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## VAN DIE REDAKSIE

### HEMOFILIESE BLOEDING EN DIE BEHANDELING DAARVAN

Bloeding is altyd skrikwekkend, veral as dit nie wil ophou nie, maar by die meeste pasiënte kan dit met betreklik eenvoudige maatreëls beheer word. Dit is egter nie die geval by aangebore bloeiing nie, want hierdie pasiënte hou aan met bloei lank nadat die bloeipunte uitgeken en afgebind is. Onlangse navorsing, wat grootliks in Brittanje gedoen is,[1-3] het egter nuwe lig op die onderwerp van die behandeling gewerp.

Voorbehoeding is natuurlik die eerste noodsaaklikheid, en veel kan gedoen word om besering te voorkom. Bloeiers kneus maklik en met hulle moet 'n mens soos met oorryp tamaties te werk gaan! Seuntjies wat bloeiers is moet nie toegelaat word om mee te doen aan al die aktiwiteite van hul maats nie, hoe graag 'n mens hulle ookal wil toelaat om normale lewes te lei. Gereelde besoeke aan die tandarts kan lastige tandetrek, as die kind ouer is, vermy, en by hierdie pasiënte moet die dokter baie konserwatief in sy houding teenoor snykundige ingreep wees. Slegs die allernoodsaaklikste operasies mag gedoen word. Vandag is die sterftesyfer as gevolg van buikoperasies by bloeiers heel moontlik bo 50 persent in feitlik enige hospitaal in Suid-Afrika. Hierdie syfer is baie groter as die sterftesyfer vir die meeste akute buik-noodgevalle wat sonder operasie met konserwatiewe moderne terapie behandel word; onverligte akute derm-obstruksie is een van die belangrike uitsonderings op hierdie algemene reël. Dan ook word die meeste van die sogenaamde akute buik-noodgevalle by bloeiers veroorsaak deur bloeduitstorting in die derm of die spierwand; gewoonlik kan sulke gevalle ook verlig word sonder snykundige ingreep.

'n Korrekte diagnose van die bloedsiekte is noodsaaklik en dit verg 'n volledige hematologiese ondersoek. 'n Eenvoudige skermtoets wat onlangs beskrywe is[4] kan die dokter in staat stel om dié pasiënte wat geen ernstige siekte van die bloeiingsoort het nie, uit te skakel, maar pasiënte wat abnormale reaksies op hierdie toets toon verg moontlik 'n tromboplastien-vormingtoets. Met behulp van hierdie metode kan die diagnose met sekerheid bepaal word en kan pasiënte wat aan *Christmas*-siekte ly uitgeken word. Dit is ook baie nuttig as die hoeveelheid antihemofiliese globulien (AHG) in die sirkulerende bloed bereken kan word. Daar is 'n hele paar metodes hiervoor wat egter nie almal dieselfde resultate lewer nie. Die betreklik eenvoudige en toereikende metode wat deur Biggs[2] beskryf is, het reeds baie nuttig geblyk by die beplanning en beheer van die behandeling. Volgens hierdie metode word dit vasgestel dat ernstige bloeiers minder as 1 persent sirkulerende AHG besit; daarteenoor

## EDITORIAL

### HAEMOPHILIC HAEMORRHAGE AND ITS TREATMENT

Haemorrhage is always frightening, especially when it persists, but in most patients it can be controlled by relatively simple procedures. This is not the case in haemophilia, for these patients continue to bleed long after the bleeding points have been identified and ligated. Recent work, much of it from Britain,[1-3] has thrown new light on the problem of treatment.

Prophylaxis is of course the first essential, and much can be done to prevent trauma. Haemophiliacs bruise easily and should be handled as one handles overripe tomatoes! Haemophiliac boys should not be permitted to share all the physical activities of their contemporaries, however much we may wish to let them lead normal lives. Regular visits to the dentist may obviate troublesome dental extractions in later years and a very conservative attitude should be adopted towards surgery. All but the most essential operations must be avoided. The mortality rate from intra-abdominal surgical operations in haemophiliacs in almost any hospital in South Africa is today probably over 50%. This is much greater than the mortality rate for most acute abdominal emergencies treated without operation by modern conservative regimes; unrelieved acute intestinal obstruction is one of the notable exceptions to this generalization. Furthermore, most of the so-called acute abdominal emergencies in haemophiliacs are produced by haemorrhage into the gut or muscle wall; these too usually subside with non-operative treatment.

