South African Medical Journal
Suid-Afrikaanse Tydskrif vir Geneeskunde
P.O. Box 643, Cape Town Posbus 643, Kaapstad

Cape Town, 23 April 1955
Weekly 2s. 6d.

Vol. 29 No. 17

Kaapstad, 23 April 1955
Weekliks 2s. 6d.

EDITORIAL

RHEUMATOID ARTHRITIS

There has been great interest in rheumatoid arthritis and diseases thought to be related to it since the discovery a few years ago that cortisone and other steroids produce symptomatic improvement in these conditions. However, the earlier hopes about such therapy have not been fulfilled, and until the true cause of these disorders becomes established the chances of curative treatment becoming available are not very great.

At present the only reason for grouping the 'rheumatic' diseases together seems to be the common site of their primary lesions in the connective and supporting tissues. The onset of rheumatoid arthritis has been attributed to a number of predisposing or precipitating factors, but these theories have mostly been based on clinical impressions and on statistically uncontrolled studies. A controlled investigation a few years ago by the Empire Rheumatism Council [1] and other workers [2] indicated that a familial history of arthritis, exposure to cold, and peripheral circulatory disorders, occurred in a significant number of the cases.

There is no good evidence that focal sepsis is of any significance in the pathogenesis of rheumatoid arthritis, although the concept is by no means yet abandoned. There is considerable evidence against a streptococcal origin of the disease, despite the high titre of haemolytic streptococcal agglutinins present in the serum in active rheumatoid arthritis and the ease with which a chrome polyarthritis can be produced experimentally. It would appear that streptococci are of no significance in the pathogenesis of rheumatoid arthritis although streptococcal infection is a possible factor precipitating the onset of the disease or its recurrences. The streptococcal agglutinins in the serum are presumably non-specific and non-antigenic in nature. There is believed to be an abnormal globulin factor in the serum in rheumatoid arthritis which accounts for the tendency of such sera to precipitate spontaneously in saline, and which probably exaggerates the action of naturally-

VAN DIE REDAKSIE

MISVORMENDE GEWRIGSONTSTEKING

Sedert dit 'n paar jaar gelede ontdek is dat cortisone en ander steroïede die simptome van misvormende gewrigsontsteking en vermoedelik verwante siektes verlig, wek hierdie toestande groot belangstelling. Die vroeë verwagtings van hierdie terapie is egter nie verwesenlik nie en totdat die juiste oorsaak van hierdie kwale vasgestel word is die kanse vir helende behandeling maar skraal.

Die enigste rede waarom ‚rumatiek'-siektes tans saamgegroepeer word, is waarskynlik daaraan te danke dat in al hierdie kondisies die vernaamste letsels in die bind- en die stutweefsels voorkom. Misvormende gewrigsontstekingaanvalle word aan 'n aantal predisponerende of presipiterende faktore toegeskryf maar hierdie teorieë is grotendeels gebaseer op kliniese indrukke en studies wat nie statisties gekontroleer is nie. 'n Gekontroleerde ondersoek wat 'n paar jaar gelede deur die Empire Rheumatism Council [1] en ander werkers [2] ingestel is, het aan die lig gebring dat 'n familiegeskiedenis van gewrigsontsteking, blootstelling aan koue en ongesteldhede van die perifeerbloedsomloop in 'n aansienlike aantal gevalle voorkom.

Daar is geen grondige bewys dat haardbesmetting 'n veroorsakende faktor in die ontstaan van misvormende gewrigsontsteking is nie, alhoewel hierdie teorie nog glad nie op die lang baan geskuif is nie. Daar bestaan heelwat bewyse teen 'n streptokokke-oorsprong, ten spyte van die hoë titer van hemolitiese streptokokke-agglutiniene wat met aktiewe misvormende gewrigsontsteking in die serum gevind word en die gemak waarmee 'n uitgebreide chroomgewrigsontsteking eksperimenteel teweeggebring kan word. Oënskynlik speel streptokokke geen rol in die ontstaan van die siekte nie alhoewel streptokokkusinfeksie moontlik as presipiterende faktor in aanvalle of hernude aanvalle ageer. Die streptokokkus-agglutiniene in the serum is vermoedelik nie-spesifiek en nie-antigenies van aard nie. Dit word gemeen dat in misvormende gewrigsontsteking 'n abnormale globulienfaktor in die serum aanwesig is, wat verantwoordelik is vir die neiging van dié serum om in 'n soutoplossing spontaan neer te slaan, en wat waarskynlik die aksie verhoog van presipitiene vir streptokokkus- en pneumokokkus-fraksies wat natuurlik voorkom.

Gordon [3] het geredeneer dat 'n groep spesifieke virusse

occurring precipitins for streptococcal and pneumococcal fractions.

