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EDITORIAL : VAN DIE REDAKSIE

PITUITARY-ADRENAL RESPONSE AFTER STEROID THERAPY

The possibility of adrenal collapse following long-term therapy with a corticosteroid drug frequently arises. A number of questions may be asked: For how long and in what dosage is it completely safe to give such drugs? Should ACTH be administered during or at the end of a course of steroids? How long will it be before the pituitary-adrenal axis will be sure to work normally? Is permanent adrenal unresponsiveness ever caused by steroid drugs? Can adrenal unresponsiveness be prevented by intermittent therapy? Among other workers, Danowski and his colleagues[1] from Pittsburgh have helped considerably in answering some of these questions.

They observed and investigated six different groups of patients—a group of 117 females who received small ('replacement-displacement') doses of steroids, a group of 3 diabetics and 42 healthy adult males who took continuous small dosage of hydrocortisone or dexamethasone for 36 months, a group of 6 patients who had taken pharmacological doses of steroids for over 4 years, 5 adults who had received large doses of steroids for proteinuria, 11 healthy adult males who received 300 mg. of hydrocortisone daily for 30 days, and finally 2 adult females with Cushing's syndrome resulting from an adrenal adenoma.

From this experience it would appear that small doses of adrenal steroids may be administered continuously for years without clinical evidence of pituitary-adrenal unresponsiveness. Thus, the ingestion of 20 mg. of hydrocortisone or related steroids in equivalent amounts (that is in replacement or replacement-displacement dosages) per day for as long as several years by 117 patients with acne, hirsutism, etc., was not attended by any events suggestive of hypopituitarism or hypoadrenocorticism. On 80 occasions these patients passed uneventfully through stressful diagnostic procedures, wedge resection of the ovaries, etc., without supplementary steroids, and indeed without their usual small doses of steroids.

Metopirone normally leads to an increase in the excretion of 17-hydroxycorticoids in the urine. This response is not present if any part of the pituitary-adrenal axis is damaged. During prolonged and uninterrupted small-dosage steroid therapy Danowski found that lack of response to intravenous metopirone might develop, but was temporary and did not indicate that surgical stress would prove hazardous. Thus, the administration of hydrocortisone (20 mg. and then 10 mg.) and then dexamethasone, 0·75 mg. per day, to 42 healthy adult males for 3 years was attended by pituitary-adrenal unresponsiveness to intravenous metopirone during, but not 5 weeks after, such therapy. Fifteen major or minor surgical procedures were performed on these men during temporary interruption of the steroid therapy without circulatory collapse or other untoward event.

The authors found further that large amounts of steroids could be given daily for at least 1 month without fear of subsequent pituitary-adrenal hypofunction. Thus the daily ingestion of 300 mg. of hydrocortisone for 30 days by 11 healthy adults did not prevent the usual steroid responses to intravenous metopirone when tested 5 weeks after completion of therapy. Furthermore, the results of their experience indicated that large daily doses might be continued for 1 year or longer before residual pituitary-adrenal hypofunction could be expected in some individuals. (Nevertheless we do not believe it should be taken for granted that everyone could take large doses of steroids for a month without any effect on the pituitary-adrenal axis.)

If large doses of steroids must be given for long periods, Danowski suggests that an intermittent schedule (3 - 5 successive days on the drug in each week) is generally not associated with pituitary-adrenal hypofunction. Thus, in 10 patients treated for up to 7½ years on such a schedule, responses to intravenous metopirone were normal in 9 and diminished, but present, in one. Thorn and his colleagues[2] have presented evidence to show that the same effect may be obtained by administering the usual 2-day dose of steroid at one time every 48 hours.

1. Danowski, T. S., Bonessi, J. V., Sabeh, G., Sutton, R. G., Webster, M. W. and Sarver, M. E. (1964): Ann. Intern. Med., **61**, 11.
2. Harter, J. G., Reddy, W. J. and Thorn, G. W. (1963): New Engl. J. Med., **269**, 591.

GENEESKUNDIGE ALMANAK : JULIE

Vroeër Quintilis genoem toe dit nog die vyfde maand van die ou Romeine was. Sedert Julius Caesar se dood is die maand na hom vernoem. Volgens oorlewering is hy deur keisersnit verlos, vandaar moontlik die term ‚caesarean section'. Sommige meen egter dat die term van die Latynse woord *caedere* kom wat beteken om te sny. Van geneeskundige belang is die feit dat díe prosedure aanvanklik slegs vir die verlossing van babas uit gestorwe moeders gebruik is, soos ook neergelê in die wet (*Lex Regia* van Numa): ‚Sie mater pregnans mortua sit, fructus quam primum caute extrahur'. Die eerste lewende kind en moeder wat op dié wyse verkry is in Engeland was in 1836 toe Knowles van Birmingham die operasie uitgevoer het.

In hierdie maand van 1818 was die Somerset Hospitaal prakties voltooi en die *Cape Town Gazette* berig dat ‚the hospital will be established on similar principles with those in Europe and he (Mr. Bailey) begs leave to remark, that nothing shall be wanting in his power, to render the same useful and comfortable'. Die dienstaat was: mnr. Abercrombie, inwonende chirurg; mnr. Lewis Jerome Bianchi, apteker; mnr. John Gordon, rentmeester; Reyland Miller, portier en ‚lunatic asylum keeper'; en mev. de Maen, matrone.

