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EDITORIAL

ABNORMAL GLOBULINS

There are certain diseases of the reticulo-endothelial system in which plasma globulins with unusual properties can be demonstrated. These proteins lack uniform characteristics and may not always appear to be responsible for symptoms.

The presence in the blood of globulins precipitable by cold was first demonstrated in 1933 in a patient suffering from multiple myeloma,[1] an observation that was soon confirmed by numerous investigators. Later, in 1947, the term cryoglobulin was introduced to describe this type of protein.[2] Recent literature contains reports of studies on patients with 'essential cryoglobulinaemia'[3] and 'cryoproteinaemia'.[4]

These cryoglobulins are proteins which precipitate on cooling. The precipitate may be wholly or partially crystalline, or it may form a solid mass, which redissolves on warming. Complete precipitation, even at 0° C, probably never occurs. An approximate estimation of the amount present can be obtained by the 'protein-cryocrit' method.[5] The blood for these studies should be drawn into warm syringes and the serum or plasma separated at 37° C.

The molecular weight of the cryoglobulins varies from that of gamma globulins (150,000—170,000) to over one million. They probably represent broad groups of abnormal globulins, and their presence is usually a secondary phenomenon which is often, but not always, associated with an increase in the total amount of globulin.

The cryoglobulins are most frequently demonstrable in the blood of patients with multiple myeloma; the discovery of cryoglobulin should in fact lead to a careful search for that condition. Small quantities which are clinically unimportant (less than 25 mg. per 100 ml. of serum) can be demonstrated quite often in the serum in many disease states.[3] No regular relationship is found between the amount of cryoglobulin and the symptoms observed in cryoglobulinaemia (essential or secondary). Sensitivity to cold, Raynaud's phenomenon, purpura, haemorrhages, mottling of the legs, dyspnoea, cyanosis, and other features, have been

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ABNORMALE GLOBULIENE

Daar is sekere siektes van die retikulo-endoteelstelsel waarby globuliene met ongewone of uitsonderlike hoedanighede in die plasma aangetoon kan word. Daar is egter geen eenvormige stel kenmerke wat vir al hierdie proteïene geld nie en, oënskynlik, is hulle nie altyd verantwoordelik vir simptome nie.

Die aanwesigheid van koudbesinkbare globuliene in die bloed is vir die eerste maal in 1933 aangetoon by 'n pasiënt met 'n veelvoudige murggewas,[1] en hierdie waarneming is kort daarna deur verskeie navorsers bevestig. In 1947 het hierdie soort proteïen die naam krioglobulien gekry.[2] Die resente literatuur bevat verslae oor pasiënte met ‚selfstandige krioglobulienemie',[3] en ‚krioproteïenemie.'[4]

Hierdie krioglobuliene is proteïene wat by verkoeling neerslaan. Die neerslag kan geheel en al, of slegs gedeeltelik, kristallyn wees, òf dit kan 'n soliede massa wees wat by verwarming weer oplos. Heel waarskynlik kom volkome besinking nooit voor nie—selfs nie eers op 0°C nie. Die hoeveelheid aanwesig kan naasteby bereken word deur die ‚proteïen-kriokrietmetode'.[5] Vir hierdie toetse moet die bloed in warm spuite afgetrek word en moet die plasma of serum op 37°C geskei word.

Die molekulêre gewig van die krioglobuliene varieer tussen dié van die gammaglobuliene (150,000-170,000) en méér as een miljoen. Waarskynlik verteenwoordig hulle breë groepe abnormale globuliene, en hul aanwesigheid is gewoonlik 'n sekondêre verskynsel wat dikwels, hoewel nie altyd nie, gepaard gaan met 'n vermeerdering van die totale hoeveelheid globulien.

Die krioglobuliene kan veral in die bloed van pasiënte met 'n veelvuldige murggewas aangetoon word; wanneer hierdie globulien ontdek word, moet dit altyd rede wees vir 'n sorgvuldige ondersoek met die oog op dié siekte. Klein hoeveelhede wat klinies onbelangrik is (minder as 25 mg. op 100 ml. serum) kom nogal dikwels by verskeie siektetoestande in die serum voor.[3] Navorsers het nog nie 'n konstante verhouding waargeneem tussen die hoeveelheid krioglobulien en die simptome van selfstandige òf sekondêre krioglobulienemie nie. Gevoelig vir koue, Raynaud se verskynsel, huidbloeding, bloedstorting, vlekke op die bene, kortasemigheid, sianose en ander verskynsels is wel by hierdie siekte waargeneem. Gunstige resultate is reeds behaal met kortikotrofien by selfstandige krioglobulienemie; hierdie behandeling veroorsaak soms 'n

observed in association with the disorder. Favourable results have been obtained in essential cryoglobulinaemia by the administration of corticotrophin; under this treatment the concentration of cryoglobulin may or may not become significantly decreased.[3]

