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EDITORIAL : VAN DIE REDAKSIE

CHEMOPROPHYLAXIS AGAINST SMALLPOX

The efficacy of vaccination and revaccination is almost universally recognized in preventing the development of smallpox in persons who have been exposed to the infection. It is an essential factor in the methods ordinarily used for the prevention or control of smallpox, and properly applied it is in the main a thoroughly satisfactory measure. Until last year no chemical compound was available that was effective against the virus of smallpox.

In 1953, in their research into chemical viricides, Thompson *et al.*[1] discovered that isatin β-thiosemicarbazone was antiviral in mice infected with vaccinia virus. Later, in searching for anti-smallpox viricides, Bauer, of the Wellcome Laboratories, London, and his colleagues[2-4] investigated related compounds and discovered drugs with greater antiviral activity, particularly N-methylisatin β-thiosemicarbazone (compound 33T57, 'marboran'). Mice were inoculated intracerebrally with variola virus and then marboran was given during the incubation period and found to have a prophylactic action against smallpox infection.

In 1963 a field test of the prophylactic action of marboran was carried out[5] on the contacts of smallpox patients admitted to the Infectious Diseases Hospital, Tondiarpet, Madras, India (the term 'contact' being limited to persons who slept in the same room as the smallpox cases). The duration of illness on the day of admission ranged from 2 to 16 days (mean 6·9 days). The results analysed comprised 1,101 contacts treated with marboran and 1,126 not so treated (controls), the two groups having similar vaccination histories and age distributions. Most of these contacts had been vaccinated in infancy and were revaccinated shortly after admission to the hospital of the relative case of smallpox. The marboran was given in a syrup, its administration beginning on the first or second day after the removal of the relative smallpox patient to hospital. The dosage varied (for instance 12G or 24G over 4 days), and a placebo of similar appearance was given to those control contacts who lived near 'treated' contacts.

Among the 1,101 contacts treated with marboran there occurred 3 cases of smallpox, all mild, with no deaths; among the 1,126 control contacts 78 cases occurred, with 12 deaths. The authors point out that their detailed figures show that these striking results were independent of any immunity acquired as the result of vaccination. They find that the drug must usually have been given during the latter half of the incubation period, and that even when that was the case it nevertheless exerted a prophylactic action; and that prophylactic treatment with marboran effectively protected smallpox contacts who had never been vaccinated.

These striking results are of such importance that every further opportunity should be taken to explore the field they open up. If they are confirmed it is possible that marboran, or some other chemoviricide, may be established as a valuable adjuvant to, or even as a substitute for, vaccination in controlling smallpox outbreaks. Especially significant is the indication in the Madras field test that marboran is an effective prophylactic when given to susceptible contacts in the later part of the incubation period—a time when vaccination or revaccination is no longer effective.

Marboran was made available by Messrs. Burroughs Wellcome for use in the 1964 smallpox outbreak in the Eastern Cape Province; and an article by Dr. Duncan Ferguson appears in this issue of the *Journal* reporting on its use as a prophylactic on the contacts of one of the cases of smallpox in the Port Elizabeth Divisional Council area. This patient had been ill for about *8 days* before he was admitted to hospital, and on the day after admission the contacts were vaccinated or revaccinated and treatment of them with marboran was begun. Of the patient's 7 household contacts 4 developed smallpox, including his wife and 2 young children. The wife died. Dr. Ferguson rightly calls this result disappointing. No cases of smallpox occurred among the other 36 'close contacts', all of whom were vaccinated and treated with marboran at the same time as the 7 household contacts. The marboran was given in capsules twice a day for 48 hours, the total amount given being 12 G for adults and children over 10 years old, 6 G for children from 1½ to 9, and 3 G for babies under 18 months.

Of two closely comparable cases of smallpox, the 8 household contacts and a large number of other contacts were vaccinated or revaccinated 4 - 5 days after the initial febrile onset, but were not given marboran; and none of these developed smallpox.

Several authors refer to the possibility that marboran, by modifying the reaction to vaccination, may inhibit the effect of smallpox vaccination.[5, 6] Landsman and Grist[7] have compared the vaccination reactions in 2 groups each of 19 or 20 medical students, one group treated with marboran and one not, and found that the reults supported the suggestion of a limited inhibitory effect. This aspect of the problem, however, requires further investigation.

Nausea and vomiting, sometimes severe, have been mentioned by several authors[5, 7, 8] as side-effects of marboran.

1. Thompson, R. L., Minton, S.A., Officer, J. E. and Hitchings, G. H. (1953): J. Immunol., **70**, 229.
2. Bauer, D. J. (1955): Brit. J. Exp. Path., **36**, 105.
3. Bauer, D. J. and Sadler, P. W. (1960): Brit. J. Pharmacol., **15**, 101.
4. Bauer, D. J., Dumbell, K. R., Fox-Hulme, P. and Sadler, P. W. (1962): Bull. Wld Hlth Org., **26**, 727.
5. Bauer, D. J., St. Vincent, L., Kempe, C. H. and Downie, A. W. (1963): Lancet, **2**, 494.
6. Ferguson, D. L. (1964): S. Afr. Med. J., **38**, 868.
7. Landsman, J. B. and Grist, R. (1964): Lancet, **1**, 330.
8. Hutfield, D. C. and Csonka, G. W. (1964): *Ibid.*, **1**, 329.

