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VAN DIE REDAKSIE

NUWE BENADERING TOT AANGEBORE AFWYKINGS

Oor die afgelope paar jaar het die etiologie van aangebore afwykings die belangstelling gaande gemaak, vandat Gregg[1] gerapporteer het dat aangebore katarak (wat altyd toegeskryf was aan oorerflike en genetiese misvorming) in baie gevalle gepaard gaan met en waarskynlik te wyte is aan rubella by die verwagtende moeder. Mediese navorsing het 'n nuwe sfeer van waarneming, met die kans op behandeling en voorkoming, betree.

Twee jaar vóór Gregg se verslag het Wolf, Cowen en Paige[2] feite voorgelê wat 'n protosoön, Toksoplasma, as 'n misvormende faktor blameer. Dit was egter Gregg se verslag wat die aandag van latere navorsers[3] geboei het—hulle was in staat om ook doofheid, hartgebreke en swaksinnigheid toe te skryf aan die baarmoederlike invloed van die rubella-virus.

Die jongste verslae kom van Cambridge, waar Millen en Woollam, uit die Departement Anatomie, die effek van kortisoon plus 'n oormaat van vitamien-A op die swanger rot bestudeer het. Hulle eerste verslag[4] rapporteer 'n groot vermeerdering in die voorkomssyfer van misvorming (36·6 persent) by die kleintjies van rotte wat aan die invloed van hierdie kombinasie onderwerp is, in teenstelling met 'n soortgelyke styging van 7·8 persent by die kleintjies van rotte wat met vitamien-A alleen behandel was en 0 persent by dié van rotte wat met kortisoon alleen behandel was. Cohlan[6] was die eerste om op te merk dat anencephalus, hidrocephalus en exencephalus méér dikwels voorkom by die werpsels van rotte wat gedurende swangerskap 'n oormaat van vitamien-A ontvang het. Die Cambridge-navorsers het hulle dit ten doel gestel om die eksperiment te herhaal, en om ook kortisoon aan die swanger rotte toe te dien.

Hulle tweede referaat[5] is nog meer indrukwekkend as die eerste; onder dieselfde omstandighede is 100 persent van die klein rotjies met 'n gesplete verhemelte gebore ná toediening van kortisoon en 'n oormaat vitamien-A aan hul moeders, terwyl 29·7 persent dieselfde afwyking getoon het op vitamien-A alleen, en nie een op kortisoon alleen nie.

In hul bespreking oor die onderwerp, herinner die skrywers ons daaraan dat Fraser *et al.*[7] opgemerk het dat ‚kortisoon 'n hoë voorkomssyfer van gesplete verhemelte veroorsaak by sekere (stamme van) rotte wat weens genetiese faktore reeds 'n neiging daartoe toon', en hulle besluit op grond van die vorige ondersoek dat ‚die aksie van kortisoon by die aanskakeling van die aksie van vitamien-A eerder 'n algemene dan 'n spesifieke werking is'. Hierdie verslag meld verder dat verskeie ander misvormings by die klein rotjies aangetref is, maar dat ‚slegs dié van die verhemelte in hierdie artikel bespreek word'.

EDITORIAL

NEW OUTLOOK ON CONGENITAL ANOMALIES

The aetiology of congenital deformities has been arousing interest in the last few years ever since the report by Gregg[1] that congenital cataract, which had always been considered a hereditary and genetic malformation, was in many cases associated with—and probably due to rubella in the mother during pregnancy. A new field of observation, with the possibility of therapy and prevention became opened to medical research.

Two years before Gregg's report, Wolf, Cowen and Paige[2] had brought forward evidence which had incriminated a protozoon, Toxoplasma, as a teratogenic agent, but it was Gregg's report that captured the imagination of later workers[3] who were able to ascribe also deafness as well as cardiac and mental deficiency to the intra-uterine influence of the rubella virus.

The most recently recorded papers come from Cambridge, where Millen and Woollam, reporting from the department of Anatomy, studied the effect of cortisone plus hypervitaminosis A on the pregnant rat. Their first paper[4] records a large increase in the incidence of teratomata (36·6%) in the offspring of the rats subjected to this combined influence as opposed to 7·8% in the young of rats treated with vitamin A alone and 0% in those of rats on cortisone alone. The original observation that anencephaly, hydrocephalus and exencephalus occur more frequently in litters from rats which had been overdosed with vitamin A during pregnancy had been made by Cohlan[6] and the Cambridge writers set out to repeat the experiment and, in addition, to give cortisone to the pregnant animals.

Their second paper[5] is even more remarkable; under the same circumstances 100% of the offspring showed a cleft palate on the combined administration of cortisone and overdosage of vitamin A, whereas 29·7% showed the same deformity on vitamin A alone, and none on cortisone alone.

Discussing the subject, the authors recall that Fraser *et al.*[7] recorded 'that cortisone produces an increased incidence of cleft palate in strains of mice in which there is already, for genetic reasons, a liability to the deformity', and conclude from the findings of the previous investigation 'that the action of cortisone in potentiating the action of vitamin A may be a general rather than a specific activity'. It is also indicated in the same paper that various other deformities

Hierdie gegewens is stof vir interessante teorieë. Gesplete verhemelte en haaslip was nog altyd toegeskryf aan 'n oorerflike fout. Dit is beskou as 'n genetiese neiging waarby die wakker klinikus die *formes frustes* kan uitken aan die kort bolip, hoog gewelfde verhemelte en kort bolipgleuf. Kinders met hierdie genetiese trekke is nie noodwendig met 'n haaslip of gesplete verhemelte gebore nie, en die nuwe navorsing dui daarop dat oorproduksie van kortisoon op 'n kritiese stadium van die moeder se swangerskap om die een of ander rede verantwoordelik kan wees vir die feit dat die verskillende gesigsdele nie sluit nie. Daar moet nou voortgegaan word met die navorsing op die gebied van die normale produksie van kortisoon tydens swangerskap en op die faktore wat hierdie produksie enigsins beïnvloed.

