by light and electron microscopy at the Anatomy School of the University of Cambridge. While some parts of the synovium showed an absence of lining cells, in other situations these were several layers thick. The cytoplasm of the synovial cells, as well as the intercellular material, was deeply stained by the periodic-acid-Schiff method, and this reaction was not abolished by previous exposure to hyaluronidase. [Such abolition was not to be expected.] A metachromatic reaction was shown only by granules in a few deeply situated cells, assumed to be mast cells. Under the electron microscope the cells of the synovial surface were shown to contain dense, granular bodies 0·05 to 0·16 μ in diameter. Some of these cells had a degenerate appearance.

The authors consider that it is these surface cells and the cells immediately subjacent rather than the cells of the deeper layers or the mast cells which produce synovial mucin. The positive periodic-acid-Schiff reaction is presumed to be due to the hyaluronic acid of the joint fluid. [The suggestion of Asboe-Hansen (Ann. rheum. Dis., 1950, 9, 149) that hyaluronic acid is derived from mast-cell heparin is in any case most unlikely owing to the great chemical differences between these two acid polysaccharides.]

G. Loewi.


The polysaccharide hyaluronate is the main cause of the viscosity of synovial fluid. This substance, a polymer of N-acetyl glucosamine and glucuronic acid, can be measured indirectly by determining the hexosamine content of synovial fluid or mucin clot. However, hexosamines also exist in combination with other synovial fluid proteins. The authors, working at the Albert Einstein College of Medicine, New York, have analysed nineteen specimens of synovial fluid from thirteen patients with rheumatoid arthritis and ten specimens from normal knees (eight of these being obtained post mortem), and determined the hyaluronate content by two independent methods:

1. Precipitation of hyaluronate as a mucin clot by acetic acid, followed by determination of the hexosamine in the clot;
2. By measuring the fall in hexosamine level in the fluid following hyaluronidase digestion and dialysis in vitro.

Control experiments showed that the hexosamine in the mucin clot was derived solely from hyaluronate and that only hyaluronate hexosamine was rendered dialyzable by hyaluronidase.

The results of the two methods agreed. The hyaluronate hexosamine content of rheumatoid synovial fluid of greater than normal volume (measured by weight) averaged 0·4 mg. per g. and constituted 30 per cent. of the total fluid hexosamine content. In normal synovial fluids these values were 1·4 mg. per g. and 85 per cent. respectively. Rheumatoid and normal synovial fluids diluted to equal concentrations of hyaluronate hexosamine were shown to have similar viscosities (by the Ostwald method). It is suggested that dilution of hyaluronate, rather than depolymerization, seems to be the main cause of the low viscosity of synovial fluid in rheumatoid arthritis.

Allan St. J. Dixon.


A number of non-specific, "acute phase" serological tests indicative of inflammatory disease have in recent years been compared with the erythrocyte sedimentation rate (E.S.R.) and some of them recommended for clinical use. In this communication from the Prince of Wales and Edgware General Hospitals, London, the authors report the results of a clinical evaluation of some of
these tests, which they consider would be sufficiently simple for routine clinical use in separating significant from insignificant rheumatic disease. These included estimation of serum levels of C-reactive protein, total protein-bound polysaccharides, mucoprotein polysaccharides, total protein, and the serum protein: polysaccharide ratio, the results being compared with the E.S.R. as determined by the Westergren method. In all, a total of 455 tests were performed on 330 patients.

In 30 per cent. of 91 cases of active rheumatoid arthritis the E.S.R. was normal, whereas in only 3-5 per cent. of cases these were the results of the new tests within normal limits. In one group of 73 cases in which the diagnosis was at first uncertain, but later became clear, 35 proved to be cases of rheumatoid arthritis; in this group the newer tests were found to be less reliable than the E.S.R.

The authors conclude as follows:

1. In established rheumatoid arthritis and ankylosing spondylitis—conditions in which laboratory tests are not much needed—the newer tests give fewer false negative results than the E.S.R.;
2. As a measure of disease activity in cases not receiving drug treatment they are as accurate as the E.S.R.;
3. As a help in solving diagnostic problems in rheumatic disease they are disappointingly unreliable.

The Winzler mucoprotein test was slightly more reliable than the others. As these tests are time-consuming they cannot justifiably be recommended.

Kenneth Stone.