STATISTIESE INDELING VAN SIEKTES, BESERINGS EN OORSAKE VAN DOOD

Die Staande Tegniese Advieskomitee, 'n subkomitee van die statutêre liggaam, die Sentrale Gesondheidsdienste en Koördineringsraad, het na 'n onlangse vergadering 'n brief aan die Suid-Afrikaanse Geneeskundige en Tandheelkundige Raad gerig waarin die Raad se aandag gevestig word op die onbevredigende wyse waarop kliniese rekords in die hospitaal deur medici voltooi word. As gevolg van die onvolledige rekords kan die voorkoms en indeling van siektes en oorsake van dood nie as 'n troue weergawe vir statistiese doeleindes aanvaar word nie. Herhaalde versoeke om die toestand te verbeter, het geen noemenswaardige verskil gemaak nie.

Die Raad is herinner aan die handige sakboekie wat kosteloos deur die Buro van Sensus en Statistiek, Pretoria, op aanvraag verskaf word en wat gebaseer is op die *Handboek van Internasionale Statistiese Indeling van Siektes, Beserings en Oorsake van Dood,* wat deur die WGO gepubliseer is. Hierin word voorsiening gemaak vir die kodifisering van siektes, wat voldoende sal wees vir statistiese doeleindes.

Die Raad het op 12 Augustus 1963 die volgende besluit geneem: ‚Dat die bewaring van kliniese rekords uiters belangrik is en dat alle geneeskundige praktisyns versoek word om hospitaalrekords behoorlik te voltooi vir statistiese doeleindes deur gebruik te maak van die kodenommers wat in die kortlys van die genoemde handboekie verskyn.'

Die Raad het 'n vriendelike beroep gedoen dat alle medici landswyd versoek word om uitvoering aan die bogenoemde besluit te gee. Indien dit nie geskied nie, sal die moontlikheid oorweeg word om dit deur middel van wetgewing 'n vereiste te maak.

Daar word gehoop dat geneeshere sonder sodanige dwang sal saamwerk.

NON-PROFIT DRUGS

Whenever the high cost of medical treatment is discussed, an accusing finger is pointed at the drug industry as being primarily responsible for this state of affairs. It is then pointed out that pharmaceutical firms show vast profits; that they flood the profession with unnecessary advertising material; that they squander on their handouts of free samples; and that they are adamant in their preference for trade names over generic names in order to promote their sales.

There is another side to the story. A recent survey shows[1] that there is a steady rise in 'service items' for the benefit of the medical profession and their patients, made without any hope of financial gain. Five years of investigation, legislation and regulation—and subjection to unprecedented public approbrium—have not curbed the pharmaceutical industry's willingness to provide the world, not only with drugs from which reasonable profit can be expected, but also with products which offer no hope of financial gain. In fact, a comparison with a similar survey in 1960 shows that the industry's willingness to devote time, money and effort to the development and distribution of life-saving, but unprofitable, products is on the increase. In 1960 there were 35 such drugs available for relatively rare diseases. This list has been expanded and now includes at least 51 such 'non-profitable' drugs. The list shows that the number of patients who constituted the entire market for each specialty in the United States ranged last year from a low of 5 to a high of 18,200. In some cases, manufacturers were unable to pin-point the number of cases other than to advise that it is very few.

Even at the high figure of more than 18,000 the market is so limited that no reasonable price could cover the cost of research, development, clinical trials, quality control, manufacturing, and distribution. For this reason, manufacturers generally either establish a nominal price or simply donate the product at the request of a physician.

In any criticism levelled at the drug companies, this service should be remembered, as also their willingness to cooperate with the profession in providing information about their products and their uses, the publication and circulation of informative scientific information, making study scholarships and grants available, financing medical and surgical lectures, and, not the least, the fact that they devote much time to experimentation in order to provide safer and more efficient remedies for the diseases that are prevalent today.

1. *American Druggist,* 20 July 1964, p. 11.

VOORKOMING VAN MIGRAINE

Metisergied, 'n alkaloïed van ergot en een van die kragtigste serotonin-antagoniste, het in die afgelope tyd buitengewone belangstelling gaande gemaak weens sy vermeende terapeutiese waarde in die voorkoming van migraine. Die resultate van 'n gekontroleerde proefneming op pasiënte wat minstens eenmaal in 14 dae 'n aanval van migraine kry, is deur Neville Southwell en sy medewerkers[1] bekendgemaak. Dit dui daarop dat die middel 'n waardevolle plek beklee in die behandeling van hierdie toestand. Die proefneming is gemaak op 53 pasiënte (41 vroue en 12 mans), met ouderdomme wat van 13 tot 62 jaar gewissel het (gemiddeld 38·9) en wat vantevore nie behoorlike verligting kon kry deur die neem van die bestaande middels nie. Van hulle het 34 die proefneming voltooi, nadat 17 weens die newegevolge van die middel uitgeskakel is, asook 'n verdere 2, wie se verslae onvolledig voltooi is. 'n Dosis van 6 mg. van metisergied daagliks is aanvanklik toegedien, maar weens newegevolge moes dit in sommige pasiënte na 3 mg. daagliks verminder word. Baie minder hoofpyn het onder die pasiënte voorgekom wat die middel gebruik het as onder dié wat die placebo geneem het. Statisties was die verskil aansienlik. Van die pasiënte wat aanvanklik metisergied ontvang het, maar gedurende die tweede helfte van die toets tot die placebo oorgeskakel is, se aanvalle van hoofpyn is ook verminder, wat dui daarop dat metisergied 'n verlengde uitwerking toon. Newegevolge wat by sommige voorgekom het, was mislikheid en versteuring van die balans. Dit het ook by 3 pasiënte voorgekom wat die placebo geneem het.

1. Southwell, N. *et al.* (1964): Lancet, **1**, 523.