Correct diagnosis of the blood condition is essential and this involves a complete haematological work-up. A simple screening test that was recently described[4] may enable one to eliminate those patients who have no serious bleeding disorder of the haemophilic variety, but patients who give abnormal results with this test may need a thromboplastin-generation test. By this means the diagnosis can be confirmed with certainty and patients with Christmas disease recognized. It is also of great help if the level of circulating antihaemophilic globulin (AHG) can be estimated. There are a number of methods of doing this which do not all give exactly the same results. A relatively simple and adequate method,

is 30 persent die hoeveelheid wat teenwoordig moet wees vir behoorlike bloedstelping. Gevalle wat minder ernstig aangetas is (die term ‚ligte gevalle' word doelbewus vermy) kan selfs tot 30 persent sirkulerende AHG besit. Hoe meer AHG die pasiënt het, hoe geredeliker kan die bloeier se gebrek aangevul word en hoe minder moeilikheid kan met bloeding verwag word.

Om die hoeveelheid sirkulerende AHG te vermeerder kan ons vars plasma, òf gekonsentreerde preparate van AHG afkomstig van mense of diere gebruik. Pasiënte met *Christmas*-siekte kan doeltreffend met plasma wat nie meer so vars is nie behandel word, of selfs met serum; dit is die rede waarom dit so belangrik is om by die diagnose *Christmas*-siekte van hemofilie te onderskei. Vars normale plasma kan maklik in 'n hospitaal bekom word, maar omdat die AHG so labiel is, is dit noodsaaklik dat dit, wanneer dit by hemofilie gebruik word, onmiddellik voor gebruik gekollekteer word. Menige klein operasie soos die trek van 'n tand of insny van 'n abses kan gedoen word ná die toedien van (ten minste) 'n liter plasma. Die plasma moet vinnig toegedien word (binne 'n uur) en die operasie moet so beplan word dat dit begin wanneer die oortapping eindig. By 'n minder ernstig aangetaste bloeier sal hierdie hoeveelheid plasma die hoeveelheid AHG tot op 30 persent te staan bring, maar by ernstiger gevalle sal dit nie so hoog styg nie, hoewel dit hoog genoeg mag loop om 'n klein operasie moontlik te maak. Dit sal by hierdie ernstiger gevalle nie toereikend wees vir groot operasies, veral buik- en borskasoperasies, nie. Die uitwerking van die oortapping sal nie lank hou nie; binne 11 uur verdwyn 50 persent reeds, en binne 24 uur gaan die meeste van die aktiwiteit verlore. Gedurende die na-operatiewe periode sal die hoeveelheid AHG gewoonlik onder 30 persent bly as die pasiënt net een oortapping daagliks ontvang, sodat oortapping meer dikwels nodig is. Die behandeling moet voortgesit word totdat die herstel goed gevorder het—dit mag 'n tydperk van 3 tot 21 dae beslaan. 'n Groot aantal bloedskenkers sal dus benodig word, en hoewel die rooi bloedselle nie weggegooi hoef te word nie maar vir ander pasiënte gebruik kan word, beteken dit tog dat daar veel van die skenkerdiens (en/of die dokter se tyd) geverg word. Die meeste pasiënte wat as bloeiers uitgeken word besit minder as 1 persent sirkulerende AHG en hierdie prosedure sal hulle dus nie red as daar enigiets ernstiger as 'n baie klein operasie gedoen moet word nie. Macfarlane en sy medewerkers in Oxford[1] was die baanbrekers in die gebruik van gekonsentreerde AHG afkomstig uit varke of beeste. Met behulp van hierdie preparate kan betreklik enorme dosisse AHG toegedien word—genoeg om 'n hoeveelheid van meer as 30 persent oor 'n aansienlike tydperk in stand te hou. Op hierdie wyse was hulle in staat om groot operasies uit te voer en 'n hele paar lewes is reeds gered. Ongelukkig is hierdie stowwe ook antigenies en hulle kan ook plaatjiearmoede veroorsaak. Die reaksies op hierdie stowwe begin ontwikkel 10—14 dae nadat die pasiënt hierdie behandeling ontvang het, en dan mag die antigeniese stof nie verder gebruik word nie. Dit is gelukkig dat pasiënte wat sensitief is vir een van hierdie stowwe nog die ander mag ontvang. As 'n pasiënt eers 'n gevoeligheid vir die stof ontwikkel het, bly hy heelwaarskynlik sy hele lewe lank gevoelig, en dus mag die stowwe nie gebruik word behalwe by die uiterste noodgevalle nie. Die pasiënte het bloot een, of

