ABSTRACTS

This section of the ANNALS is published in cooperation 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


The author reports the results in 78 patients suffering from rheumatic fever who were followed up after tonsillectomy for 1 to 2 years. Protracted relapsing rheumatic carditis was diagnosed in 37 (47 per cent.), while the disease was inactive in 41 (53 per cent.); a proportion of the latter group showed evidence of valvular lesions and circulatory failure of Grades I and II. After tonsillectomy 58 per cent. of the patients improved, 29 per cent. failed to do so, and 13 per cent. deteriorated.

Tonsillectomy appears therefore as only one of the measures to be employed in the treatment of acute rheumatism and the author suggests the following course of treatment, which should last 1½ to 2 months:

1. Two 10-day courses of penicillin or tetracycline separated by a 5 days' interval.
2. A search for and elimination of septic foci.
3. Administration of ascorbic acid (0·1 to 0·2 g.) vitamins B, and B1 (0·001 g. of each), and 0·1 g. of vitamin P, all these doses being given three times a day for 3 or 4 weeks.
4. Either "pyramidon", 0·24 g. six to nine times a day for 3 or 4 weeks (with frequent blood examinations), or 0·5 g. of aspirin six to eight times a day for 2 to 3 weeks, gradually reducing the dose, or 0·15 g. phenylbutazone three times a day to a total dose of 18 g.
5. 20 to 40 units ACTH (corticotrophin) daily up to 1,000 units, or cortisone, 0·025 g. four times daily for 4 weeks.
6. In the absence of circulatory failure, small blood transfusions of 75 to 125 ml. every 5 days.
7. Administration of bromides and caffeine to maintain the tonus of the nervous system.

If there is circulatory failure treatment should include cardiac supportive therapy, such as tincture of strophanthus, Bekhterev's mixture, or digitalis, and a low-carbohydrate diet, limited salt and fluid intake, and ample calcium. Finally physiotherapy and remedial exercises are given as indicated.

Uniform improvement was achieved in 252 patients thus treated, of whom 87 per cent. had valvular disease. The erythrocyte sedimentation rate returned to normal in 55 per cent. and was reduced to 10 to 20 mm. in one hour in a further 28 per cent. Since the introduction of the above method of treatment the mean mortality has fallen from 14 per cent. (the rate in 1953-54) to 3·1 per cent., and the incidence of subacute bacterial endocarditis has been reduced practically to nil. S. W. Waydenfeld.


Rheumatic fever may occasionally be complicated by various types of cerebrovascular accident, such as thrombosis, non-thrombotic softening, subarachnoid haemorrhage, cerebral haemorrhage, and less often cerebral embolism. Since any of the cerebral arteries may be affected the clinical picture is highly variable. In the absence of evidence of hypertensive disease or of syphilis an erroneous diagnosis may easily be made. The author states that cerebrovascular complications occur more often and are more severe in rheumatic fever than in other collagen diseases, probably owing to its protracted course and associated cardiac lesions. The condition must be differentiated from infections of the central nervous system, aneurysm, or influenza haemorrhagic encephalitis. S. W. Waydenfeld.


Chronic Articular Rheumatism

(Rheumatoid Arthritis)


A study of the relationship between spontaneous erythropoietic activity and disease is reported from Södersjukhuset, Stockholm. Samples of bone-marrow tissue from 54 patients, of whom 23 had rheumatoid arthritis and the remainder various other diseases, were cultured. The cellular layer was obtained by centrifugation and diluted to a count of 30,000 to 50,000 cells per c.mm. This material was divided into six separate samples: two with added serum from the same patients, two with 1 per cent. of a splenic extract stated to have an erythropoietic effect (Goldberg and others, *Acta physiol. scand.*, 1950, 22, Suppl. 77), and another two with added amino-acid solution similar in composition to the splenic extract. After 4 to 5 hours of culture a cell count was made to determine an increase or otherwise in the number of cells.

No difference in activity was found between the bone-marrow cultures from patients with rheumatoid arthritis and those from patients with other disorders. When, however, splenic extract was added, a significant enhancement of activity occurred in the cultures from cases of rheumatoid arthritis, but not in those from the controls. With the amino-acid solution there was a similar increase in erythropoiesis in cultures from the arthritic group, but results in the other cases were inconclusive.

[Unfortunately, no normal controls appear to have been included in this series.]