From the Medical Clinic of the University of Freiburg the author reports the evaluation of a quick and simple method of demonstrating the presence of rheumatoid factor in serum. The test is called the capillary precipitation test (C.P.T.). The antigen employed is a commercial solution of human γ globulin (16 per cent.) diluted with borate-saline buffer and heated at 63° C. for 30 minutes, a procedure which is believed to result in molecular aggregation. The patient's serum is not inactivated. Serum and γ-globulin solution are drawn up successively into a glass tube 8 cm. long and of about 5 mm. bore, care being taken to avoid the inclusion of an air-bubble between them. After 2 hours' incubation at 37° C. the tubes are refrigerated overnight and examined for precipitate at the point of contact of the two fluids. This test was carried out in parallel with the Rose-Waaler haemagglutination test, the latex fixation test of Singer and Plotz, and the author's "boundary layer reaction" (Z. Rheumaforsch., 1958, 17, 206). This last test is similar to the C.P.T., but is stated to be capable of providing a quantitative result; it employs heated γ globulin at 0-5 per cent. concentration and the patient's serum is diluted 1 : 6. Sera from 224 patients with various rheumatic disorders, 40 patients with non-rheumatic inflammatory disease, and 20 healthy subjects were examined.

In rather more than 75 per cent. of cases the result of the C.P.T. agreed with those of the other tests. In 16 per cent. of cases the result of the C.P.T. was negative when of the other tests were positive—this usually occurred with the serum of patients who were probably not suffering from rheumatoid arthritis. The C.P.T. tended to give negative results in cases in which the titre of rheumatoid factor in the haemagglutination and latex fixation tests was low. Some correlation between the amount of precipitate formed and the titre of the latex fixation test was obtained when the γ-globulin concentration employed was 2-5 per cent.; with strengths of 5 per cent. or more, however, false positive results were obtained.

It is concluded that this test cannot at present replace the more elaborate reactions usually employed in testing for the rheumatoid factor.

G. Loewi.


In this study from the Stanford University School of Medicine, sera from healthy persons and from rheumatoid arthritics were separated into fractions by continuous flow electrophoresis on a paper curtain. Each fraction was used as the particle-coating substance in the latex-fixation test against a high titre rheumatoid serum. After the reactant had been discovered, a measurement of its concentration was made by determining the highest dilution which would give a definite reaction. Reactant was present in the gamma globulin fractions of all sera tested in fairly equal concentrations. The rheumatoid factor was a fast-moving gamma globulin. Fractions containing large amounts of rheumatoid factor, showed also a high concentration of reactant. Two inhibitors of the rheumatoid reaction were found in normal serum. The first inhibitor was present in the gamma globulin fractions and was probably reactant. The second inhibitor was more powerful than the first and was discovered in fractions containing alpha and beta globulins. It was absent from sera containing large amounts of rheumatoid factor. Further study of this second inhibitor may lead to improved methods for the diagnosis of rheumatoid arthritis if it can be shown to be present in diminished amounts in cases in which the rheumatoid factor itself cannot be demonstrated.

G. W. Csonka.


In this study from the Södersjukhuset, Stockholm, concentration of synovial fluid protein, acid glycoproteins, and sialic acid were estimated in 22 cases of rheumatoid arthritis and in seventeen cases of osteo-arthritis. The electrophoretic protein patterns in serum
and synovial fluid were in close agreement in cases of rheumatoid arthritis, and this relationship was also found in osteo-arthritis, although the total protein content of synovial fluid was found to be much lower than that of serum. This may indicate that the type of permeability change in the synovial tissue is similar in both diseases. The sialic acid content of synovial fluid was closely related to the total protein content. Determinations of sialic acid did not help in the differentiation between fluids from cases of osteo-arthritis and rheumatoid arthritis. Acid glycoproteins are known to be increased in the serum of rheumatoid arthritics. In osteo-arthritis the values were much lower in both serum and synovial fluid, and it is thought that this fact may be of value in differential diagnosis. The $\alpha_2$ fraction of the synovial fluid decreased in both groups 2 to 4 days after intra-articular hydrocortisone treatment. In rheumatoid arthritis, the $\alpha_2$ and the beta fraction also decreased.

G. W. Csonka.

Comparative Distribution of Proteins and Glycoproteins of Serum and Synovial Fluid. 


Arthr. and Rheum., 2, 162. 24 refs, 3 tables, 9 figs.