Macroglobulins are classified as a different group of abnormal globulins. They are proteins of a very high molecular weight, detectable only by ultracentrifugation. They differ in amino-acid composition from patient to patient. Trace amounts are found in normal sera examined by the ultracentrifuge. Small increases are frequently observed in hepatic cirrhosis, nephrosis and other conditions, but in multiple myelomatosis, of which cryoglobulinaemia is characteristic, the serum has seldom been found to contain macroglobulins. They may appear in the absence of detectable disease.

The syndrome of macroglobulinaemia, first described by Waldenstrom in 1944, has recently been reviewed.[5] In this syndrome the clinical features include lassitude, dyspnoea, bleeding from mucous membranes, pallor, oedema, enlarged liver and spleen, and mild enlargement of lymph nodes. The bone marrow shows infiltration with small atypical lymphocytic cells. The condition may have to be differentiated from certain other haematological syndromes by ultracentrifugal analysis. Treatment of the condition has been unsatisfactory, but death may not occur for several years if severe anaemia, infections and haemorrhages can be controlled or prevented.

The abnormal proteins of cryoglobulinaemia and macroglobulinaemia are probably produced in the reticulo-endothelial system. Occasionally the abnormal plasma-protein may include both a cryoglobulin and a macroglobulin. Their presence is not specific for any disease entity. The infections which are common in the presence of one or other of these two kinds of abnormal blood-globulin, are probably associated with failure of antibody formation.

1. Wintrobe, M. M. and Buell, M. V. (1933): Bull. Johns Hopk. Hosp., **52**, 156.
2. Lerner, A. B. and Watson, C. J. (1947): Amer. J. Med. Sci., **214**, 410.
3. Wolpe, R. *et al.* (1956): Amer. J. Med., **20**, 533.
4. Witschafter, Z. T. *et al.* (1956): *Ibid.*, **20**, 624.
5. MacKay, I. R. *et al.* (1956): *Ibid.*, **20**, 564.

belangrike vermindering in die konsentrasie van krioglobulien.[3]

Die makroglobuliene word as 'n ander groep van die abnormale globuliene beskou. Hulle is proteïene met 'n baie hoë molekulêre gewig, en kan alleenlik met die ultra-uitswaaimetode waargeneem word. Hulle aminosuursamestelling wissel van die een pasiënt tot die ander. Spoorhoeveelhede kan by ultra-uitswaai in normale serums aangetoon word. 'n Geringe vermeerdering word dikwels opgemerk by lewerskrompeling, niersiekte en ander aandoenings; dit word egter baie selde waargeneem dat die serum makroglobuliene bevat by 'n veelvuldige murggewas waarvan krioglobulienemie kenmerkend is. Hulle mag voorkom sonder dat enige siekte bespeur kan word.

Die sindroom van makroglobulienemie, wat in 1944 vir die eerste maal deur Waldenstrom beskryf is, is onlangs weer bespreek.[5] By hierdie sindroom kom kliniese tekens soos afgematheid, kortasemigheid, bloeding uit die slymvliese, bleekheid, edeem, vergrote lewer en milt, en matige vergroting van die limfknope voor. Die beenmurg toon insyfering deur klein atipiese limfosietselle. By sommige gevalle moet hierdie siekte deur ultra-uitswaai onderskei word van ander bloedsiektes. Dusver was behandeling van hierdie siekte maar onbevredigend, maar die pasiënt kan nog jare lank leef as ernstige bloedarmoede, besmettings en bloedings beheer of voorkom word.

Die abnormale proteïene van trio- en makroglobulienemie word waarskynlik deur die retikulo-endoteelstelsel voortgebring. Die abnormale plasmaproteïene kan by uitsonderlike gevalle beide krio- en makroglobuliene insluit. Hulle teenwoordigheid beteken nie noodwendig 'n bepaalde siekte nie. Die besmettings wat so dikwels voorkom as die bloed een van hierdie twee abnormale globuliene bevat, staan waarskynlik in verband met 'n versteuring in die vorming van teenliggaampies.