G. Loewi.


Popliteal cysts communicating with the knee-joint are common in patients with rheumatoid arthritis. Such cysts, which were extensive, reaching well down the calf and lying either between muscles or between muscle and tibia, were seen in four patients admitted to the Hospital for Special Surgery, New York, all of whom had had rheumatoid arthritis for some years and had been treated with steroids. Considerable hydrarthrosis was present originally; this was followed later by tender swelling of the calf suggesting thrombophlebitis. The cystic nature of the calf swellings was not always apparent clinically, but arthograms clearly showed their extent and their communication with the knee-joint. In three cases the cysts were excised, with recurrence in two and involvement of the other leg later in one. The cyst walls were fibrous without specific cellular lining; in places a palisade-like arrangement of fibroblasts and collections of lymphocytes and plasma cells were seen. It was uncertain whether the cysts developed by herniation of the synovial cavity of the knee between semimembranosus and gastrocnemius muscles, or by the breaking down of a dividing wall between the joint cavity and a preformed cyst. It is suggested that steroid therapy may have played a part in causing weakness and stretching of the fibrous wall of the synovial cavity and of the cyst.

J. A. Cosh.


The results of long-term administration of phenylbutazone in 315 patients with rheumatoid arthritis and the findings at the end of 4 years are described in this paper from the London Hospital. In the majority of patients the dosage ranged from 100 to 400 mg. daily, but of twelve who had up to 1,200 mg. daily for short
periods, two developed intolerance to the drug. In some cases treatment brought about a remission and in others it was ineffective. At the end of 3 months the drug was discontinued in 37 per cent. of the patients, after 2 years in 80 per cent., and after 3 years in 88 per cent. Intolerance was the commonest reason for discontinuing the drug, particularly in the early stages of treatment. Symptoms of intolerance were observed in 15-9 per cent. of the patients during the first 3 months and in only 27-7 per cent. at the end of 3 years; after 3 years no further cases of intolerance were encountered. Gastrointestinal symptoms and rash were the commonest toxic manifestations, but stomatitis, oedema and blood dyscrasias were also observed. At the end of 3 months, 198 of the patients were taking phenylbutazone, seven of them being in remission; at the end of 2 years, the figures were 62 and two respectively, and at the end of 3 years, 45 and 10 respectively. The number of patients in whom the drug was ineffective and therefore withdrawn was ninety in the first 3 years and in three in the fourth year; only 38 patients continued to take the drug after 4 years. The incidence of remission was highest between the 6th and 24th months of treatment, but some remissions were observed up to 3 years. The authors consider that the longer the patient takes phenylbutazone the less likely is the development of intolerance. They regard this as an indication for continuing treatment for a long time in the hope of achieving a remission and avoiding steroid therapy with its very toxic effects. William Hughes.


This is an account of nineteen cases of acute septic arthritis in aged or chronically ill patients seen during a 5-year period at the King County and Seattle Veterans Administration Hospital, Washington. In fifteen cases the diagnosis was based on the culture of organisms from the synovial fluid, in one case organisms were identified in a smear of the joint fluid, and in three cases the presentation and clinical course were characteristic. The patients’ ages ranged from 45 to 77 years. In sixteen cases the arthritis was monarticular and in three polyarticular. The knee-joint was most commonly involved, then the shoulder, interphalangeal joints, ankle, and elbow, in that order. In nine cases the infecting organism was Staphylococcus aureus, which in some cases was resistant to the usual antibiotics, and in at least three of these there was reason to believe the infection had been acquired in hospital. The next commonest organism was the pneumococcus. In twelve cases the infection appeared to be blood-borne from infection elsewhere (pneumonia, empyema, superficial infection, osteomyelitis). In six cases the infection entered the joint by penetrating trauma, which in three cases was intra-articular therapy. Four patients had chronic rheumatoid arthritis and eight were chronic alcoholics.

In eleven cases conservative therapy with antibiotics was used and the results appeared to be as good as in cases treated by open drainage in addition to antibiotics. If adequate antibiotic therapy was instituted promptly the results were good. The diagnosis was difficult in some cases owing to failure to realize that an increase in joint symptoms was not due to an exacerbation of pre-existing arthritis or disease. The importance of paracentesis of the joint whenever there is doubt is stressed. The “leukocrits” of joint fluid from successive paracenteses were valuable for following progress. Vancomycin proved helpful in some of the cases due to resistant staphylococci. C. Bruce Perry.


Results of Treatment with Antimalarials in Rheumatoid Arthritis. (Resultados obtenidos pelo uso de antimaláricos na artrite reumatóide.) GAMARSKI, J. (1960). Rev. bras. Med., 17, 599. 11 refs.


(Aoste-Oarthritis)


*(Ankylosing Spondylitis)*


*(Miscellaneous)*


This account of "Hippocratic fingers" (H.F.) and hypertrophic osteoarthropathy (H.O.A.) is based on 350 cases studied at the Hôpital Hôtel-Dieu, Paris. Over 80 per cent. of the patients were males. The changes seen in H.F. are regarded as the first stage in the development of H.O.A., which in its complete form also shows hypertrophy of the trophi of the portions of the upper and lower limbs, pains in the joints, bilateral proliferative periostitis, and peripheral neuro-vascular disorders (cyanosis, excessive sweating, and paraesthesia). These two conditions and other related syndromes have been grouped under the general term "dysacromelas".