In this paper from the Mayo Clinic, the distribution of proteins and glycoproteins, determined by zone electrophoresis of the serum and synovial fluid in 71 patients with various rheumatic diseases and in ten patients without rheumatic disease, is compared. In cases of rheumatic disease there was a greater increase in globulins than in albumin, so that the distribution of proteins in synovial fluid approached the distribution of proteins in serum. Selective alteration in the $\alpha_2$ glycoprotein of synovial fluid compared with the $\alpha_2$ glycoprotein of serum was shown by the $\alpha_2$ glycoprotein gradient:

Percentage Concentration of $\alpha_2$ Glycoprotein in Serum

Percentage Concentration of $\alpha_2$ Glycoprotein in Synovial Fluid

The value for the $\alpha_2$ glycoprotein gradient was highest in patients without rheumatic disease and lowest in patients with synovitis and systemic rheumatic disease; the patients with synovitis not associated with systemic disease gave intermediate values. The reduction in the $\alpha_2$ glycoprotein gradient in disease is thought to result from increased permeability of the synovial membrane. The $\alpha_2$ glycoprotein gradient showed no change after the intra-articular injection of hydrocortisone acetate in three patients. G. W. Csonka.

Studies of Complement Fixation with Tissue Antigens in Rheumatic Subjects. (Untersuchung der Komplementbindung mit Gewebeantigenen bei Rheumakranken.)


Z. Rheumaforsch., 18, 144. Bibl.

Extracts of heart, tonsil, lymph node, and granulomatous tissue obtained at biopsy or necropsy from persons with rheumatic disorders were prepared and exposed to ultrasonic radiation to reduce their anti-complementary effect and thus increase their activity as antigens. With these antigens a total of 599 complement-fixation tests (Wassermann technique) were performed on sera from patients with rheumatic diseases, from patients with non-rheumatic diseases, and from healthy subjects. The mean proportion of positive reactions with the four antigens was highest in the rheumatic group (45 per cent.) and lowest in the control group (14.7 per cent.).

Because of its lack of specificity this test is considered to be of little value for diagnostic purposes in rheumatology. It may, however, be useful in investigating problems of organ specificity. G. W. Csonka.

Effect of Histamine on the Polysaccharide System of Blood Serum. 


Acta rheum. scand., 5, 108. 26 refs.

Rheumatic Pneumonitis: Pathologic Features. 


J. pediat., 54, 60. 8 figs, 15 refs.

Rheumatic Pneumonia. A Clinical, Radiologic, and Pathologic Study of Seven Cases. (La pneumopathie rheumatismale. Étude clinique, radiologique, anatomo-pathologique à propos de sept cas personnels.) 


Acta clin. belg., 14, 20 figs, 40 refs.

Macroglobulins and Connective Tissue Disease. 


Arthr. and Rheum., 2, 266. 9 refs.

Rate of Hyaluronic Acid Production by Human Synovial Cells studied in Tissue Culture. 


Arthr. and Rheum., 2, 259. 2 figs, 12 refs.

Paper Electrophoresis of Serum Proteins in the Prognosis and Control of Treatment of Rheumatic Fever. (Znaczenie elektroforezy białkowej bialek surowicy w rokowaniu i kontroli leczenia choroby Bouillaudii.) 


Electrophoretic Studies of Synovial Fluid and Serum in Patients with Rheumatoid Arthritis treated with Hydrocortisone. (Badania elektroforetyczne płynów wychodzących z kłuków i surowicy chorych na gościc pierwotniowej) 


ABSTRACTS


ACTH, Cortisone, and Other Steroids

Inhibitory Effect of Triamcinolone on Adrenal Function.  

Inhibition of the secretion of hydrocortisone, which is normally caused by injection of certain steroid hormones, has proved a useful means of demonstrating an intact pituitary-adrenal axis, and in some cases helps to distinguish between adrenocortical neoplasia and hyperplasia. A disadvantage of the technique is that many of the steroids, when given in suppressive doses, contribute significantly to the metabolites, the levels of which in the urine and plasma are used as an index of adrenocortical activity.

In this paper from the Postgraduate Medical School of London a study is reported of the ability of triamcinolone to depress the secretion of hydrocortisone by the adrenocortex in a healthy male aged 31 years, and a girl aged 16 years, with cirrhosis of the liver without ascites. The urinary excretion of corticosteroids and the plasma hydrocortisone level were estimated for a control period of 2 days. The subjects were then given 8 mg. triamcinolone four times a day for 5 and 11 days respectively, and the urinary excretion of steroids and the plasma hydrocortisone level again determined at intervals. Triamcinolone caused marked depression of hydrocortisone secretion and did not produce a significant amount of plasma or urinary chromogen. ACTH (corticotrophin) gel given while the subjects were still receiving triamcinolone immediately restored hydrocortisone secretion, indicating that the drug did not act directly on the adrenal cortex. Toxic effects of the steroid necessitated cessation of the trial in one additional subject.