1 Julie 1858. Beide Charles Darwin en Alfred Russel Wallace (1823 - 1913) se referate voorgedra aan die Linneaanse Vereniging. Terwyl Darwin se *Origin of Species* in voorbereiding was, ontvang hy 'n manuskrip van Wallace *On the tendency of Varieties to Depart indefinitely from the Original Type.* Die basis van Darwin se idees was bondig daarin saamgevat, maar Darwin se beskrywing was meer akkuraat en bevat ook 'n volledige, logiese beredenering. Die artikel van Wallace het byna, uit fyngevoeligheid, vir Darwin gedwing om sy publikasie te onttrek, en die kompromis van gesamentlike referate is getref op advies van Darwin se vriende, Lyell en Hooker.

6 Julie 1885. Die lewe van die negejarige Joseph Meister, wat deur 'n hondsdol hond gebyt is op veertien plekke, word gered deur Louis Pasteur, met sy pasontdekte serum teen hondsdolheid. Dit sou sy roem ook gou na die verre Rusland laat versprei waar rabies onder die wolwe 'n groot risiko ingehou het vir die boerebevolking.

12 Julie 1813. Claude Bernard gebore. Grondlegger van die moderne fisiologie en die eksperimentele metode. Vader van die begrip dat die konstantheid van die milieu interieur 'n vrye lewe verseker: ‚La constance du milieu interieur est la condition de la vie libre'.

12 Julie 1821. Sir Charles Bell lewer referaat voor die Royal Society ‚On the Nerves, giving an account of some experiments on their structure and functions, which lead to a new arrangement of the System'.

16 Julie 1916. Sir Victor Horsley oorlede. Britse grondlegger van die neurochirurgie. Sedert die Steentydperk het trepinasie die enigste kraniale chirurgiese prosedure gebly. Horsley het, deur 'n antiseptiese was voor te berei in medewerking met P. W. Squire, die probleem van bloeding uit die skedelbene oorkom (Horsley se Was: byewas 7 dele, amandelolie 1 deel). Verwyder in 1887 'n spinale tumor, die eerste van diè soort ingreep.

18 Julie 1849. William Osler gebore. Sy ouers wou hom Walter Farquhar doop, maar omdat sy geboorte saamval met die fees van die Oranje-manne wat die slag van Boyne (1688) gedenk, is hy William gedoop ter ere van Willem van Oranje. Hoewel hy een van die eerste beskrywers van die bloedplaatjies was, word hy, soos Herman Boerhave, merendeels onthou as mediese onderwyser en klinikus by uitstek. Sy liefde vir die klassieke tale en die geskiedenis het moontlik bygedra tot sy besondere filosofiese insig in die probleme van die geneeskundige praktyk.

22 Julie 1822. Gregor Johann Mendel gebore. Hierdie Oostenrykse monnik was ontevrede met die onsistematiese en luksraak resultate wat hy met hibriedes in die kloostertuin behaal het. Hy kies toe 7 kenmerke in ertjies, o.a. vorm van die ryp sade, kleur van die ertjies, posisie van blomme, ens., vir 'n sistematiese studie van sy resultate. Uit 7,324 ertjies so gekruis, is 5,474 rond en 1,850 grof. Hierdie 3:1 verhouding is in die meeste ander karakters in die eerste geslag gevind, terwyl die tweede geslag die 9:3:3:1 verhouding in geërfde eienskappe toon wat deur dominante, heterogene mengsel, en ressesiewe oorerwing van kenmerke verklaar word. So sleep hierdie monnik die wiskunde in die biologie in, en lê die grondslag van genetika waaruit die geneeskunde ook mettertyd sou baat.

23 Julie 1773. Abraham Colles gebore te Milmount, Kilkenny. President van die Ierse Kollege van Chirurge in 1802, d.w.s. vòòr hy 29 jaar oud was. Beskrywe Colles se fraktuur in 1814 ‚On the fracture of the Carpal Extremity of the Radius' in die *Edinburgh Medical and Surgical Journal.* Dit was byna 80 jaar voor die ontstaan van radiologie as hulpmiddel in ortopediese diagnose. Beskryf ook die fassia van Colles.

23 Julie 1828. Jonathan Hutchinson te Selby, Yorkshire, Engeland gebore. (Sien Junie se aantekeninge.)

24 Julie 1937. Redaksionele artikel in die *Suid-Afrikaanse Tydskrif vir Geneeskunde* verwys na die tekort aan Afrikaanse bydraes, en wys ook daarop dat die fout by die skrywers en nie by die redaksie lê nie.

25 Julie 1825. Pierre Charles Potain gebore te Parys. Vòòr Potain se ontdekking van die metode van aspirasie van vog uit die borskas, was ope insnydings vir pleurale dreinasie gebruik met skrikwekkende resultate. Sy metode van aspirasie deur 'n naald maak ook later die neem van naaldbiopsies van die pleura moontlik wat verdere beveiliging van die hantering van pleurale effusies inhou.

25 Julie 1963. Ugo Cerletti, ontdekker van elektrokonvulsie-terapie, oorlede in Rome op die ouderdom van 86 jaar.