1. Wintrobe, M. M. en Buell, M. V. (1933): Bull. Johns Hopk. Hosp., **52**, 156.
2. Lerner, A. B. en Watson, C. J. (1947): Amer. J. Med. Sci., **214**, 410.
3. Wolpe, R. *et al.* (1956): Amer. J. Med., **20**, 533.
4. Witschafter, Z. T. *et al.* (1956): *Ibid.*, **20**, 624.
5. Mackay, J. R. *et al.* (1956): *Ibid.*, **20**, 564.

SALUTE TO ITALY

We have great pleasure in publishing, in English, in this issue of the *Journal* four articles kindly supplied by distinguished representatives of Italian Medicine. This gesture reciprocates the action, taken on 24 February 1953 by *Minerva Medica*, the medical journal of Turin, in publishing an issue exclusively devoted to South African Medicine and comprising several articles, translated into Italian, by South African medical authors. The exchange has been effected by the South African Council for the Exchange of Medical Sciences (Chairman, Dr. A. Shedrow), which has also been responsible for the appearance of South African issues of medical journals in other European countries. The selection of the articles by Italian authors published in our present issue was made by Prof. Tomaso Oliaro, editor-in-chief of the *Minerva Medica* group of journals, to whom we are greatly obliged.

The four articles are from the pens of Prof. B. Bastai (with Dr. M. Crepet), Prof. G. De Toni (of Genoa), Prof. Piero Fornara (of Novara), and Prof. Luigi Villa (of Milan, with Dr. C. B. Ballabio and Dr. G. Sala); and we have the pleasure of publishing with these articles messages from the Hon. Tiziano Tessirori, the Italian Minister of Health, and from the Hon. J. F. T. Naudé, Union Minister of Health, and a letter from Prof. Tomaso Oliaro.

On 9 May 1953, in recognition of the above-mentioned South African issue of *Minerva Medica* we wrote: 'It is our duty and pleasure to offer our hearty thanks to the *Minerva Medica* and to recognize with gratitude this notable expression of the goodwill of Italy and its medical profession towards our own country and profession. It is a manifestation of the international solidarity of Medicine, which indeed "knows no frontiers". We particularly value it as coming from that country and people who were in the van of the Renaissance and have ever been in the forefront of the Arts and Sciences and of Medicine. We greet our Italian colleagues, and we offer our salutations to their great nation'. We take the present opportunity of repeating and emphasizing these sentiments.

THE DOCTOR'S RIGHT TO DISPENSE

It is announced in the daily press that a meeting has been arranged, and will take place in Pretoria on 11 August, between the South African Medical and Dental Council and the South African Pharmacy Board, to discuss the claims that have been made by chemists and druggists concerning the right (or duty) of the doctor to supply medicines needed by his patients. The pharmacists' desires were embodied in the clause which was drafted for the Medical, Dental and Pharmacy Amendment Bill and which would have made it illegal for medical practitioners to supply medicine for their own patients within 5 miles of a municipality where a chemist's shop exists. This clause was deleted by the Government before the Bill was introduced last session, and the session came to an end before the Bill had advanced beyond the first-reading stage. The Minister of Health (the Hon. J. F. T. Naudé) was reported as hoping that the time before the next parliamentary session might be used for discussions between the professions interested in the clause.

The Association has expressed its willingness to take part in discussions, and the meeting between the Medical and Dental Council and the Pharmacy Board will be none the less welcomed on account of the fact that these bodies are for the protection not only of the rights and duties of the professions concerned with the prescribing and dispensing of medicines but also of the welfare of the public, and comprise other members besides doctors and pharmacists. No doubt the meeting will be the occasion of plain speaking. The views expressed in the *Journal*[1] on 9 June may be taken to be those held by doctors in general. They regard their traditional right to dispense and supply medicine for their patients as absolute, and they do not dispute that in the last resort it is also their duty. It is not many years since the majority of general practitioners dispensed their own medicine, and if most of them in town practice have chosen instead to give prescriptions to be dispensed by chemists they have done so on their own initiative and in the exercise of their undoubted right. The profession resents this attempt by chemists and druggists to bring legislative compulsion in this matter upon the ancient profession of medicine.

It is by a natural development that most doctors have virtually ceased to dispense, and it is only in accordance with the same development that a minority are continuing to dispense, whether by their own choice or because it is necessary for the reason that there is no chemist available. The development should be allowed to proceed without statutory intervention. If, indeed, ethical abuses are occurring in connexion with dispensing by doctors, as the chemists seem to allege, the South African Medical and Dental Council, which is concerned with the interests of the public as well as of the profession, is well able to deal with individual cases on complaint.

1. Editorial (1956): S. Afr. Med. J., **30**, 534.