Gordon [3] has argued that a group of specific viruses with selective affinity for connective tissue may be the cause of the disorder in rheumatic diseases and, though it seems unlikely that the lesions of rheumatoid arthritis are due to a virus,[4, 5] this cause cannot as yet be definitely excluded.

The Empire Rheumatism Council in its investigation [1] found no significant relationship between psychic trauma and the onset of the disease. There are some who classify rheumatoid arthritis as a psychosomatic disorder, but most physicians do not regard the disease as having this origin although emotional disturbances are accepted as having a relationship to fluctuations in the disease. There is no evidence definitely to connect avitaminoses with the disease; a deficiency of ascorbic acid is more likely a result rather than a causal factor in rheumatoid arthritis. As regards endocrine dysfunction evidence is available that abnormal steroid metabolism may be present, but whether this is a result of the disease or a cause it is impossible to state at present. Although the adrenal steroids modify the reaction their effects are not specific and they have not yielded direct information on the aetiology of rheumatoid arthritis; their therapeutic effects have of course given a great stimulus to the study of the pathogenetic mechanisms.

The term 'collagen-vascular diseases' has been used for the group which includes rheumatoid arthritis, rheumatic fever, polyarteritis nodosa, and dermatomyositis. There is a non-specific disturbance involving connective tissues, especially the extracellular elements, which is observed microscopically as a form of 'fibrinoid' degeneration and a profound physicochemical alteration of the interfibrillar ground-substance and possibly of the scleroprotein fibres also. A knowledge of the nature of this basic change might throw light on the pathogenesis of these disorders. The subject is obviously one of great complexity. The evidence seems to support the view that the inflammatory and toxic features of rheumatoid arthritis result from primary disintegration of collagen. The concept of rheumatoid arthritis as one of the connective-tissue diseases does not however necessarily imply a unified aetiology for the whole group.

A lengthy and excellent review on the aetiology and pathogenesis of rheumatoid arthritis has recently been published,[6] in which not only the factors referred to above are discussed fully but also other aspects of rheumatoid arthritis, such as the question of hypersensitivity of the tissues and Selye's concept of disorders of adaptation. Our knowledge of rheumatoid arthritis has greatly advanced in recent years but the factors predisposing to or maintaining the disease have not been clearly established.

1. Empire Rheumatism Council (1950): Brit. Med. J., **1**, 799.
2. Short, C. A. *et al.* (1949): Ann. Rheum. Dis., **8**, 313.
3. Gordon, M. (1948): Lancet, **1**, 697, 740.
4. Levinsky, W. J. and Lansbury, J. (1951): Proc. Soc. Exp. Biol., **78**, 325.
5. Bauer, W., Clark, W. S. and Dienes, L. (1951): Practitioner, **166**, 5.
6. Dresner, E. (1955): Amer. J. Med., **18**, 74.

met 'n selektiewe affiniteit vir bindweefsels vir rumatiekkwale verantwoordelik mag wees en alhoewel dit onwaarskynlik is dat die letsels van misvormende gewrigsontsteking aan 'n virus te wyte is [4, 5] kan dit nog nie definitief as 'n oorsaak uitgeskakel word nie.

Die ondersoek van die Empire Rheumatism Council het geen noemenswaardige verwantskap tussen psigiese trauma en 'n aanval van hierdie siekte aan die lig gebring nie. Daar is diegene wat misvormende gewrigsontsteking as 'n psigosomatiese kwaal bestempel, maar die meeste geneeshere glo nie dat dit die oorsprong van die siekte is nie alhoewel dit aanvaar word dat daar 'n verhouding bestaan tussen emosionele steurings en wisselings in die siektetoestand. Dit is nie definitief bewys nie dat daar enige verband tussen hierdie siekte en 'n vitamiengebrek is nie; dit is meer waarskynlik dat 'n tekort aan vitamien C eerder 'n gevolg as 'n oorsakende faktor in misvormende gewrigsontsteking is. Wat die onreëlmatige werking van die buislose kliere betref is dit bewys dat abnormale steroïde-metabolisme aanwesig mag wees maar tot nog toe is dit onmoontlik om te konstateer of dit die gevolg of die oorsaak van die siekte is. Alhoewel byniersteroïde die reaksie beïnvloed is hul uitwerking nie spesifiek nie en verstrek hul nie direk inligting oor die etiologie van misvormende gewrigsontsteking nie; vanselfsprekend het hul terapeutiese gevolge die studie van die patogenetiese meganismes aangewakker.

