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THE HAGEMAN FACTOR

People who perform silly tests must expect that sometimes they will get silly answers. In certain hospitals a patient who is admitted for almost any disease may be put through the diagnostic sieve. Since there is no shortage of laboratory tests this work up may only be limited by the patient's ability to pay for these tests. In many cases an extensive laboratory investigation is essential for diagnosis and treatment; occasionally a rather 'unnecessary' investigation yields surprising results. One such example led to the discovery of the Hageman factor.

There are apparently patients who have a very prolonged coagulation time although they give no history of severe haemorrhage. The relative insensitivity of the clotting time has been known for a considerable time. Many patients who are undoubtedly bleeders have a normal coagulation time. Probably if one were to investigate a large number of people who state that they bleed excessively, only a minority would be found to have a prolonged coagulation time. Even in the group of unquestioned haemophilics there are a considerable number who have normal coagulation times.[1,2] But one does not normally expect to find a prolonged coagulation time in a person who has no bleeding tendency. Yet cases such as this have been described.[3-5] In all these cases 'routine pre-operative' coagulation times were performed and the results were received with surprise. In none of these cases had excessive bleeding been a feature of the clinical story. Some of the cases had had major surgical procedures performed without incident before the test was made, and after the test surgery was also safely performed. The fact that the clotting time can be lengthened to 3 times the normal without indicating a significant haemorrhagic tendency raises the suggestion that the test as usually performed may have no practical significance, and that glass containers may introduce serious irrelevance. This would certainly be true if the discrepancy was encountered with any degree of frequency. It is, however, excessively rare, and pathologists who have time to look for such cases probably need to be provided with more useful occupation![6] However, investigations carried out on the blood of patients presenting this rare phenomenon have provided evidence of very great interest both from a practical and theoretical point of view.

The first patient in whom this phenomenon was investigated in detail was a certain Mr. Hageman; hence the name. The condition is apparently familial and a similar deficiency has been discovered in the blood of Peking ducks.[7] The blood of these patients is apparently insensitive to the effect of glass contact. That glass contact affects the coagulation of the blood has been known for a considerable time. In 1901 Bordet and Gengou[8] found that the clot-promoting effect of glass could be shown even after the bulk of the blood cells had been removed, and this work has been amply confirmed.[9-12] This clot-promoting effect of glass was demonstrable also in plasma which had been absorbed with barium sulphate (or aluminium hydroxide) and which had been heated to 56°C for 30 minutes.[11,12] Plasma so treated was devoid of most clotting factors but still contained the Hageman factor and the so-called Rosenthal's factor (PTA). Why glass should act in this way is not clear, but Ratnoff and Rosenblum[7] believe that an inhibitor is removed by contact with glass. They believe that glass exerts its clot-promoting effect by releasing Hageman factor from inhibition. Plasma from patients (or animals) deficient in Hageman factor impedes the clot-promoting effect of glass on normal plasma. However, once glass had been allowed to exert its effect on normal plasma the addition of Hageman-deficient plasma does not appreciably inhibit clotting. Margolis[12] reported that the accelerator which appeared when plasma was treated with glass was labile, since its activity appeared to be destroyed by some agent in the plasma. The concept is that the fluidity of the blood in the blood vessel is maintained by the presence of inhibitory substances directed against the Hageman factor and that exposure of blood to glass removes this inhibitor. The uninhibited Hageman factor then initiates or promotes clotting.

This clot-promoting effect of glass is present in plasmas devoid of antihaemophilic factor, Christmas factor, plasma thromboplastin antecedent (PTA), factor V, factor VII and Stuart factor, as well as in patients treated with dicoumarol or patients with liver disease. It is not implied that glass cannot act on factors other than Hageman factor (especially the blood platelets), and even blood from patients with Hageman-factor deficiency may show accelerated coagulation on agitation with glass.[7]