In hulle oorsig van die invloed van die rubella-virus op die fetus, het Aycock en Ingalls[8] sekere statistieke voorgelê wat daarop dui dat wanneer die moeder gedurende die eerste 6 weke van haar swangerskap Duitse masels kry, daar 'n hoë voorkomssyfer van katarak by die babas gevind word. As sy dit gedurende die eerste 9 weke kry, kom doofheid voor en, tussen die 5de en 10de week, kan dit hartgebreke en swaksinnigheid veroorsaak. Dit blyk dat die rubella-virus slegs op 'n kritiese stadium van sy ontwikkeling op die vrug inwerk, en moontlik is dit ook die geval met kortisoon. Navorsing moet gedoen word om die juiste tye (wanneer die vrug geaffekteer kan word) vas te stel sodat middels toegedien kan word—om die oorproduksie van kortisoon gedurende hierdie kort tydperk te bestry—aan die verwagtende moeder wie se familiegeskiedenis 'n hoë voorkomssyfer van gesplete verhemelte en haaslip toon.

Volgens die oorlewering, die volkskunde en ouvroue-praatjies sonder tal, word haaslip veroorsaak deur 'n besering of skok wat die verwagtende moeder opdoen, maar aangesien hierdie ‚gesaghebbendes' amper alle aangebore defekte só verklaar, het die mediese beroep nog nooit juis daarvan notisie geneem nie, en dokters was maar altyd geneig om die skouers op te haal. Maar vandag weet ons dat die kortisoonproduksie styg as gevolg van sekere soorte skok en skrik en weens die gevolglike spanning, en dit is heel moontlik dat die dokters verkeerd is en dat die ouvroue tog reg het.

1. Gregg, N. McA. (1941): Trans. Ophthal. Soc. Austral., **3,** 35.
2. Wolf, A., Cowen, D. en Paige, B. (1939): Science, **89,** 226.
3. Swan, C., Tostevin, A. L., Moore, B., Mayo, H. en Barham Black, G. H. (1943): Med. J. Austral., **2,** 201.
4. Millen, J. W. en Woollam, D. H. M. (1957): Brit. Med. J., **2,** 196.
5. Woollam, D. H. M. en Millen, J. W. (1957): *Ibid.*, **2,** 197.
6. Cohlan, S. Q. (1953): Science, **117,** 535.
7. Fraser, F. C., Kalter, H., Walker, B. G. en Fainstat, T. D. (1954): J. Cell. Comp. Physiol., **43,** Suppl., p. 237.
8. Aycock, W. L. en Ingalls, T. H. (1946): Amer. J. Med. Sci., **212,** 366.

were encountered in the young, but that 'only those affecting the palate were considered in the present communication'.

All this leads to very interesting speculations. Cleft palate and harelip have always been considered as being due to some hereditary fault. It was a genetic tendency in which *formes frustes* could be recognized by the astute clinician in the short upper lip, the highly arched palate and the short philtrum. Not every child with these genetic characteristics was born with a harelip or a cleft palate and the new work suggests that for some reason or another, overproduction of cortisone by the mother during a critical stage of the pregnancy may be responsible for the failure of the various facial processes to unite. The field is now open for research on the normal production of cortisone during pregnancy and on the factors responsible for maintaining or altering this production.

In considering the effect of rubella virus on the foetus, Aycock and Ingalls[8] brought forward figures which indicated that rubella contracted in the first 6 weeks of pregnancy led to a high incidence of cataracts in the babies, during the first 9 weeks to deafness and in the 5th-10th week to cardiac and mental deformities. The rubella virus seems to act on the embryo at a critical stage of its development only, and the same may be true of cortisone. Research to establish the exact time relations of this stage is necessary so that drugs to combat the overproduction of cortisone during this short critical period might be given to pregnant women whose family history shows a high incidence of cleft palates and harelips.

Tradition, folklore and innumerable old wives' tales have insisted that harelip is caused by some injury or fright sustained by the expectant mother but, as almost every congenital defect has been ascribed by the same authorities to the identical cause, medical opinion has not paid great respect to this theory and doctors have tended to pooh pooh the old wives' tales. In view of the fact that the production of cortisone is now well known to be increased by certain forms of fright and its resultant stress, it may well be that the doctors will turn out to be wrong, and that the old wives may be right after all.

1. Gregg, N. McA. (1941): Trans. Ophthal. Soc. Austral., **3,** 35.
2. Wolf, A., Cowen, D. and Paige, B. (1939): Science, **89,** 226.
3. Swan, C., Tostevin, A. L., Moore, B., Mayo, H. and Barham Black, G. H. (1943): Med. J. Austral., **2,** 201.
4. Millen, J. W. and Woollam, D. H. M. (1957): Brit. Med. J., **2,** 196.
5. Woollam, D. H. M. and Millen, J. W. (1957): *Ibid.*, **2,** 197.
6. Cohlan, S. Q. (1953): Science, **117,** 535.
7. Fraser, F. C., Kalter, H., Walker, B. G. and Fainstat, T. D. (1954): J. Cell. Comp. Physiol., **43,** Suppl., p. 237.
8. Aycock, W. L. and Ingalls, T. H. (1946): Amer. J. Med. Sci., **212,** 366.