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
- Non-articular Rheumatism, including Disk Syndromes, Sciatica, etc.
- Rheumatoid Arthritis
- Pararheumatic (Collagen) Diseases
- Still's Disease
- Connective Tissue Studies
- Osteo-Arthritis
- Immunology and Serology
- Spondylitis
- Biochemical Studies
- Inflammatory Arthritis
- Therapy
- Gout
- 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.

Acute Rheumatism


In a former paper (Pediatrics, 1962, 30, 712; Abstr. Wld Med., 1963, 33, 404) certain criteria were formulated by the authors with the object of gauging the potential danger of rheumatic fever developing in any Group-A streptococcal epidemic occurring in populations at risk so that mass prophylaxis could be instituted in time to abort the epidemic. The criteria were based on the finding of an index case of rheumatic fever and then the application of the following principles:

1. A Group-A prevalence rate of 30 per cent. or more,
2. A preponderance (50 per cent. or more) of typable strains,
3. At least one-third of the typable strains must be represented by one particular strain.

In the spring of 1961, an epidemic of streptococcal infection associated with a high incidence of rheumatic fever occurred among schoolchildren in Dickinson, North Dakota, and was found to yield all these criteria; mass prophylaxis was instituted, with the result that the epidemic was aborted (J. Pediat., 1966, 69, 40; Abstr. Wld Med., 1966, 40, 456). The present paper from the U.S. Department of Health, Education, and Welfare, Greeley, Colorado, and the Children's Memorial Hospital, Chicago, reports the follow-up of some of the children involved. During the period October, 1961, to May, 1962, no index case of rheumatic fever was diagnosed, nor were the three criteria fulfilled simultaneously as they were during the epidemic. Although the carrier rate of Group-A streptococci declined in the autumn and early winter of 1961, there was a slight rise later, but without a corresponding rise in typable organisms. The most striking feature was the disappearance of the epidemic strain (Group A, Type 5) from the school population. No rheumatic fever developed during this endemic period.

The authors consider therefore that their criteria may still be valid indications for mass prophylaxis of rheumatic fever in a threatened epidemic in a civilian population, and indeed they state that these criteria were once more applied to an epidemic of streptococcal infection associated with the findings of index cases of acute rheumatic fever which occurred in South Dakota in 1965. Mass prophylaxis was introduced and again the epidemic was aborted successfully.

H. Stanley Banks


Immunology of Acute Rheumatism. (Nouvelles données sur la pathogénie immunologique du rhumatisme articulaire aigu.) Halpern et al. (1967). Presse méd., 75, 209.


Rheumatoid Arthritis

An attempt was made to withdraw prednisolone therapy at the rate of 1 mg. a month from 25 female and ten male patients whose disease had been “adequately suppressed for at least 3 months”. They were aged 21 to 78 years, the disease duration was 2 to 30 years, and they had received corticosteroids for 1 to 16 years at a mean dose of 3.5 mg. to 15 mg. daily. It was considered that there was “a reasonable chance” that their dosages could be lowered, if not stopped, without loss of symptom control. In the event the dose given was lowered for all the patients but complete withdrawal was not possible for 70 per cent. (The period of observation was not given but it must have been at least 2 to 3 years). Of ten patients who stopped therapy, nine took a mean period of 1.5 months for each 1 mg. reduction. These patients, as a group, did not differ from the others in respect of the details given above. Of particular interest was the reactivation of arthritis in “quiescent” joints that accompanied a reduction of dose in most patients. Many adrenal function tests were performed during the course of the withdrawals (see Daly, J. R., Myles, A. B., Bacon, P. A., Beardwell, C. G., and Savage, O. (1967). Ann. rheum. Dis., 26, 18); these showed that eight subjects who had stopped prednisolone therapy had insulin hypoglycaemia tests of pituitary-adrenal function within the normal range. The authors suggest that, if the 10.30 a.m. plasma “cortisol” concentration is within the normal range, then the withdrawal of prednisolone therapy may be safely continued without recourse to other tests of pituitary-adrenal function.

H. F. West


In 1964 (Arthr. and Rheum., 7, 467; Abstr. Wild Med., 1965, 37, 126) the authors put forward the theory that ulnar deviation and volar subluxation at metacarpophalangeal joints seen in patients with rheumatoid arthritis are due to the action of the long flexor tendons on diseased ligaments around the joint. In this paper from the Departments of Physical Medicine and Rehabilitation and of Mechanical Engineering, University of Michigan, Ann Arbor, they review this theory and explore some of the implications as they involve the management of the deformity. They emphasize that the force carried by the flexor tendon at the flexor tendon mouth to the metacarpophalangeal joint is six times the finger tip pinch force required for this action. When there is active disease of these joints the flexor forces should therefore be reduced to a minimum by instructing the patient to use the fingers as hooks for lifting and to handle objects which encourage extension of these joints: joint flexion can also be limited by splintage. Pinching or grasping should be minimized and the patient should be encouraged to use the hand as a scoop when picking up an object or to hold the object between his two palms so that the fingers are spared; the common practice of instructing him to exercise his fingers by squeezing a rubber ball is condemned. The authors suggest that the disappointing long-term results of arthroplasties of these joints may be due to failure to recognize the importance of the displacement of the tendons.