These concepts are important in at least two ways. The first is technical. In an investigation of the calcium clotting time in a patient with possible bleeding disease it is essential to standardize at least the presence or absence of blood platelets and also the amount of glass contact. Margolis[13] has recently introduced a kaolin clotting time which does just this, and he reports that the clotting time of recalcified plasma then gives reproducible results and is of value in the diagnosis of patients with bleeding disorders. But an even more important concept might arise from these phenomena. Any factor which plays a part in maintaining the fluidity of blood in blood vessels is obviously of immense potential importance in the study of disease processes. The concept of the pre-thrombotic state is well established. Numerous studies have been made in an attempt to provide laboratory confirmation of a tendency to form thrombi in blood vessels. In potentially thrombotic states such as, for instance, occur after operations there is an increase of plasma fibrinogen and of blood platelets. But we remain unable to recognize the patient who will develop the vascular thrombus. To be able to do so would be of immense prac-

tical importance and it is conceivable that studies such as those mentioned above may throw some light in this rather obscure field.

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DIE MIGRAINEGESTELDHEID

Een van die chroniese toestande wat taamlik algemeen voorkom en wat dikwels omrede van sy wisseling van vorm misgekyk word, is migraine. Dit is 'n toestand wat van kleins af kan voorkom en dikwels lewenslank kan duur, maar wat baie keer ook in sy natuurlike geskiedenis en verloop belangrike wisselvorme en vormveranderinge toon.

By kinders wat onderhewig is aan migraine, is daar soms 'n neiging om ‚naar-hoofpyne' te kry met die grootste nadruk op die naarheid. Dit is om hierdie rede dat migraine in hierdie vorm gewoonlik gewyt word aan eetvoorvalle en versteurings van spysvertering. Omdat hierdie soort ‚spysverteringsaanvalle' sporadies voorkom en van verbygaande aard is, word daar gewoonlik nie veel meer aandag daaraan geskenk nie as om te sê dat die kind versigtig moet wees met wat hy eet.

Hierdie aanvalle van ‚naar-hoofpyn' by kinders wat onderhewig is aan migraine gaan dikwels in die middelste jare—tussen 20-45—oor in die tipiese paroksismale migraine-aanval. So 'n aanval word dan gewoonlik voorafgegaan deur gewaarwordinge wat die vorm kan aanneem van ligflikkeringe, versteuring van gesig (gewoonlik van die een of ander deel van die gesigsveld), parestesie, fotofobie en oorgevoeligheid vir geluide en gerase, gevoelens van verwyderd te wees, ens. Vyftien tot 20 minute later volg dan gewoonlik die bekende skeelhoofpyn wat op hierdie stadium gewoonlik die opvallendste kenmerk van die aanval is, ofskoon naarheid en braking dikwels met die hoofpyn saamgaan. Die aanvalle kan lig wees of in hewige vorm voorkom sodat die pasiënt volstrek onbevoeg is om enigiets te doen.

Teen ongeveer die ouderdom van 40-50 tree dikwels die volgende faseverandering in waarby die naarheid en die hoofpyn van die eerste twee fases op die agtergrond tree en die sogenaamde migraine-ekwivalente prominent op die voorgrond kom. As die dokter nie baie goed bekend is met die geskiedenis van die pasiënt nie, is dit gewoonlik hier waar die basiese migrainegesteldheid misgekyk kan word.

Ekwivalente aanvalle kan nou voorkom sonder hoofpyn en daar is gewoonlik die volgende bygaande simptome: Ongewone prikkelbaarheid, 'n gevoel van verwyderdheid, 'n gevoel van gejaagdheid, besondere honger en oordrewe eetlus, gaperigheid en dwarrelende gedagtestrominge met helder beelde en herbelewenisse uit die verlede. Hierdie ekwivalente verskynsels kan ook in ligte graad voorkom sodat die pasiënt self die toestand nie eers herken nie (en ander mense dink hy is net moeilik of prikkelbaar of temperamenteel), of die ekwivalente verskynsels kan in so 'n erge graad voorkom dat die hele ondervinding skrikwekkend vir die pasiënt is en hom vreesbevange laat met twyfel oor sy eie geestesgesondheid.

Dat migraine hierdie soort verloop het in die drie fases wat ons geskets het, is taamlik algemeen, maar dit kom nie noodwendig so voor nie. Migraine is 'n toestand wat by uitstek deur vormwisseling gekenmerk word. Dat die toestand ook in 'n sekere soort persoon voorkom, ly geen twyfel nie. Die migrainelyer is dikwels 'n fynbesnaarde, intelligente persoon wat die geneigdheid toon om met die aanvalle van hoofpyn ook spastiese toestande van die kolon te kry.