In this series infective respiratory disease was present in more than 50 per cent. of patients with H.F., but H.O.A. occurred more commonly in association with lung cancer, 80 per cent. of the patients with H.O.A. being diagnosed as suffering from cancer of the lung and 10 per cent. as suffering from a malignant tumour of the pleura. In the study of this condition laboratory investigations were not found to be of particular value, although urinary steroid excretion was often low in those patients who had developed gynaecomastia, which occurred much more often in those with H.O.A. than in those with H.F.

The author concludes that simple clubbing of the distal phalanx is likely to be due to a chronic infection or fibrotic disease of the chest and that the complete changes of H.O.A. are more often brought about by a tumour of the lung. Gynaecomastia combined with H.O.A. is highly suggestive of intrathoracic malignant disease. He accepts the view that the local abnormalities are due to functional changes in the precapillary circulation of the extremities and that the visceral changes are due to vascular shunts in the pulmonary circulation or the physiological equivalent thereof. The pathogenesis of the connexion between the thoracic starting-point and the distal receiving-point is unknown, although it is postulated that there seems to be a predisposing factor in certain individuals.

A. Gordon Beckett.


At the Department of Rheumatology, Karolinska Sjukhuset, Stockholm, specimens from the throat of 700 patients, who were examined during a period of 2 years (1957-59), were cultured. The antistreptolysin-O titre (A.S.O.) was estimated in the serum of every patient. Of the 43 strains recovered, 39 could be grouped serologically according to Lancefield's system. Almost half of the strains were isolated during an epidemic of Asian influenza (November, 1957, to March, 1958). The proportion of Group-G strains was unduly high (about 50 per cent., while that of Group-A strains was low (about 25 per cent.). A rise in A.S.O. may be caused by infection with C and G strains, but not by B strains, the pathogenicity of which appears to be very low. Immunological response is known to increase in rapidity and strength from birth to 10 to 20 years, but elevation of the A.S.O. titre does not run parallel with the clinical course of rheumatic fever, a rise often persisting after subsidence of clinical symptoms.

After listing the criteria by which post-infectious rheumatism is diagnosed, the author points out that the proportion of Group-G strains was so high (about 65 per cent.) and that of Group-A strains so low (about 18 per cent.) that it is unlikely that the latter can be mainly responsible for that condition; in rheumatic fever, on the other hand, Group-A strains are undoubtedly incriminated.

D. Preiskel.

The authors of this paper from the University of Pittsburgh School of Medicine, Pennsylvania, report their findings on examination of 142 specimens from 136 patients of synovial tissue obtained from knee-joints affected by rheumatic disease by means of the instrument for punch biopsy described by Polley and Bickel (*Ann. rheum. Dis.*, 1951, 10, 277; *Abstr. Wild Med.*, 1952, 11, 70). Specimens were taken from three different sites from the suprapatellar bursa distended either with synovial fluid or by the introduction of 40 to 60 ml. 0.85 per cent. sodium chloride solution. The histological appearances were compared with those of 75 specimens taken at necropsy from open knee-joints clinically free from disease. Correlation of “sclerotic atrophy” with advancing age was obtained. The punch biopsy specimens were grouped according to histological appearances into:

1. No disease;
2. Non-specific synovitis;
3. Questionable rheumatoid arthritis (focal accumulations of lymphocytes, small numbers of plasma cells, minimal oedema, fibrosis, and vascular proliferation, and occasional deposits of fibrin or fibrinoid);
4. Rheumatoid arthritis (more pronounced inflammatory focal reaction, prominent number of plasma cells, and, in some cases, pronounced vascular proliferation); and
5. Other “specific” synovitis (gout, scleroderma, and neuropathic joint disease).

Of 26 patients with rheumatoid disease and active involvement of the knee, the changes in 24 were considered to be “at least in the category of questionable rheumatoid arthritis” and in seventeen “were sufficient to place the patients in the category of rheumatoid arthritis”. None of the patients with clinically inactive disease gave evidence of active synovitis. Relative acuteness of the inflammatory process was related to the presence of large amounts of fibrin or fibrinoid and numbers of neutrophil polymorphonuclear leucocytes. The authors state that these changes are not specific for rheumatoid arthritis, “being noted as well in cases of systemic lupus erythematosus and psoriatic arthritis. Marked hyaline thickening, atrophy and vascular sclerosis of the synovium were observed in a number of patients with progressive systemic sclerosis (diffuse scleroderma), and are changes which appear to be pathognomonic of this disease. While urate deposits were detected in the synovium of a number of patients with long-standing gout, the lack of these in many patients with well documented disease (including several with acute gouty arthritis and gouty arthritis. Punch biopsy of the synovium has proved to be a simple, safe and practical procedure which may supply information of considerable value in the study and diagnosis of joint disease”.

There was only one complication of the procedure; a man with myeloma and a bleeding tendency had pain and swelling of the knee which subsided following aspiration of bloody synovial fluid from the distended joint.