V. Wright


From the Medical College of Virginia, Richmond, a detailed report is presented of the case of a white man aged 64 years in whom both typical rheumatoid nodules and gouty tophi were demonstrated. After an initial attack of typical gout in one great toe multiple similar
attacks occurred, followed by symmetrical episodic polyarthritis in the wrists, shoulders, elbows, knees, and proximal phalanges. Nodules were removed and shown histologically to be of the rheumatoid type “featuring a necrotic eosinophilic centre surrounded by strikingly palisaded spindle cells with large hyperchromatic nuclei”. Tissue removed from one elbow showed typical rheumatoid changes, as did synovial tissue obtained by needle biopsy from the knee. The ESR was consistently increased and tests for the rheumatoid factor by the latex and sensitized human and sheep cell techniques were positive in high titre. There were no tophi on the ears, but in material from tophi on the distal phalanges of the index fingers birefringent sodium urate crystals were demonstrated. The serum uric acid level varied between 9 and 13·2 mg./100 mg. and there was increased urinary excretion of urate. Satisfactory relief of symptoms was obtained with colchicine, with relapse on its withdrawal. Administration of allopurinol caused an immediate exacerbation. The authors consider the concurrence of rheumatoid nodules and gouty tophi in the same person to be extremely rare and have been able to find only four other cases in the literature. —Harry Coke


Still's Disease
This is a very full report of 544 patients all of whom had developed joint symptoms before the age of 15 years; 299 had been treated by the Rheumatism Foundation Hospital before the age of 15. The average time since the onset of the disease to the point of study was 16 years (range 3 to 50 years) and conclusions were based on a personal follow-up in 372 cases, questionnaires in 92, and hospital records in the others. From this excellent review, it would appear that the number of children affected by rheumatoid arthritis in Finland is from 6 to 8/100,000, and that the peak ages at onset are from 1 to 4 and 9 to 14 years. The results of the various radiological, serological, and clinical studies are similar to previous published work and, as in so many series, about one-third of the cases show serious residual involvement. No specific therapy appeared to influence this, but function could be maintained provided suitable physiotherapy and, if necessary, operative therapy was instituted early.
B. M. Ansell


ABSTRACTS

Osteo-arthritis


Spondylitis


**Inflammatory Arthritides**


In previous papers the authors of this report from the Institut Pasteur, Paris, have shown that the "virulence" of streptococci (that is, their ability to cause rapid death by septicaemia) is genetically determined. "Pathogenicity" (the ability to cause lesions which are not necessarily fatal) is difficult to study in the case of virulent organisms, because these rapidly kill the experimental animals; avirulent organisms, on the other hand, are quickly eliminated and so cause no lesions at all. The authors have surmounted this difficulty by giving their mice 0.1 ml. of a rabbit anti-mouse-macrophage serum; 1 hour later they injected the animals intraperitoneally with Strain 1824 *Streptococcus pyogenes*; doses of 10^9 to 5 x 10^9 organisms, only a few of which were virulent, were used. Less than 25 per cent. of the mice treated in this way died.

Segmental swelling of the tail developed in 45 (15 per cent.) of 300 mice thus infected; various limb joints became inflamed in 17 (6 per cent.); in nine (3 per cent.) there was cachexia associated with the development of cardiac lesions characterized by enlargement of the heart and marked thickening of the pericardium, which adhered to the pleura. A further 150 mice showed enlargement of the heart without pericarditis. The percentage of mice showing lesions was related to the quality of the macrophage antiserum, for when a pool obtained from more strongly immunized rabbits was used 20 per cent. of the mice suffered noticeable arthritis. Similar results were obtained in experiments in which organisms of Strain 36212 were used.

Serial histological sections of pericardium, pleura, and synovial membrane showed granulomatous lesions, vascular congestion, and infiltration with lymphocytoplasmonic cells. Rarely, areas of necrosis were seen. In all cases the myocardium showed interstitial and peri-vascular infiltration. No renal lesions were found. Type 24 *Streptococcus pyogenes* was always recovered from the cardiac or articular lesions. Various control experiments demonstrated that neither normal nor anti-macrophage serum in themselves had any effect on mice.

The authors conclude that although the cardiac lesions did not have the characteristic histological appearance of the Aschoff body, the sites and synchronized appearance of the lesions suggest that the experimental syndrome produced in mice was very similar to rheumatic fever in man.  

*Harry Coke*


Reiter’s syndrome is often associated with the cutaneous lesions of keratosis blennorrhagica, and the clinical resemblance of these to some forms of psoriasis has led the authors of this paper, from the University of Texas Medical Branch, Galveston, and Forth Worth, Texas, to try the therapeutic effect of folic acid antagonists in Reiter’s syndrome with cutaneous manifestations.

Six patients were studied: all were severely affected with arthropathy and keratosis blennorrhagica; other forms of treatment had failed. One patient responded rapidly to aminopterin (0.5 mg. daily for 6 days followed by a second 6-day course after 3 days), but a second patient failed to respond. Three patients were given methotrexate in a dose of 2.5–5 mg. daily for two to four 6-day courses. There was excellent improvement in the skin lesions in two of these cases, and in another both the skin and the joint lesions responded excellently. The remaining patient responded unsatisfactorily at first, but when after an acute exacerbation of his illness he was given two 7-day courses of methotrexate at a dose of 5 mg. daily in place of the 2.5 mg. used initially the skin lesions cleared almost completely and the joints improved. No complications occurred with methotrexate. The authors conclude that even though the course of Reiter’s syndrome is variable a trial of methotrexate may be beneficial in severe cases, especially for the cutaneous manifestations.

