South African Medical Journal : Suid-Afrikaanse Tydskrif vir Geneeskunde

Cape Town, 17 November 1962 Volume 36 No. 46 Deel 36 Kaapstad, 17 November 1962

EDITORIAL : VAN DIE REDAKSIE

THE ANTIVIRAL ACTION OF INTERFERON

The discovery and study of interferon have opened a significant chapter in virology and perhaps in clinical medicine, and the medical profession is following developments with great interest. An interesting review of present knowledge on the subject was made by Dr. A. Isaacs, of the National Institute for Medical Research, London, in his Almroth Wright Lecture given at the Wright-Fleming Institute on 21 May 1962, which was published in shortened version in the *British Medical Journal* of 11 August 1962.[1] In this lecture Isaacs brought under review the relevant work of himself and his colleagues and of other workers in the 5 years that have passed since he discovered interferon in collaboration with J. Lindenmann.

He said that interferon is produced by the cells of many different vertebrates when infected with any of a large number of different viruses. In virus-infected cultures interferon produces in the cells a resistance to destruction by the virus; and, with the accumulation of interferon in the cultures, complete cure of the virus infection may ensue.

Very young chick embryos are much more sensitive to the infection of certain viruses than older chick embryos, and the development of resistance corresponds in time with the production of interferon as the result of casual non-lethal virus infections. It is concluded that interferon plays an important part in recovery from virus infections in general, distinct from the part played by specific antibodies which operate in certain virus infections.

It has been found that virus infections both *in vitro* and *in vivo* are greatly influenced by variations in temperature. For instance some viruses in chick embryo cells grow best at 35°C. and others at 42°C. Poliovirus and poxvirus strains that can grow at higher temperatures are often more virulent than those that cannot. Facts of this kind suggest that fever, through its action on the growth of the virus, may play a part in recovery from virus infection; and the question has arisen whether the fever mechanism (and therefore the virulence of any particular virus) is related to the sensitivity of virus growth to temperature.

Investigation into this question has shown, with certain viruses studied in 10-day chick embryos, that the higher the optimal growth temperature the less resistant is the virus to interferon. Other experiments, dealing with the production of interferon rather than sensitivity to interferon, have been carried out in England and America. They showed, both with measles virus and poliovirus, that an avirulent strain caused a higher yield of interferon in a culture of human amnion cells than a virulent one. Another series of experiments was made on the hypothesis that a relationship of this kind might be general among viruses and, further, that viruses with a high optimal temperature for growth would give a smaller yield of interferon than those with a lower optimal temperature. And this in fact was the result obtained. It was also found, at any rate with avirulent strains, which grow less well at temperatures over 37°C., that the viruses under examination gave their best yield of interferon at the higher temperature.

Virulence, of course, is not a property of the virus alone but of the virus in relation to a particular kind of cell. Thus, the virus of Newcastle disease, which is virulent for chick embryos but not for man, grows well in cultures of chick cells (and inhibits interferon production), but does not grow in cultures of human thyroid cells (but stimulates these cells to produce interferon in high titre). Infection of chick cultures with the virulent Newcastle disease virus also blocks the production of interferon by the avirulent Chikungunya virus which would have occurred in the absence of the virulent virus. On the other hand, strains of influenza virus, which do not grow well in chick cells, do not inhibit this production of interferon caused by the Chikungunya virus. It appears, then, that a virulent virus operates by actively inhibiting the production of interferon. Moreover, it is better able to effect this inhibition at higher than at lower temperatures.

Three factors, then, were mentioned which decide whether a virus-cell interaction will result in the multiplication of the virus or in the production of interferon. These are: the virus (or, better, the virus virulence), the cell, and the temperature. Isaacs proceeds to mention 3 more factors. The fourth is the presence of interferon itself. Cells treated with interferon respond to virus infection by producing more interferon rather than by producing more virus. A fifth is the oxygen tension. Cells incubated in an atmosphere of nitrogen have been found to behave like cells treated with interferon, virus multiplication being completely inhibited while interferon production is not affected. The sixth factor is the pH. It has been shown that a pH of 6·8 inhibits the multiplication of certain polioviruses in the same way as a rise of temperature; and that at pH 6·8 cells infected with Sandbis virus produce more interferon than at pH 7·4 and are more sensitive than at pH 7·4 to the antiviral action of interferon. Isaacs indicates that still other factors can be added to the list.