*Harry Coke.*


The authors discuss the relationship between these diseases on the basis of published papers. Keratosis blennorrhagica may follow either Reiter’s syndrome or a gonococcal infection, and they suggest the name be abandoned in favour of the term “Reiter’s syndrome” with modifying terms, e.g. Reiter’s syndrome with keratoderma. *W. E. S. Bain.*


The hind foot-pads of rats were injected with a single dose of heat-killed tubercle bacilli suspended in mineral oil. About 65 per cent. of animals developed severe arthritis and other lesions of the mucous membranes and skin, while 15 per cent. also developed iridocyclitis. Most animals had an acute non-granulomatous uveitis, but a few showed features of granulomatous uveitis with iris nodules and mutton-fat keratic precipitates. These manifestations were thought to be a delayed hypersensitivity reaction as no organisms could be cultured from the ocular tissues. The possible relationships between this symptom complex in the rat and Reiter’s disease, Behcet’s syndrome, and ankylosing spondylitis are discussed. *R. F. Fisher.*


ANNAI S OF THE RHEUMATIC DISEASES

Gout


Gout has been described as an occupational disease among workers engaged in the collection, drying, and preparation of dung at poultry farms, an industry which is now carried out on a large scale, the dung being used for the manufacture of uric acid. In spite of the wearing of protective clothing, considerable opportunities exist for the absorption of uric acid through the lungs, gastrointestinal tract, and possibly also the skin.

After doing this work for 2 or 3 years the workers developed pains in the joints, especially of the hands and feet, accompanied by crepitus, while firm tender tophi in the fingers and toes were observed in some cases. Signs of increased muscular excitation were present and Chvostek's sign was positive. Toothache and dental caries were frequently complained of. The urine contained a high concentration of urates and the blood uric acid level was raised in 43 out of 52 persons examined, the actual values being correlated with the duration of exposure to this type of work. On change of occupation manifestations of the disease disappeared. Basil Haigh.


tisimo, 12, 181. 13 figs, 57 refs.


Pararheumatic (Collagen) Diseases


In the first part of this paper from the University of Southern California School of Medicine, Los Angeles, the author presents an excellent summary of his personal clinical experience of 400 cases of systemic lupus erythematosus (S.L.E.) and of the principles he has applied in therapy. [But the majority of rheumatologists and others unfamiliar with the author's previous writings will hesitate to accept his opening sentence, which states: "Systemic lupus erythematosus . . . is a malignant variant of rheumatoid arthritis."] The second half of the paper records the results of the treatment with dexamethasone (9α-fluoro-16α-methylprednisolone) of fifty patients suffering from S.L.E. and compares the side-effects observed in this series with those in previous series treated respectively with methylprednisolone (40 cases), triamcinolone (29), and prednisone and prednisolone (37). [The method of sequential comparison adopted by the author is inaccurate to many authorities as a valid basis for comparison. Further, the period of treatment varied from one to 15 months and the steroid therapy was supplementary to other forms of treatment; thus 24 patients received salicylates to the point of mild toxicity and seventeen were taking antimalarial drugs. Again, 29 patients received dexamethasone as their initial steroid therapy, but 21 were transferred to this drug from treatment with other steroids. Also reference is made to one of the author's series in which 38-7 per cent. of the patients exhibited spontaneous improvement before steroid therapy was even begun. Lastly, no detailed analysis of the severity or of the duration of the disease before steroid treatment was started in these fifty cases is given.]

The dosage of dexamethasone varied from 1 to 6 mg. daily, usually in two divided doses, but in two critically ill patients a dosage of 24 mg. daily was employed for 2 to 3 weeks. The pattern of clinical improvement with dexamethasone paralleled that in previous series in which other steroids were used. However, a higher percentage of dexamethasone-treated patients (especially those initially treated with the drug) exhibited Cushingoid features, more insomnia, and a greater degree of pitting oedema—28 per cent. compared with a mean of 3.6 per cent. for the other steroid preparations. In a special study of the incidence of peptic ulcer, fourteen patients underwent base-line radiographic studies before the start of dexamethasone therapy and these, together with thirteen others, were examined radiographically at varying intervals thereafter. [It is difficult from the information provided to understand the rationale for selecting the patients or deciding the time intervals between the radiographs.] This study revealed six new peptic ulcers after periods of therapy ranging from 2 to 18 months, all of which were symptomatic. In all, eleven patients receiving dexamethasone had epigastric discomfort, five had a demonstrable ulcer, and one had a haematemesis, although three preceding radiographs had been normal. The author concludes that the incidence of peptic ulcer after dexamethasone therapy is no greater than after treatment with prednisone, methylprednisolone, or triamcinolone. There is a suggestion that the incidence of ulcer is greater when the patient is receiving a larger dosage of the steroid.

The final conclusion is that in the treatment of S.L.E
Steroid preparations previously tried, but that it produces an appreciably higher incidence of side-effects, particularly pitting edema and insomnia, and for this reason, it is not to be preferred to other steroids.