*Benjamin Schwartz*


Gout
Calcification of cartilage may occur as a primary condition or as a consequence of hypocalcaemia, trauma, or degenerative and infective states. It also occurs in ochronosis and there are isolated reports of its appearance in patients with rheumatoid arthritis, systemic lupus erythematosus, and haemochromatosis. The authors of this report, which comes from the Department of Radiology of the University of California, San Francisco, produce evidence that calcification of the meniscus and to a lesser extent of the articular cartilage of the knee is common in patients with gout. They reviewed the case records and radiographs of 58 patients seen between 1958 and 1965 and from these they selected 39 cases of primary gout for study. Radiographic studies of the knees were available in 31 of these cases (29 males, 2 females) and of these ten showed meniscal calcification (3 of these 10 also showed calcification of an articular cartilage of the knee or of the triangular cartilage of the wrist.) Radiographs of other limb joints were negative: the spine was not included in this study. Comparison of the groups with and without calcification revealed little difference in age, level of uric acid, and duration of gout but those with calcification had more severe gout as judged by the number and size of tophi present. The incidence of such calcification in a normal elderly population (average age 80 years) had been found by previous workers to be only 7 per cent. and the calcification present was attributed to degenerative processes. Thus the present incidence of ten cases of calcification out of 31 is far greater than would be expected in the general population.

The authors consider that calcification of the cartilage seen in gout is a secondary process caused by the gouty arthritis and that its appearance is not coincidental as has been suggested in the literature. The deposit of calcium is light and the predominant involvement of the knee is attributed partly to the long surface presented by this joint to the x-ray beam.

K. C. Robinson

Renal damage in gout has been reported in 22 to 87 per cent. of cases. It is generally accepted that serious renal impairment in gout is often preceded by asymptomatic proteinuria.

The authors carried out inulin clearance and para-aminohippuric acid tests on fourteen cases of gout with normal urine analysis and blood urea, and in four of these the kidneys showed definite evidence of damage. From this they argue the risks of renal damage from gout and the need of extra fluids, diet and reduction of acidity of the urine, but do not attempt to evaluate the xanthine oxidase inhibitor allopurinol.

G. D. Kersley


Ask-Upmark, 6 figs, 11 refs.


Renal Complications of Gout. (Complications rénales de la goutte.) PRUNIER (1967). *Presse méd.*, 75, 139.


Bone Disease


A woman aged 60 with bilateral calcium phosphate nephrolithiasis was found to have hyperparathyroidism. After removal of an adenoma, painful swellings occurred in the ankle, hand, and elbow. Serum uric acid levels were normal before and after the operation: levels of Ca and phosphorus had become normal. X-ray showed typical chondrocalcinosis. No biopsy was done and the process resolved with colchicine treatment. The authors refer to 22 cases of chondrocalcinosis and hyperparathyroidism, out of a total of 243 chondrocalcinosis cases recorded in the literature, and discuss possible mechanisms. *E. G. L. Bywaters*


ABSTRACTS


Non-Articular Rheumatism


The literature on cervical injury and the cervical pain syndrome does not mention the part played by the anterior cervical muscles in the development of such pain. At the Hitchcock Clinic, Hanover, New Hampshire, the authors first examined 35 normal persons aged 18 to 50 years in order to obtain a range of normal strength for these muscles. They were tested by manual resistance from the supine position with the neck in the mid position, and then with the head rotated to the left or right, and the authors found that seven of these 35 normal individuals had definite muscle weakness though they were asymptomatic. Next a group of 49 patients with cervical and/or upper thoracic pain with known cervical flexor weakness and another group of 66 patients with similar symptoms but without known cervical flexor weakness were studied. The age range of these 115 patients was 9 to 71 years and the various diagnoses are listed. Significant cervical muscle weakness was found in 95 (including the 49 who were originally selected because of this finding); the remaining sixteen showed no weakness.


The literature on low back pain is voluminous but little has been said about the role of muscle weakness as a contributory factor. At the Veterans Administration Hospital, Palo Alto, California, the authors studied trunk flexion and extension and hamstring muscle tightness in 32 male patients with low back pain and compared them with 32 normal controls matched for age, sex, weight, and height. A second group of twenty patients with low back pain were similarly matched with 25 normal controls and examined for abdominal and psoas muscle strength to assess the relative importance of these muscles in total trunk flexion. [For the methods of assessment the original paper should be consulted.]

There was considerable overlap of data between patients and controls but on the whole the patients had weaker trunk muscles than the controls, the flexors and extensors being equally affected. Hamstring muscle tightness, which was assessed in terms of hip flexion, was significantly greater in the patients than in the controls.

It is concluded that chronic low back pain that is not associated with bone or disk disease is often accompanied by generalized weakness of the trunk muscles. Whether the muscle weakness is the cause or the result of the pain could not be assessed but the use of supports or belts is considered to be contraindicated unless immobilization is the aim. Exercises aimed at strengthening both flexor and extensor muscles of the trunk are regarded as essential. The postural role of the hamstrings is discussed but it is not clear how tightness here aggravates back pain in the erect position.