Tot so ver het ons nou nog net die konstitusionele, idiopatiese migrainegesteldheid beskryf. Die moontlikhede van ander veroorsaking van migraineagtige hoofpyne soos byvoorbeeld, subarachnoïde bloedings, ens., moet nie uit die oog verloor word nie.

Wat die behandeling van die toestand betref, moet ons dink aan voorsorgsmaatreëls en aktiewe terapie. Onder die voorsorgsmaatreëls moet die volgende genoem word: Waak teen emosionele spanning, besondere koue, lank staan, die glans van skerp lig, die eet van kos wat 'n aanval van spastiese kolon kan veroorsaak, en moontlik ook die eet van sjokolade en ryk varkvleis. Omdat glans so 'n algemene prikkel is, is dit goed vir migrainelyers om 'n ligte getinte glas te dra in 'n sonbril, of 'n ligte getinte lens as hulle brildraers is.

Wat die spesifieke terapie by aanvalle betref, hang alles af van die aard van die aanval. Daar is veral drie middels wat afsonderlik of in kombinasie gebruik kan word, wat per inspuiting of deur die mond gegee kan word, en wat baie effektief is, veral as hulle vroeg in 'n aanval toegedien word. Die basiese bestanddele van hierdie middels is ergotamien, kaffeïen en fenobarbitone. Hierdie middels is vandag in baie preparate verkrygbaar. Veral middels wat ergotamien bevat, behoort, om die maksimale uitwerking te hê, toegedien te word sodra daar aanmannings van die aanval is en nog voordat die hoofpyn te voorskyn kom—indien dit moontlik is.

Omdat migraine chronies van aard is, moet daar altyd gewaak word teen die gebruik van gewoontevormende middels vir migrainelyers. Die regte benadering van die toestand, die sorgvuldige tref van voorsorgsmaatreëls en spoedige aktiewe terapie kan baie doen om die lewe van die migrainelyer minder onaangenaam te maak.

'GENERAL PRACTICE SERIES'

The theory and practice of modern medicine has advanced with such rapid strides that it would be no exaggeration to say that the whole face of medicine has changed. This change has been especially noticeable in the fields of anaesthetics, operative procedures and in the drug treatment of disease, but it has also had a very important bearing on the

practice of medicine by the general practitioner. In spite of this, however, it remains true to say that we have not completely outgrown the usefulness of the time-honoured art of clinical medicine.

In order to try to give some guidance in the numerous problems of management and treatment with which the modern general practitioner is confronted, and in order to arrive at a re-evaluation and a synthesis between proved clinical methods of treatment and the newer scientific approaches, we have invited distinguised contributors to provide a series of signed articles which it is hoped will be helpful to the practitioner. These articles will be published at fortnightly intervals.

‚ALGEMENE PRAKTISYNSREEKS'

Die teorie en die praktyk van die moderne medisyne het met sulke rasse skrede vooruitgegaan dat dit geen oordrywing sal wees nie om te sê dat die hele medisyne wesenlik verander het. Hierdie verandering is veral merkbaar op die gebiede van die narkose, operasietegnieke en die behandeling van siektes met medisyne, maar dit het ook 'n baie belangrike neerslag gehad op die mediese praktyk soos beoefen deur die algemene praktisyn. Ten spyte hiervan bly dit egter tog nog waar om te sê dat ons nog nie die waarde van die ou beproefde kuns van die kliniese medisyne ontgroei het nie.

Met die doel om te probeer om leiding te gee ten opsigte van die baie probleme aangaande die hantering van pasiënte en behandeling waarmee die algemene praktisyn te doen kry, en in die hoop om tot 'n herwaardering en 'n sintese te geraak tussen kliniese metodes van behandeling en die nuwere wetenskaplike benaderings, het ons 'n aantal bekende medewerkers gevra om 'n reeks getekende artikels te skryf wat, na ons hoop, van nut sal wees vir die algemene praktisyn. Hierdie artikels sal al om die ander week gepubliseer word.