R. E. Tunbridge.


From the Mercy and County Hospitals, San Diego, California, the authors report four well-documented cases of systemic lupus erythematosus (S.L.E.) occurring in two sisters of Italian ancestry and in a mother and her married daughter of Mexican origin. The fifteen previously reported cases of S.L.E. showing a familial incidence are briefly reviewed. [The authors do not attempt to explain the relationship.] R. E. Tunbridge.


Diffuse scleroderma is a progressive disease of connective tissue which leads to prolonged disability and is often fatal. Any organ may be affected, the sequence of events being always the same—edema, followed first by connective-tissue proliferation and sclerosis of collagenous bundles, and finally by atrophy. In this report from the General Hospital, Washington, D.C., the author reviews 25 cases seen over the last 16 years and considers the radiological changes encountered in the light of accounts in the literature.

The heart is often enlarged and triangular with diminished pulsation, and at necropsy the cardiac muscles show irregular areas of fibrosis not related to disease of the coronary arteries; the heart was affected in eight of the present cases. In the lungs, affected in seven cases, there is diffuse interstitial infiltration with degenerative cystic lesions; these may expand into pneumatoceles and their rupture may cause a pneumothorax. The author considers this pulmonary fibrosis to be a primary manifestation of the disease. The alimentary tract was involved in fourteen cases, this being characterized by dilatation and decreased intestinal peristalsis, with delay in transit of barium. Such changes are most common in the oesophagus; they were also observed in the small intestine and colon, but no striking abnormalities were seen in the stomach. Bone abnormalities, present in six cases, frequently resulted in absorption of the terminal phalanges of the fingers and, less commonly, those of the feet. Similar changes were noted in the distal ends of the radius and ulna. Attempted remodelling during quiescent phases may produce a conical deformity of the affected bone ends. The presentation of the disease by joint symptoms may be attributed to involvement of synovial membranes. Skin contractures often result in subluxations and dislocations of the interphalangeal and metacarpal-phalangeal joints. Calcinosis of the soft tissues was also observed four times in the present series.

Marked thickening of the periodontal membrane, when this occurs provides a strong radiological indication of the disease

R. O. Murray.


The authors have summarized the various ophthalmological manifestations of the collagen diseases, emphasizing the importance of these signs in diagnosis and prognosis.

In periarteritis nodosa, small deep chorido-retinal foci are found, associated with micro-anerysms, haemorrhages, and cotton-wool exudates. Bilateral, symmetrical retinal detachments are sometimes seen, in some cases early in the disease. Occlusion of the central retinal artery and primary optic atrophy are rare complications. As a result of cardio-vascular or renal involvement, a typical retinopathy may complicate the picture.

Temporal arteritis is frequently the only manifestation of generalized arterial involvement. Pseudo-papillae- oedema is the most common manner in which it presents, other signs being retrobulbar neuritis and primary or secondary optic atrophy. Occlusion of the central artery of the retina is a less common presenting sign.

Lupus erythematosus may present with superficial or deep retinal haemorrhages, areas of chorioiditis, papil- l oedema, or aneurysmal or obliterator aterial lesions.

Serum sickness may also be associated with a retino- pathy of a collagen type.

Dermatomyositis is rarely associated with a late exudative retinopathy.

In generalized scleroderma a retinopathy is not seen, but lagophthalmos sometimes occurs and cataract may form.

B. Jay.


A case of linear scleroderma en coup de sabre, with ipsilateral atrophic iris lesions, is described. The morbid process appeared a few months after severe psychic troubles and the eye lesions developed within several months. Their character showed their neurotrophic origin, which is especially distinct in linear scleroderma. The authors believe that linear scleroderma en coup de sabre is not identical with spontaneous Romberg's atrophy, although both those morbid processes show a distinct connexion with the nervous system.

W. H. Melanowski.


Périarteritis Nodosa in an Infant. (Périarterité noueuse


Neuraminic Acid and Polysaccharides in the Serum Protein Fractions in Collagen Diseases (Scleroderma and Lupus Erythematosus). (Kwas neuraminowy i surowicy w tzw. kolagenozach (twardziny i liszaju rumieniowatym). DZULYŃSKA, J., JABŁOŃSKA, S., MAZURKIEWICZ, W., and PIEKARSKA, Z. (1961). Pol. Tyg. lek., 16, 1. 8 figs, 31 refs.