Pararheumatic (Collagen) Diseases


In this paper the authors report their long-term observations of 37 patients with proven sarcoïdosis treated at the Veterans Administration Hospital, Bronx, New York. In four patients (Group 1) only the hilar lymph nodes were affected; in sixteen (Group 2) there was pulmonary disease with or without thoracic lymph node enlargement; in the remaining seventeen (Group 3) at least one other organ system, as well as the lungs, was affected. All the patients in Group 3 were non-Caucasian, compared with only a quarter of the patients in each of the other groups. The prognosis varied according to the degree of involvement. During the period of observation, which was more than 6 years in most cases, five patients in Group 3 died and nine were disabled, whereas in Group 2 only three died and one was disabled, and in Group 1 all the patients remained fit.

Remissions and exacerbations were common in Group 3, but changes in the pulmonary lesions bore no relation to those in other organs. The commonest extrapulmonary lesions were in the skin, liver, and spleen. Calcium metabolism was disturbed in six patients, two of whom had evidence of severe pyelonephritis.

The authors analysed serial chest radiographs. These showed that enlarged mediastinal nodes might persist unchanged for years while the patients remained clinically well. No case of pleural effusion was seen. There was no relation between the extent of pulmonary infiltration and the eventual outcome of the disease. Shrinkage of lung volume, the appearance of multiple small bullae, and upward retraction of the lung roots were irreversible and associated with pulmonary disability. If complete resolution occurred it did so within 3 years.

Necropsy was performed on seven of the eight patients who died. The lungs showed parenchymal and peribronchial fibrosis, with marked bronchial dilatation. Microscopically there was sarcoidosis, but the absence of infection was striking.

The results of pulmonary function tests correlated well with the degree of clinical disability, and these tests had prognostic significance. There was no conclusive evidence that steroid therapy prevented pulmonary insufficiency, though subjective and objective improvement occurred in some patients with secondary bronchitis, which may be an indication for such therapy.

B. Herszenhorn


Clinical and pathological studies on 105 patients with joint involvement that developed during the course of systemic lupus erythematosus (SLE) are reported in this study from the Research Institute of Rheumatism, Academy of Sciences of the U.S.S.R., Moscow.

This series consisted of 102 females and three males between the ages of 17 and 55 years who were diagnosed as having SLE on clinical grounds, on the presence of LE cells in the blood and antinuclear factor in the serum, and also on necropsy findings. The patients had been under observation for 1 to 5 years.

During this time 97 per cent. had some joint involvement which included arthralgia, acute asymmetrical polyarthritis, subacute polyarthritis which tended to be symmetrical, and chronic polyarthritis complicated by deformities. Myalgia, myositis, and tenosynovitis were also common findings. Radiographic examination of the joints showed that bone rarefaction was the commonest manifestation (60 per cent. of cases); moreover, narrowing of the joint space, small marginal erosions, and subluxations were seen in 18 per cent. of those patients with chronic and subacute polyarthritis. Gross deformity or destruction was not seen. Histology of the joint tissues showed no villous hypertrophy, no pannus, and a paucity of cellular infiltrate. The characteristic features of lupus synovitis—the disintegration of cell nuclei and formation of haematoxylin bodies—were seen most frequently during the active phase of the disease. Fibrinoid and degenerative changes rather than proliferative changes predominated. The deformity and destruction that does occur in these cases is considered by the author to be the result of damage to associated muscles.
and tendons. In conclusion, he discusses the possible cause of the joint lesions in SLE. 

J. S. Malpas

Positivity of the L.E. Phenomenon in Various Stages during the Course of Systemic Lupus Erythematosus. [In Czech.] Vachtenehim, J. (1967). Vnitřní Lék., 13, 52. 10 refs, 1 fig.


Connective Tissue Studies


The synovial leukocytes of nearly all patients with rheumatoid arthritis contain inclusion bodies which, it has been suggested, are aggregated y-globulin-rheumatoid-factor complexes. Such complexes might cause degeneration of the ingesting leukocytes with consequent release of their lysosomal enzyme and hence the production of further inflammation. Particles of leukocytes, thought to be DNA, have in fact been demonstrated in the joint fluid of patients with rheumatoid arthritis, and in this paper from Harvard Medical School, Boston, and other centres in the U.S.A. The authors report their investigation of the hypothesis that in the rheumatoid patient any joint injury causing inflammation may set in motion a self-perpetuating process involving altered nuclear material and anti-nuclear antibody. They made an analysis of the immunoglobulin classes of antinuclear factor (ANF) in paired synovia-serum samples from patients with various rheumatic diseases and also performed immunofluorescent studies on cytoplasmic inclusions in a few cases.
ANF of one or more of the immunoglobulin classes was found in both the serum and the synovia of seven out of 21 patients with definite or classical rheumatoid arthritis, in the serum only (in low titre) of four patients, and in the synovia only of two; it was not found at all in the remaining eight patients. Rheumatoid factor (RF) was found in the serum and synovia of twelve patients, in the serum only of four, and in neither the serum nor the synovia of three (the synovia of two patients was not tested but RF was found in the serum in one of these cases). The levels of synovial haemolytic component and second component of complement (C'2) activity in the patients with rheumatoid arthritis was moderately or markedly reduced in nearly all cases.