Die benaming ‚kollageenvatsiektes' is vir dié groep gebruik wat misvormende gewrigsontsteking, rumatiekkoors, knopvormige slagaarontsteking en dermatomyositis behels. Daar is 'n nie-spesifieke steuring wat die bindweefsel, veral die buitesellulêre elemente, raak wat onder die mikroskoop as 'n vorm van fibrienagteruitgang en 'n groot fisies-chemiese verandering van die tussenfibrillêre grondstof (en moontlik ook van die skleroproteïenvesels) gesien word. Kennis van die aard van hierdie basiese verandering mag lig op die ontstaan van hierdie siekte werp. Hierdie onderwerp is ongetwyfeld 'n baie ingewikkelde een. Die gegewens blyk die opvatting te staaf dat die ontstekings- en vergiftigingseienskappe van misvormende gewrigsontsteking op die primêre disintegrasie van die kollageen volg. Die mening dat misvormende gewrigsontsteking 'n bindweefselsiekte is, behels nie noodwendig die opvatting dat die oorsaakleer vir die hele groep dieselfde is nie.

'n Breedvoerige en puik oorsig van die oorsaakleer en die siekte-ontstaan van misvormende gewrigsontsteking is onlangs gepubliseer,[6] waarin nie net die bogemelde faktore ten volle bespreek word nie maar ook ander aspekte van misvormende gewrigsontsteking soos byvoorbeeld die kwessie van oorgevoeligheid van die weefsels en Selye se opvatting van aanpassingsmoeilikhede. Ons kennis van misvormende gewrigstontsteking het in onlangse jare baie gevorder maar die faktore wat hierdie siekte in stand hou of daartoe predisponeer is nog nie duidelik vasgestel nie.

1. Empire Rheumatism Council (1950): Brit. Med. J., **1**, 799.
2. Short, C. A. *et al.* (1949): Ann. Rheum. Dis., **8**, 313.
3. Gordon, M. (1948): Lancet, **1**, 697, 740.
4. Levinsky, W. J. and Lansbury, J. (1951): Proc. Soc. Exp. Biol., **78**, 325.
5. Bauer, W., Clark, W. S. en Dienes, L. (1951): Practitioner, **166**, 5.
6. Dresner, E. (1955): Amer. J. Med., **18**, 74.

POLIO VACCINE

The results of the great American experiment with the Salk polio vaccine were announced at the University of Michigan on 12 April, and from the messages which were published in the South African press the next day it appears that the hopes of the promotors of the mass test have been realized. As in all field tests of this kind, the interpretation of the results is a problem for statisticians. The controversy that arose out of the early results—and indeed the later results—of the use of B.C.G. as a prophylactic against tuberculosis will be remembered. The medical profession in South Africa are therefore compelled to wait until the official reports from America reach this country before they can come to final conclusions. These reports are expected to arrive shortly; copies may indeed be available here by the time this issue of the *Journal* is published.

The press messages report Dr. Thomas Francis, who is in charge of the evaluation, as saying that the vaccine was found to be 80 or 90 per cent effective in preventing paralytic polio, but other disconnected figures are given which cannot be interpreted without fuller details. It is stated that the results varied for the 3 types of poliovirus. The question of the duration of immunity has received attention and the messages include the statement that the effect was maintained with but moderate decline after 5 months. The vaccine was found to be very safe in use, the messages stating that only 0·4 of 1 per cent of the children injected suffered from minor reactions and that major reactions were almost entirely absent.

In view of these statements the official reports may be awaited with a high degree of confidence, for the mass experiment was designed and the results analysed in order to give trustworthy replies to the questions to which answers were wanted. They will be of particular interest in South Africa because the work of producing a polio vaccine similar to the Salk vaccine is far advanced at the laboratories of the Poliomyelitis Research Foundation where, although the vaccine has not yet been tested on human beings, enough of it is in stock to vaccinate the whole population of the Union. South Africa is one of the few countries in the world which have seriously attacked the task of producing a prophylactic polio vaccine.

The news about the polio vaccine naturally provokes comparison with anti-diphtheria inoculation. In both the routine is a series of 3 injections at intervals of a few weeks, with a possibility that 2 injections may be adequate, especially if later reinforced by a 'booster' dose. The practical problems therefore appear to be similar. The case for universal protective inoculation of children is not the same in the two diseases. In diphtheria the deaths that occur in the community when the disease is uncontrolled are far more numerous than ever happen from poliomyelitis. Poliomyelitis becomes epidemic at certain times and places, but at any one time it is in an endemic phase in most parts of the world, when the amount of mortality for years on end, and even the number of cases, may be practically negligible. The dread which polio inspires in the community when it becomes epidemic in a country is due to the disabling crippling that is the common sequela of a paralytic attack. The impression that this made on South Africa a few years ago was reflected in the public response to the appeal for funds to combat the disease.

It may be expected that in America, where the present mass experiment has been followed with enormous nation-wide interest, a relatively complete inoculation of the child population against polio will soon be under way, and the manner in which the prophylactic will be used in other countries will no doubt be influenced by the further experience which will thus be gained. The remarkable feature of immunization against the greater menace of diphtheria is that, in spite of its long-proven efficacy, in most parts of the world—South Africa included—public apathy has been sufficient to prevent the virtual abolition of diphtheria which a universal acceptance of inoculation in childhood would secure.