Non-Articular Rheumatism


General Pathology


The rheumatoid factor of rheumatoid arthritic sera is known often to form a precipitate with aggregated gamma-globulins (A.G.G.). A preparation of A.G.G. of F.II human serum fraction was made and all sera from 200 patients with various diseases and eighty healthy subjects were found to form a precipitate with it, with the exception of sera from ten new-born babies, whose mother’s serum was positive. Investigations were made as to the relationship of complement to this precipitation reaction. Decomplementation of a serum by admixture with an heterologous antigen and antibody system prevented precipitation with A.G.G. In the precipitation reactions the supernatants showed a decrease in titre of complement up to the point of maximal precipitation, but increased again beyond this zone down to the anti-complementary effect of A.G.G. itself. At least one step in the reaction had a dependence on temperature. Fractional inactivation of the components and of end-piece and mid-piece of complement suggested the possible identity of precipitating factor for A.G.G. with the first component. Since fixation of the first component is known often to require calcium ions and to be inhibited by the chelating agent sequesterin, quantitative precipitations were made with a serum containing 0.01 M. sequesterin. The precipitate was thereby increased, while the anti-complementary action of the supernatant was decreased but not completely inhibited. “These findings indicate that the precipitating factor, although suggestively similar to the first component of complement, is distinct from it as well as from the other hitherto known components of complement.” Recovery from the precipitate of a globulin entity having a sedimentation constant of S_20 10.5 was made by centrifugation, and which entity again formed a precipitate with A.G.G.

Harry Coke.


This paper from the Royal Bath Hospital, Harrogate, Yorks, records another satisfactory experience with the simple slide test utilizing the commercial preparation of latex particles coated with a globulin for the diagnosis of rheumatism. The results, which were read macroscopically at one minute, were compared with those of the differential agglutination (D.A.) test. Of 603 sera examined, 232 gave a positive result by the latex slide (L.S.) test, and of these only four failed to give a positive D.A. reaction, which is defined as a differential titre of 1:16 or greater. No serum giving a positive D.A. reaction failed to give a positive L.A. test result. After clinical classification, 85 per cent. of those classified as “definite or probable” rheumatoid arthritis gave positive...
L.S. test results, while of those classified as “possible” rheumatoid arthritis 44 per cent. did so. The incidence of false positive reactions was assessed at 3.8 per cent. in cases without any suggestion of rheumatoid arthritis, and at 5.3 per cent. in those of osteoarthritis. Only occasional positive reactions were obtained in the sera of patients with such conditions as ankylosing spondylitis, Still’s disease, and psoriasis with arthritis. The percentage of positive results was lower in early cases, in long-standing cases, and those in which the arthritis was “mild in extent”. In relation to clinical activity of the disease 88 per cent. of those with active disease gave a positive result, as compared with 54 per cent. of those with inactive disease. No correlation was found between L.S. test results and disease activity as measured by the erythrocyte sedimentation rate or haemoglobin level, but positivity was related to the radiographic bone changes and the presence of nodules. The test is shown to be simple to perform, easy to read, and qualitatively as satisfactory as the more extensive and time-consuming erythrocyte agglutination methods.

Harry Coke.


Skin Test for the Diagnosis of Rheumatoid Activity. (Un test cutaneo per la diagnosi di attivita reumatica.) RUBBIANI, V., and MATTIOLI, G. (1960). Reumatismo, 12, 221.


ACTH, Cortisone, and Other Steroids

This paper from the University Medical Clinic, Geneva, reports the results of treatment of 250 cases of various types of “rheumatism” with tablets containing 50 mg. phenylbutazone and 1.25 mg. prednisone. Previous work on this combination of drugs is described. There was no control group, but the criteria of improvement were laid down before the start of treatment. By these, improvement occurred in from 50 to 75 per cent. of cases of osteo-arthritis of the limbs, periartthritis of the shoulder, non-articular rheumatism, low back pain, and rheumatoid arthritis. On the other hand little benefit was obtained in sciatica and cervical osteo-arthritis, especially the chronic forms of these. The average daily dose was between two and six tablets a day. Side-effects, which were minimal, included three cases of skin irritation, several of minor gastric upset, and one case of reactivated duodenal ulceration. It was found that some cases could be treated with these tablets for as long as 11 months.

G. S. Crockett.

Treatment of the Dermatoses with 6-Methyl-Prednisolone

From the University Skin Clinic, Giessen, Germany, comes this report on the efficacy of treatment with 6-methylprednisolone of 62 patients, most of whom were suffering from such conditions as eczema, psoriasis, dermatomycosis, and urticaria, while a few had primarily dermatological diseases such as systemic lupus erythematosus and sarcoidosis. The duration of therapy ranged from 10 to 74 days (average 23 days) and the total dose of the steroid from 80 to 2,384 mg., the dosage depending largely upon the type and severity of the disease in each case. Investigations carried out before and during therapy included determination of blood pressure, blood sugar and serum protein and electrolyte levels. There appeared to be no major alterations in any of these values as a result of the therapeutic regimen, except that the serum potassium level was lowered in eighteen cases. However, only one patient, in whom this level was 13-6 mg. per 100 ml., developed symptoms. There was a general increase in the feeling of well-being and no important complications occurred. The dosage of methylprednisolone was between 50 and 75 per cent. of that of prednisolone, while it was considered that the former was more easily utilized. The importance of supplementary potassium therapy is emphasized.