ANF was found in the synovia of one out of nine patients with degenerative arthritis, in the synovia and serum of one out of twelve patients with gout or pseudogout, in the serum of one patient with staphylococcal arthritis, in the synovia of one patient with Hodgkin's disease (complicated by an infective arthritis), and in the serum of one patient with psoriatic arthritis; the synovia of this last patient also contained RF. Reduced levels of synovial haemolytic complement or C'2 activity were occasionally found in patients suffering from other arthritides.

The synovial leucocytes from four patients with rheumatoid arthritis contained γG, γM, and β1C globulin (a moiety of the third component of complement) more frequently than did those from three patients with other arthritides. Contrary to the authors' expectations, however, nuclear antigenic determinants capable of reacting with the ANF obtained from the serum of a patient with systemic lupus erythematosus were found in the inclusion bodies of only one rheumatoid patient, and the authors are unable to explain this failure to demonstrate nuclear antigens by the immunofluorescent technique.

V. Wright


Several studies of the connective tissue cells in rheumatoid arthritis have been made, and it is known that these cells proliferate unrestrainedly and produce an excess of hyaluronic acid. The authors of this paper, from the University of Michigan Medical School and the Rackham Arthritis Research Unit, Ann Arbor, Michigan, have investigated the effects of hydrocortisone on synovial tissue connective cells maintained in culture. The cells came from eight patients with rheumatoid arthritis and thirteen patients with other types of disease, and were obtained at operation or biopsy.

No morphological difference between the cells from rheumatoid and nonrheumatoid subjects could be discerned, and both types produced large amounts of hyaluronic acid. However, the rheumatoid cells grew more slowly, and five of the strains secreted hyaluronic acid of slightly lower intrinsic viscosity than normal, while that secreted by two other strains was of considerably higher viscosity.

It was found that hydrocortisone exerted its greatest effect at a concentration of 1-0 μg/ml. in the culture medium, and this concentration was therefore used in experiments. In the normal strains hydrocortisone stimulated cell mitosis, reduced the mean cell volume, and decreased the rate of synthesis of hyaluronic acid. These effects were all much less prominent or even completely absent in the case of the rheumatoid cells. In preliminary observations of other types of arthritis it was found that cells from patients with traumatic arthritis or rheumatoid spondylitis responded to steroids in the same way as normal strains.

Inoculation of cellular and medium components from three rheumatoid strains caused no cytopathic effects in primary rhesus monkey kidney cultures, and no mycoplasma organisms could be found before or after the passage of these materials through such cultures.

E. G. L. Bywaters


From the National Institutes of Health, Bethesda, Maryland, the authors report the finding of distinctive giant cells in synovial tissue (obtained at operation) from nine out of nineteen patients with sero-positive rheumatoid arthritis. No such cells were found in nine specimens from patients with sero-negative rheumatoid arthritis or in four patients whose serological reactions were not known, nor were they found in control specimens from healthy subjects (25) or patients with traumatic or other synovitis (7) or infective arthritis (2) or from pigs with villous synovitis (6).

The giant cells were ovoid and measured approximately 40 μ in the greatest dimension, with up to twelve peripherally-placed nuclei. These resembled the nuclei of the mononuclear lining cells. There were numerous cytoplasmic granules, well stained by the PAS method; their histochemical reactions suggested a neutral mucosubstance with a minor esterified lipid component. Haemodesirin was occasionally found. The cells displayed acid phosphatase activity. Where giant cells were found there was hyperplasia of the lining cells of the synovium, the giant cells themselves being usually at a distance of 25–100 μ from the synovial surface. On electron microscopy the fine structural characteristics of the giant cells were basically similar to those of the macrophage-like cells which form the predominant component of the synovial surface.

G. Loewi


Temporary immobilization of normally movable joints often results in permanent loss of motion but the actual mechanism which causes this and the exact changes in joint structures which are responsible for decreased
mobility are unknown. The causative pathology can be divided into two main categories, extra and intra-articular—and the intra-articular stiffness involves basic changes in the physical properties of collagenous tissue. The mechanism by which immobilization leads to permanent immobility must be understood if prevention and satisfactory treatment are to be possible. Once these changes are defined, ways by which they can be reversed will become apparent, and prevention and treatment of small joint stiffness will be more predictable and successful than other methods.

While attempting to solve some of these problems it has been helpful to make several hypotheses which can be proved or disproved by experimental methods. The first such hypothesis assumes that decrease in joint motion is due to changes in collagenous tissue, proved by dissection of numerous human stiff finger joints and animal limbs, and relief of joint immobility only occurs when the dense connective tissue of the joint capsule or collateral ligaments is divided. A second hypothesis is based on the assumption that two basic changes appear possible in collagenous tissue and either or both cause joint stiffness. These are changes in the amount of collagen present and changes in its elasticity, and in the opinion of the author, the latter plays no part in joint stiffness.

The capsule, volar plate, and collateral ligaments of finger joints are tough, non-elastic membranes and the cause of interarticular joint immobility appears to be the result of shortening or fixation of these structures; the conclusion is reached that new collagen synthesis or reabsorption or both must be the fundamental processes by which interarticular joint stiffness is produced.