P. A. Nasmyth.


This paper from the Hôpital Laennec and the Institut National d’Hygïène, Paris, describes a study of adrenocortical function in 53 women with obesity, none of whom was manifestly suffering from Cushings’s disease. In most cases the excretion of 17-ketosteroids, like that of 17-hydroxycorticosteroids, was abnormally low or at the lower limit of normal, though low readings for 17-hydroxycorticosteroids occurred more commonly than low readings for 17-ketosteroids. This partial adrenal insufficiency was considered to be purely functional, due to confinement to bed and restrictions of hospital life.

The excretion of aldosterone was studied in five cases while the subjects were given successively a normal sodium intake, a moderately low-sodium diet, and a high-sodium diet. In two cases the subjects were then given a very low sodium intake (200 mg. daily) and in one a high sodium intake (6 g. daily). The amount of aldosterone excreted and its variation with the amount of sodium in the diet were within normal limits. It is concluded that the amount of extracellular fluid in the obese is normal and that the excess fluid and sodium in such cases are held in the interstitial spaces. In the obese subject given a high sodium intake the excess was not eliminated so that there was a marked rise in weight, although in other respects the diet remained restricted. In this sense obesity is comparable to oedema with salt retention. In two cases the excretion of aldosterone was studied at different points in the menstrual cycle. There was frank hyperaldosteronism during the second half of the cycle, comparable with the hyperaldosteronism that has been observed in obese women during periods of gain in weight.

A. G. Mullins.


The authors have studied the morphological and histochemical changes in the cells of the adrenal cortex in four cases of Cushing’s disease. Three of the specimens were taken from glands totally or partially resected and operation and one from a patient who died of pneumonia in a late stage of the disease.

The hyper trophy and hyperplasia of the adrenal cortex found in this disease are due to the excessive production of corticotrophin by the pituitary gland as a result of the poor output of hydrocortisone. The effect of this is to produce an intensive synthesis and secretion of androgens such as 4-androstenedione, androstenedione, and 11 hydroxyandrostenedione. Two stages of hypertrophy were observed:

1. Accumulation of lipids in the cells (initially in the zona glomerulosa) and increased secretion of corticosteroids, particularly of glucocorticoids;
2. Reduction of lipids and perverted biosynthesis of steroid hormones, with increase in the neutral 17-ketosteroids and decrease in oestrogens.

The two stages are characterized by corresponding histochemical changes.

The authors advocate large doses of cortisone or hydrocortisone in the treatment of the disease to suppress the reaction of the pituitary and the consequent excessive production of virilizing and neutral steroids. They consider that resection of the adrenal glands is justifiable only in the first stage of cortical hypertrophy.

The article is illustrated by five photomicrographs reproduced in colour.

L. Firman-Edwards.


From the University of Geneva the authors report the clinical and metabolic effects of dexamethasone (9α-fluoro-16α-methyl prednisolone), a recently introduced corticosteroid. It was found that dexamethasone was six to eight times more active than prednisolone and did not give rise to sodium or water retention. One case of heart failure is described in which a water diuresis was obtained with dexamethasone. Care, however, must be taken in its use for diabetics, since impaired carbohydrate tolerance results.

Dexamethasone is considered by the authors to be the most effective suppressor of ACTH (corticotrophin) by
its action on the anterior pituitary. They found that a single oral dose of 1-0 mg. could reduce the plasma 17-hydroxycorticoid level to zero within 8 hours. No serious side-effects were noted, except in one patient, a young man aged 21, who developed severe melaena due to ulceration of the colon while receiving a dosage of 10 mg. dexamethasone daily. Caution is therefore urged in the use of this steroid. I. M. Lewis Baird.

**ABSTRACTS**

**Dexamethasone in the Treatment of 100 Patients. Comparison with Prednisone and 6-Methylprednisolone.**


The authors describe the various attempts that have been made to modify the corticoids, especially prednisolone, so as to remove their anti-inflammatory action. These have included halogenation (substituting fluor in the C₆ position), deshydrogenation (between C₁ and C₂), methylation (in various positions, with resulting different effect on sodium retention and anti-inflammatory action), and hydroxylation—the addition of an OH group in C₁₆ causes reduction or disappearance of sodium retention.