Allene Scott.


It is known that after prolonged treatment with corticosteroids the adrenal cortex responds subnormally to stimulation with ACTH (corticotrophin). The experiments reported in this paper from the Institut Pasteur, Lyons, were designed to determine the duration of this insufficiency and whether it could be prevented or reduced by including ACTH or testosterone in the therapeutic regimen. The plasma 17-hydroxy cortisol levels were first determined at 0, 2, 4, and 6 hours during the intravenous infusion of 25 mg. ACTH in 3 healthy subjects, thus establishing the normal response to such an infusion of ACTH.

A similar infusion of ACTH given to 34 patients 12 hours after cessation of treatment with prednisone alone for various periods, ranging from 20 days to 10 months, gave a uniformly subnormal response. When the test infusion was delayed for 36 hours after cessation of treatment with prednisone, four out of six patients gave a subnormal response, but when 60 hours were allowed to elapse before the test infusion, three out of six patients gave a subnormal response. In a third group of six patients only two gave a subnormal response when 64 hours were allowed to elapse between cessation of treatment and the test infusion, while of six patients who received 15 to 20 mg. prednisone daily for periods ranging from 19 days to 31/2 months supplemented by 50 mg. testosterone every 5th or 7th day all gave a subnormal response to the test infusion of ACTH given at 12 hours. However, when treatment with prednisone was supplemented with 20 mg. ACTH-zinc (a retard preparation) every 5th or 7th day, the response to the test infusion 12 hours after cessation of the treatment was normal in four of six patients.

P. A. Nasmyth.

[An English translation of this paper was published simultaneously in the U.S.A. (J. Pediat., 1960, 57, 471). No acknowledgment of this fact is made in either journal.]


At the Facultad de Ciencias Medicas, Buenos Aires, Argentina, the authors have studied the action of ACTH (corticotrophin), cortisone, and prednisone on human skin. For this they used skin from six healthy volunteers, and from thirty patients with local diseases capable of temporary improvement on hormone therapy. The three hormones were administered parenterally by mouth, and hydrocortisone ointment was applied locally. The results obtained in both normal and diseased skin were constant. Normal skin showed progressive atrophy of the collagen bundles and fibres, thinning and
fragmentation of the reticular and elastic fibres, and disappearance of the interfibrillar mucopolysaccharides. The basement membrane appeared to become thin and lose its continuity, while the periodic-acid-Schiff reaction became weaker. Fibroblasts lost nucleoprotein granules from their cytoplasm and the nuclei were pyknotic. In scleroderma and sclerodema adultorum the hypertrophied collagen bundles and the elastic tissues became dissociated, the zones of hyalinization became reduced, and the mucopolysaccharide in the papillary corium disappeared. The glycoprotein, the reticular fibres of the basal membrane, and the hyalinized arterioles were unchanged. Fibroblasts seemed less hypertrophied and lost their cytoplasmic nucleoproteins. Some mast cells lost their granules. All these changes seemed to reach their peak about 4 weeks after treatment, and appeared more marked with prednisone than with corticotrophin or cortisol. The changes were apparently reversible, as the skin returned to normal when administration ceased.

[This paper is illustrated with extremely clear plates.]

G. B. Mitchell-Heggs.


Prolonged suppression of adrenocortical function is observed after cessation of long-term glucocorticoid therapy. The reactivation achieved by administration of adrenocorticotropic hormone (ACTH) may not be maintained when treatment is discontinued. In this paper from Georgetown University School of Medicine and Georgetown University Hospital, Washington, D.C., a study is reported of the urinary excretion of 17-ketosteroids and 17-hydroxysteroids in three patients who had received long-term glucocorticoid therapy. The first patient had rheumatoid arthritis for 22 years and had been receiving 50 to 75 mg. cortisol daily for the preceding 7 years. Liver and kidney function were normal but for 3 days following the abrupt withdrawal of corticoid therapy steroid excretion was below normal.

A standard 8-hour infusion of ACTH at the end of this short withdrawal period produced an increase in the excretion of 17-ketosteroids and 17-hydroxysteroids, but the response was subnormal. Sustained stimulation with intramuscular ACTH gel resulted in a urinary excretion of 17-hydroxysteroids which was above the normal level, but excretion of 17-ketosteroids although increased, barely reached normal levels. When stimulation was discontinued the output of steroids fell below normal and 11 days after sustained stimulation there was a subnormal response to the standard ACTH test. A similar study was carried out in two other patients who had been receiving cortisol for 2$\frac{1}{2}$ and 3 years, respectively. The results were almost identical with those obtained in the first patient, but in these last two patients a longer time was allowed to elapse between withdrawing corticoid therapy and beginning sustained stimulation with intramuscular ACTH gel. The maximum time between withdrawal and sustained stimulation was 7 days and during this time there was no evidence of a spontaneous return to normal excretion of 17-hydroxysteroids or 17-ketosteroids. Only one of the three patients gave an adequate response to the 8-hour ACTH test 10 days after stopping sustained stimulation with intramuscular ACTH gel.