Prevention or selected removal of new collagen synthesis by biophysical or biochemical processes would seem to hold greater promise for the control of joint stiffness than surgical means. Identification of the fundamental process by which joint stiffness occurs, is the first step in developing such measures. **A. Kates**

**Hydrothermal Shrinkage and the Ageing of Collagen.** 

The hydrothermal shrinkage of collagen is a first order phase transition essentially the same as melting. The temperature at which shrinkage can first be detected (Ts) increases with the age of the donor animal, but when the Ts is determined isometrically, as here reported, age makes no difference. Nevertheless, there is a fivefold increase in the force of contraction of rat tail tendon of animals 2 years old compared with animals 2 months old. This is only partly due to the increase in collagen per unit of wet weight as collagen ages: the remainder is attributed to forces lateral to the axis of the peptide chains.

**L. E. Glynn**

**Articular Cartilage.** (Le cartilage articulaire. Problemes d'histophysiologie et de physiopathologie.)

**Comparative Study of Roentgenographic Techniques for Detection of Calcium Pyrophosphate Dihydrate Deposits (Pseudogout) in Human Cartilage.** 

**Fine Structure of Articular Cartilage in Mice receiving Cortisone Acetate.** **SILBERBERG et al.** (1966). *Arch. Path.,* 82, 569.


**Human Tendon Collagen—both Soluble and Insoluble in Citrate—and its Reactions to Normal and Rheumatoid Sera.** (Extracción de colágeno de tendón humano en sus fracciones citrosoluble e insoluble y sus reacciones inmunológicas frente a sueros normales y de pacientes con artritis reumatoidea.) **CARUSO, A. C., and SALOMONE, J.** (1965). *Arch. argent. Reum.,* 28, 10. 1 fig., 17 refs.


**Limited Cleavage of Native Collagen with Chymotrypsin, Trypsin, and Cyanogen Bromide.** **BORNSTEIN et al.** (1966). *Biochemistry (Easton, Pa),* 5, 3803.


Immunology and Serology


Neonatally established tolerance to human γ-globulin (an ethanol-fractionated preparation or pure IgG) could be terminated by injection of an active rheumatoid factor (isolated by column fractionation) but not by a similar preparation rendered inactive by ageing. Four groups of thirty tolerant mice were challenged at 80 to 85 days after birth with rheumatoid factor (RF) or γ-globulin as an aqueous suspension or emulsified in Freund's adjuvant. Tolerant mice which received IgG in adjuvant did not produce antibody detectable by gell diffusion or indirect haemagglutination except to a minor component of human γ-globulin. Mice in which tolerance was terminated by injection of RF showed by day 90, using either technique, antibody specific for IgG. The author considers that termination of tolerance may result from RF combining with human γ-globulin fragments or, more probably, by the antigenicity of RF itself being potentiated by the formation of RF-γ-globulin complexes following localization in mesenchymal tissue in the mice.

**N. R. Ling**


Measurement of the ESR in freshly-taken plasma invariably shows higher values than plasma that has been kept in an incubator at 37°C for several hours, and it is thought that the heat inactivates some factor in the plasma so that the ESR is "stabilized". This stabilization reaches a maximum in 12 hours at the above temperature.

At the University Medical Clinic, Cologne, this finding has been used to test the effect of incubation of plasma at 37°C for 4 to 5 hours on the ESR in 30 patients suffering from either neoplasms or a variety of infections, the results being compared with a control ESR figure of over 20 mm in 2 hours. It was found that in the patients with infections both the 4- and 5-hour values were much lower than the control value, whereas in the patients with tumours the values at both times did not differ greatly from the control value. Thus the factor in the plasma which increases the ESR in the presence of infection is more readily inactivated by heat than that associated with neoplasms. The test gave a correct differential diagnosis between infections and tumours in 80 per cent. of cases, but it could not distinguish between acute and chronic infections, tuberculosis, or "rheumatic" infections, no significant difference being observed in the behaviour of plasma.

Various lipases of animal and vegetable origin were added to the plasma and these produced a rapid and sustained heat stabilization; this suggested to the authors that lipase activity of some kind is the limiting factor in the heat stabilization of the ESR.

**E. Lester**


C-Reactive Protein Test in Rheumatic Diseases. DELLA-MARTINA, F. (1967). Rheumatism, 23, 22. 4 refs.


Biochemical Studies


Our inability to monitor directly either the in-flow to the adenohypophysis of the factor or factors that control its synthesis of ACTH or the rate at which it secretes ACTH has led to the use of many indirect means of studying the regulation of ACTH synthesis and release. This review describes and to some extent evaluates the means that have been used. The complexity of the subject is revealed by the author's reference to more than 400 publications. One of the problems reviewed, which remains complex, is the interpretation of the effects of Metopiron (Metyrapone) administration. Apart from this the subject matter is derived almost entirely from studies of laboratory animals and is of more interest to the laboratory physiologist than to the scientifically-minded physician. Needless to say Vitamins and Hormones should be found (and usually is) in every department in which medical scientists work. H. F. West


At the First Medical Clinic of the University of Kiel the authors have compared the 24-hour urinary excretion of hydroxyproline (as a measure of collagen catalbolism) of 25 patients with various connective tissue diseases with that of twenty healthy control subjects. Twenty of the patients had rheumatoid arthritis, two scleroderma, one dermatomyositis, one rheumatic fever, and one visceral lupus erythematosus; all were given a diet free from gelatin and most were bedridden and were receiving various types of treatment. [Their age range is not stated.] The controls, who were aged 22 to 84 years, received a gelatin-free diet, but most of them carried on with their normal day's work. Repeated estimations of hydroxyproline excretion were made in most cases, the assay being carried out by Stegemann’s method.