He ends with the suggestion that perhaps interferon production is essentially a reaction of cells to a foreign nucleic acid, by analogy with antibody production as a reaction of the body to a foreign protein, and that virus virulence is in some way related to a subtle change in the viral nucleic acid by which it comes to seem less foreign to the new host.

1. Isaacs, A. (1962): Brit. Med. J., **2**, 343.

KWASHIORKOR — NOU 'N VERPLIGTE AANMELDBARE SIEKTE

Ons het alreeds by 'n vorige geleentheid[1] daarop gewys dat een van die mees verontrustende probleemgesteldhede in die beoefening van die moderne medisyne die feit is dat daar so 'n groot aantal toestande is waaraan ons baie sou kon doen as die omstandighede gunstig was, maar waaraan ons nou nie veel kan doen nie omdat die maatskaplike agtergrond soos 'n versperrende berg voor ons lê.

As 'n pertinente voorbeeld van hierdie toestand van sake het ons die probleem van ondervoeding by kinders genoem. Op die grond van verslae wat al meer dikwels in die mediese pers verskyn, is dit duidelik dat daar in hierdie land 'n baie groot aantal babas en klein kindertjies is wat gedoem is tot gebrekkige liggaamlike en geestelike ontwikkeling eenvoudig omdat hulle nie genoeg kos kry nie.

Een van die ernstige en dramatiese siektetoestande wat op grond van ondervoeding ontstaan, is kwashiorkor. In 'n studie van ongeveer 1,000 Kleurlingkinders oor 'n tydperk van 'n jaar, het Snyman en Murray,[2] byvoorbeeld, gevind dat kwashiorkor en uittering by 8·4% van dié kinders voorgekom het. Hierdie syfer word skrikwekkend as ons dit sien teen die agtergrond van die bevinding van Scrimshaw en Béhar,[3] wat aangetoon het dat vir elke *enkele* geval van kwashiorkor in die bevolking daar ten minste 'n *honderd* gevalle van onderliggende proteïengebrek is — 'n toestand waarna as pre-kwashiorkor verwys kan word.

Dit is dus met genoeë dat ons kan meld dat twee groot stappe onlangs gedoen is om 'n uitweg te probeer soek uit hierdie bedroewende toestand van sake. In die eerste plaas is kwashiorkor in terme van Goewermentskennisgewing Nr. 1481, wat in die *Staatskoerant* van 14 September 1962 verskyn het, nou 'n *verpligte aanmeldbare siekte verklaar* in the Republiek van Suid-Afrika. Hierdie progressiewe stap sal na verwagting nie net lei tot vroeër diagnose van gevalle nie, maar ook van hul behandeling.

Die ander positiewe stap dui nie net op diagnose en behandeling van toestande van ondervoeding nie, maar ook op 'n voorbehoedende benadering. Die proefskema ter bestryding van voedingskwale wat die Departement van Volksgesondheid verlede jaar in Pretoria, Durban en Kaapstad begin het om melkpoeier deur middel van plaaslike owerhede onder nie-blanke kinders tussen die ouderdomme van 6 maande en 5 jaar te versprei, het sulke bemoedigende resultate opgelewer dat die koste om dié program op 'n landwye skaal uit te brei, as heeltemal geregverdig beskou word. Daar is dan ook vanjaar R20,000 vir dié doel bewillig en, na verneem word, sal die Staat in die volgende begroting nog 'n bedrag vir dié doel beskikbaar stel.

Verslae wat reeds van plaaslike owerhede ontvang is, is besonder bemoedigend — sodanig so dat die moontlikheid van Staatsweë oorweeg word om die melkpoeierskema landwyd uit te brei — ook na die Bantoegebiede.

Hierdie soort benadering moet as 'n positiewe stap in die bekamping van tekortsiektes ten sterkste aangeprys word. Om regtig sukses te behaal, sal dit egter nodig wees om die gewete van die *hele gemeenskap* te prikkel sodat hierdie, en ook talle ander siektetoestande, wat, as hulle ongekontroleerd voortwoed, veel aan onkoste vir die Staat en menslike ontbering vir almal kos, verhoed kan word voordat dit nodig is om hulle te behandel.

1. Van die Redaksie (1961): S.Afr. T. Geneesk., **35**, 683.
2. Snyman, J. D. en Murray, A. B. (1961): *Ibid.*, **35**, 595.
3. Scrimshaw, N. S. en Béhar, M. (1959): Fed. Proc., **18**, 82.