P. A. Nasmyth.


Cushing's syndrome associated with bilateral adrenal hyperplasia can be satisfactorily explained by supposing that it results from an increased secretion of adrenocorticotropic hormone (ACTH). However, it has not been possible to demonstrate a measurable increase in blood concentration of ACTH in such patients, and it has therefore been doubted that this is the explanation of the syndrome. In an investigation at the University of Utah College of Medicine, Salt Lake City, the effect on the plasma 17-hydroxycorticosteroids of infusing amounts of ACTH insufficient to produce a measurable rise in the plasma levels of the hormone was determined in seven normal young men. The amount of ACTH to be infused in each individual was determined by measuring the maximum quantity which could be infused intravenously for the 4 hours from 8 a.m. to noon without causing a rise in the plasma 17-hydroxycorticosteroid concentration. This was found to range from 1·5 to 5 i.u. per day. The appropriate concentration of ACTH was then infused constantly for 4 days. In two of the subjects 1 mg. dexamethasone was given orally every 8 hours to suppress endogenous ACTH. In four of the seven subjects, and including the two given dexamethasone, the plasma 17-hydroxycorticosteroid level was raised during the 4-day infusion. In five of the subjects the response of the plasma 17-hydroxycorticosteroid level to maximal stimulation with ACTH 2 hours after completion of the 4-day infusion was greater than it was when the same test was made before the infusion. It was concluded that the absence of a measurable increase in blood ACTH concentration in Cushing's syndrome associated with adrenal hyperplasia is not a valid objection to the hypothesis that the condition is due to a constant secretion of ACTH. P. A. Nasmyth.


An investigation was carried out at the Mayo Clinic to determine the incidence of peptic ulceration in patients with rheumatoid arthritis and the effect, if any, which steroid therapy has on this incidence. A total of 2,114 patients in whom rheumatoid arthritis was diagnosed in the 2 years 1954 and 1957 were divided into two groups:

1. 1,237 patients who had received systemic steroid therapy;
2. 877 who had not been given such treatment.

In addition, a number of patients in Group 1 who had clinical signs of hypercortisonism as a result of treatment were separately studied. The ages of the majority...
of the patients ranged from 40 to 69 years, but 49 patients were aged under 10 and 18 over 80. The authors note that in 1947—before steroids were available—23 (3.3 per cent.) of 830 patients with rheumatoid arthritis had peptic ulcer. In 1954, of 627 arthritis given steroids 42 (6.7 per cent.) had peptic ulcer compared with 34 (6.8 per cent.) of 501 not so treated. In 1957, the figures were 51 (8.4 per cent.) of 610 and 37 (9.8 per cent.) of 376 respectively. In the subgroup of 331 treated arthritics with hypercortisonism the incidence of peptic ulcer was 5.7 per cent. in 1954 and 9.9 per cent. in 1957. Of 93 steroid-treated patients with ulceration seventeen (18.3 per cent.) had a gastric ulcer, while in the 71 patients with ulceration not so treated five (7 per cent.) had gastric ulcer. Of a group of 65 patients given intra-articular injections of steroids in 1954, two had peptic ulcer, and of 44 so treated in 1957, four had peptic ulcer. In all six cases the ulcers had been present before treatment started and were not aggravated by it. Of the 1,237 patients treated with steroids, fourteen had severe gastro-intestinal haemorrhage and three had perforation; of the 877 not so treated nineteen had haemorrhage but none had perforation.

The authors quote figures to show that the incidence of peptic ulcer in patients with rheumatoid arthritis seen at the Mayo Clinic and the Massachusetts General Hospital before the introduction of cortisone was 3.3 to 4.7 per cent. In the general population of North America it has been reported to be 1 to 3 per cent., and to 4.7 per cent. in the general population of North America it has been reported to be 1 to 3 per cent., and to 4.7 per cent. in Massachusetts it has been reported to be 1 to 3 per cent., and to 4.7 per cent. in the general population of North America it has been reported to be 1 to 3 per cent., and to 4.7 per cent. in the general population of North America it has been reported to be 1 to 3 per cent., and to 4.7 per cent. in the general population of North America it has been reported to be 1 to 3 per cent., and to 4.7 per cent. In females. They consider that the most significant finding in their investigation is the increase in the incidence of gastric ulcer—18 per cent. of the peptic ulcers in the steroid-treated patients being gastric as against 7 per cent. in those not so treated. Whether the increase in the incidence of peptic ulceration among arthritis from 3.3 per cent. in 1947 to 8 per cent. for the two years 1954 and 1957 combined is real or is due to better diagnosis cannot be decided.

William Hughes.

Long-term Corticotherapy in Inflammatory Rheumatism.