The control subjects excreted a mean of 25-0±43-3 mg./day, the lowest value being 15-0 mg. and the highest 240-0 mg. It was noted that when corticosteroids were given hydroxyproline excretion tended to fall. In eleven controls and thirteen patients hexosamine excretion was also measured, but with very variable results (controls 217-6±73-3 mg./day; patients 241-6±73-3 mg./day).

The author suggests that estimation of hydroxyproline excretion provides a useful measure of rheumatic inflammatory activity.

[The value of this study would have been enhanced by the use of bedridden controls with non-rheumatic diseases.] G. Lowe


Therapy


Intra-articular injection of corticosteroids is becoming increasingly popular in the treatment of rheumatoid arthritis. From the University of Michigan Medical School, Ann Arbor, the authors report the occurrence of cutaneous atrophy over the affected joint in eight patients treated by this means during the period 1963-5 (a total of 1,706 intra-articular injections had been given in the arthritis clinic concerned during this time). The eight patients (5 males and 3 females) were aged 12 to 42 years; the diagnosis was rheumatoid arthritis according to ARA criteria in six cases, psoriatic arthritis in one, and Reiter's disease in one. All eight patients had previously received intra-articular injections without the development of cutaneous atrophy and one patient was receiving oral prednisolone at the time it developed. The atrophy occurred only over the joint into which the injection had been given (wrist, ankle, and interphalangeal joints of the fingers). The corticosteroid used was triamcinolone in five cases, methylprednisolone in two, and hydrocortisone in one. Atrophy was first noted 1 to 4 months after injection, the changes in the affected areas consisting in erythema and thinning of the skin with loss of hair, telangiectasia, accumulation of pigment, and atrophy of subcutaneous fat. The atrophy lasted for up to 24 months in one case and although the authors believe the condition to be reversible it was still present after 30 months in another case.

The authors also studied the effects of injecting the corticosteroids in question into the skin of adult rabbits. Injection was followed by skin atrophy in each case. The first changes were observed 2 weeks after injection and were most pronounced at 4 weeks; recovery occurred within 8 months; triamcinolone produced more persistent atrophic effects compared with hydrocortisone. Loss of hair and cutaneous atrophy were the most noticeable features. Atrophy was more extensive when corticosteroids were diluted with saline solution than when used as supplied by the manufacturers.

The authors point out that the cosmetic lesion in such cases is clearly of iatrogenic origin. This can have undesirable medicolegal consequences when the disfiguring atrophy occurs over exposed joints in females. Cutaneous atrophy has never been observed over the larger joints and the authors consider that the condition may be due to overspill from injecting too much of the corticosteroid preparation into relatively small synovial spaces.

William Hughes


A double-blind controlled trial of flufenamic acid was carried out on nineteen patients with definite rheumatoid arthritis according to ARA classification who were treated as outpatients at The Royal Infirmary, Sunderland, Co. Durham. The drug was administered by mouth in a dosage of 200 mg. thrice daily to ten of the patients and a placebo was given in the same way to the other nine patients, the trial period lasting 8 weeks. No other medication was given concurrently. The two patient groups were comparable in terms of age and length of history of arthritis. All patients were assessed weekly beginning 1 week before the trial started, such assessments including laboratory estimation of ESR, serum alanine transaminase levels, urine cell counts, and estimation of the number of disease-active joints and of grip strength.

The patients who received flufenamic acid showed a significantly greater improvement in grip strength (P<0.05) than did the controls but no difference was noted in the number of joints affected, the average joint score falling in both groups, nor were there any significant changes in the ESR, urine cell counts, or serum alanine transaminase levels (two patients from each group did have abnormal values for the last-named test but these were thought to be due to a laboratory error).

Seven patients (including four who took part in the controlled trial) were given periods of treatment of up to a year in a dosage of 200 to 300 mg. flufenamic acid/day; three of them developed diarrhoea on the higher dosage but this subsided when the dosage was reduced to 200 mg./day. In all cases laboratory findings have remained satisfactory and the clinical condition good. Estimations of the plasma levels of flufenamic acid were made on four patients, three of whom received 100 mg. thrice daily and these levels were found to range between 4 and 6 μg./ml. 2 hours after taking the last dose of the drug. All these patients had received flufenamic acid for at least 6 months and these findings are taken to indicate that absorption remains satisfactory with prolonged treatment.