At the Hôpital Saint-Anne, Paris, one of these compounds, 6α-methyl-prednisolone (6-MP), was tried on 61 patients with rheumatoid arthritis or other arthroses; it seemed to produce improvement similar to that obtained with prednisone, but not always in the same patients, nor were the side-effects of 6-MP always of the same order as those caused by prednisone. The second compound tried was 16α-methyl-9α-fluoroprednisolone (dexamethasone) and this was given to 100 patients, of whom 52 had osteo-articular affections, 29 had allergic conditions, eleven had endocrine disorders (five had Addison's disease, four hypopituitary, and two the adenogenital syndrome), and eight had varied disorders, including colitis, hypoglycaemia, cirrhosis, and pleural carcinomatosis. Most of the patients were adults aged over 45 and the daily dosage of dexamethasone varied from 0-2 to 4 mg.

For the patients with osteo-articular disease, treatment was continued for up to 9 months, the average dose of dexamethasone being between 1 mg. and 3 mg. daily. It was shown that the ratio of effective action of prednisolone to dexamethasone and of 6-6 to dexamethasone was between 5 and 7 (that is, dexamethasone proved to be five to seven times more effective). In the patients with respiratory and skin allergy, doses not exceeding 1-5 mg. daily controlled the condition effectively. In the five cases of adrenal insufficiency, dexamethasone was found to be ten times more active than prednisone, and in the two cases of the adenogenital syndrome over forty times more active.


Among the 100 patients treated with dexamethasone described above (see previous Abstract) the undesirable side-effects observed were studied in the following groups:

1. Tissue effects, including rounding of the face, slight Cushing appearance, hirsutism, acne, increase in weight, purple striae, and skin infection.
2. Psychological effects, such as euphoria, irritability, insomnia, hypomania, headaches, paraesthesias, and giddiness.
3. Visceral conditions, including effects on the heart (dyspnoea, precordial pain, palpitations, hypertension), effects on the blood vessels (purpura), effects on the digestive tract (increased appetite, sensation of taste, excessive thirst, nausea, postprandial pain, meteorism, or gastric haemorrhage), and decalcification of bone.
4. Metabolic effects, particularly those on the sodium, potassium, water, calcium, and phosphorus levels.
5. Effects on the metabolism of proteins and carbohydrates, including the production of hyperglycaemia, particularly in diabetic patients.
6. Glandular effects—of which, however, none was observed.

The authors' general conclusions are that the side-effects of dexamethasone and 6-methyl-prednisolone are not only rarer and much less marked than, but also qualitatively different from, the comparable side-effects of prednisolone, prednisone, and other corticoids. Effects on the heart appear to be completely absent, and digestive disturbances were also rarer, although no final conclusion could be reached as regards gastric haemorrhage, since the number of patients was small. The metabolic effects were similar to those of prednisone. The powerful anti-ACTH action of the drug did not seem to cause adrenal insufficiency. They therefore conclude that these two new corticoids, and especially dexamethasone, are far superior in their action to prednisone, prednisolone, and other earlier forms, and also have a considerably wider margin of safety. V. C. Medvei.

**Combined Treatment with Antibiotics and Corticosteroids.**


A study of the literature concerning the use of corticosteroids in acute infections reveals a conflict of opinion, some authors holding that they diminish the resistance of the infected organism and reduce the antimicrobial activity of antibiotics, while others assert that there is a synergic effect, the hormones reducing reactivity and inflammatory processes while the antibiotics suppress the infection.

The present authors conclude from their own experience that for the treatment of certain infective processes, particularly those in which allergic phenomena predominate (such as tuberculous pleurisy), and of protracted severe sepsis (such as osteomyelitis), the combination of steroids and antibiotics is superior to the use of antibiotics alone. Indeed, several cases are cited in which complete control was not attained until antibiotic treatment was supplemented with cortisone or corticotrophin (ACTH). Two illustrative cases of infective
endocarditis, two of osteomyelitis, and one of cholangitis with general sepsis are described in full.

L. Firman-Edwards.


Other General Subjects

At the Cleveland Clinic Foundation, Ohio, the local response to injection of serotonin in 23 patients with rheumatoid arthritis was compared with that in sixteen healthy controls. In the patients only uninvolved joints were injected. The dosages of serotonin were 0.01 mg. intra-articularly into the proximal interphalangeal joints of the fingers, 0.05 or 0.1 mg. periarticularly near a proximal finger joint, and 0.1 mg. intradermally on the back of the hand. Diffuse painful oedema and erythema with cyanosis, sometimes spreading over the back of the hand and the wrist and lasting 1 to 2 hours or more, developed in twenty of the patients but in only one of the controls. Antagonists to serotonin given intravenously abolished the cyanosis in 10 minutes. Similar results were obtained in fifteen patients with systemic lupus erythematosus or scleroderma. It is concluded that patients with rheumatoid arthritis and related disorders are less able to inhibit serotonin than are healthy subjects.

J. A. Cosh.