J. A. Cosh


Duke (1910) described the bleeding time test and this was later utilized by Minot and Lee (1920) in their description of what is now called the Minot-von Willebrand syndrome, but the significance of the bleeding time in haemostasis is still poorly understood. Salicylates are a known cause of gastric bleeding, but no definite
causal effect has been demonstrated, though a promising line of research was started by Quick (Fed Proc, 1966, 25, 498), using aspirin as test material. The present paper from Marquette University School of Medicine, Milwaukee, Wisconsin, reports the effect of 0·33–1·3 g. doses of aspirin and 1·15 g. of sodium salicylate on the bleeding time of normal students and patients with the Minot-von Willebrand syndrome. When 0·65 g. aspirin was given to the normal subjects the bleeding time remained within the upper limit of normal but when 1·3 g. was given to these subjects there was a small but significant increase in the bleeding time in 50 per cent. of cases: no such increase occurred when 1·15 g. sodium salicylate was given. The bleeding was significantly prolonged in all the patients with Minot-von Willebrand syndrome following 0·65 g. aspirin, a finding which has been made the basis for an aspirin tolerance test to detect patients with this syndrome.

It is postulated that the prolonged bleeding time in the Minot-von Willebrand syndrome results from the lack of a vague, undefined plasma factor which is independent of the normal coagulation mechanism and that aspirin depresses the activity of this agent. It is further postulated that the action of aspirin is determined by the acetyl linkage and not by the salicylate content. The practical value of the test appears to lie in the detection of subclinical cases of the syndrome and it is emphasized that the findings in these tests in no way detract from the use of aspirin as a therapeutic agent—"It remains one of the safest analgesics and it can increase the bleeding time should not limit its same therapeutic use."

Ian Hutton


The management of advanced degenerative arthritis of the hip, especially when bilateral, remains an unsolved problem. Although the Austin-Moore prosthesis has become of established value in femoral neck fractures where the acetabulum is healthy, its place in cases of osteo-arthritis of the hip is less certain and most authorities agree that, when acetabular remodelling is carried out, the results cannot be expected to be more than fair.

In this series 33 such operations in 28 patients were carried out, and thirty relevant hips in 25 patients were examined at least one year post-operatively. The best effect of the operation was in relief of pain, although in some cases pain after operation was described as discomfort at rest and aching on exercise. There was not a marked improvement in range of movement, and with time there was a tendency for the arthroplasties to stiffen up.

Improvement in activity as judged by capacity for work was confined to unilateral cases and the operation appeared to have a greater effect in reducing pain than in improving mobility or walking ability, especially in bilateral cases.

Stability was the one factor in which most patients considered they were worse off, and this instability may be associated with the shortening that occurs, and with it the shortening of the abductus. Loosening of the stem of the prosthesis, early migration along the line of the axis of the neck, and new bone formation in the capsule, were complications noted radiologically.

It is concluded that at the present stage of progress in the development of arthroplasty, the use of the Austin-Moore prosthesis with acetabular reaming has very limited indications.

A. Kates


Surgical treatment of chronic arthritis of the hip is usually a compromise between relief of symptoms and preservation of function in the joint, and replacement of femoral head and acetabulum by metal prostheses
cemented into bone gives both relief of pain and restoration of a useful range of joint movement.

There is a large group of elderly patients with stiff painful hips in whom neither McMurray osteotomy nor arthrodesis is satisfactory, but who will benefit by an arthroplasty.

A replacement ball-and-socket type of artificial joint has been developed at Norwich during the past 15 years, and consists of a modified Thompson prosthesis as the femoral component, articulated with an acetabular prosthesis, and cement is used to anchor both components to bone. The prostheses are constructed of chrome-cobalt alloy.

Operation is performed through an antero-lateral approach, and post-operatively active exercises are commenced the day after operation. Usually by the end of the first week, the patient can walk with crutches, and full weight-bearing is achieved at the end of a fortnight; length of stay in hospital varies from 2 to 3 weeks.

The results have been encouraging: 47 of the first fifty cases had excellent or good results.

The very few difficulties met after this operation were due to technical faults, and all were corrected at revision.

There has been very little trouble from infection; one patient had superficial infection which cleared with antibiotic treatment, and a second hip developed a sinus reaching into the joint.

The question “How long will they last?” can be answered only by the passage of time, but experience of this procedure since 1956 is encouraging. This series has a success rate of over 90 per cent. but with the present state of our knowledge it is strongly advised that the operation be reserved for older people. A. Kates


Reaction of Patients with Inflammatory and Non-Inflammatory Joint Changes to Treatment with Sulphurated Spring Waters. (Reaktion von Kranken mit entzündlichen und nicht entzündlichen Gelenkveränderungen auf Behandlung mit einer Schwefel-Sol-Thermalquelle.) EVERS, A. (1967). *Z. Rheumaforsch.*, 26, 73. 5 refs.


Early Effects of Hydrocortisone on rapidly labelled Rat Liver Ribonucleic Acids. VENKOV et al. (1967). *Nature (Lond.*), 213, 807.


Kidney Failure due to Phenybutazone. (Les accidents rénaux de la phénybutazone.) BLOCH-MICHEL et al. (1966). *Presse méd.*, 74, 2671.


Relation between Cholesterolemia and the Uricemia caused by Ingestion of Ribonucleic Acid. (Relación entre la colesterolemia y la uricemia elevada por la ingesta de ácido ribonucleico.) GRAMAJO, R. J., CIEGOORIANSKY, J., PAVE, L., and SALOMONE, J. (1965). *Arch. argent. Reum.*, 28, 14.

Role of Knee Synovectomy in Complex Treatment of Infectious Non-Specific Polyarthritis. PAVLOV, V. P. (1966). *Vop. Reum.*, No. 4, p. 64. 6 refs.