described by Biggs,[2] has proved very useful in planning and controlling therapy. By this technique severe haemophiliacs have been shown to have less than 1% circulating AHG, as against 30%, which is the level required for adequate haemostasis. Less severely affected cases (the term 'mild' is deliberately avoided) may have anything up to 30% circulating AHG. The more AHG he has, the easier is the haemophiliac's deficiency correctable and the less trouble with haemorrhage is to be anticipated.

In order to raise the level of circulating AHG we can use either fresh plasma or concentrated preparations of AHG derived from human or animal sources. Patients with Christmas disease can usefully be treated with plasma which is not so fresh or even with serum; hence the importance of this differentiation in the diagnosis. Fresh normal plasma can be made readily available in most hospitals, but because the AHG is very labile it is essential when it is to be used for a haemophiliac that it be collected immediately before use. Many minor operations like the extraction of teeth or the incision of abscesses can be conducted after the infusion of (at least) a litre of plasma. This must be rapidly transfused (within an hour) and the operation timed to start as the transfusion finishes. This amount of plasma will raise the level of AHG in a less severely affected haemophiliac to 30% but in the more severely affected patient the level will not reach so high. It may, however, be high enough to allow minor surgery to be performed; it will not suffice for major, especially intra-abdominal and intrathoracic, surgery. The effect of transfusion will not last for very long; in 11 hours about 50% will have disappeared, and the bulk of activity will be lost within 24 hours. During the post-operative period, if the patient only receives one transfusion a day, the level of AHG will be below 30% for most of the time, so that more frequent transfusions will be required. Treatment must be continued until healing is well advanced and this may be for a period of 3–21 days. A large number of donors will thus be required, and while the red cells need not be discarded but can be used for other patients, the drain on the donor service (and on the doctor's time) will still be considerable. The majority of patients classed as haemophiliacs have less than 1% circulating AHG and this procedure will not serve if they require anything more than a minor operation. Macfarlane and his co-workers at Oxford[1] have pioneered the use of concentrated AHG derived from pig or beef sources. By the use of these substances relatively enormous doses of AHG can be given, sufficient to maintain levels of over 30% for a considerable time. In this way they have been able to carry out major surgery and a number of lives have already been saved. Unfortunately these materials are antigenic and may also cause thrombocytopenia. Reactions to the material start to develop after the patients have received treatment for 10–14 days and preclude the further use of the offending substance. Fortunately, patients sensitive to one of these substances can

miskien twee, ekstra kanse ontvang; in elk geval is die stof nie maklik bekombaar nie. Stof van menslike oorsprong is reeds voorberei[5] maar dit is nog nie heeltemal bevredigend nie en die voorrade is moontlik nog meer beperk.

Dit is altyd wenslik om die uitwerking van oortapping te bereken deur die AHG-hoogte 15 minute na die voltooiing van die oortapping te meet. Indien die hoogte nie genoeg gestyg het nie, het die preparaat wat gebruik is minder AHG dan beweer word (en die meeste van die sogenaamde antihemofiliese preparate wat vandag bemark word kom in hierdie klas voor), of anders reageer die pasiënt nie normaal nie. 'n Stollingsteenstof in die bloedsomloop, wat nogal dikwels by hemofilie voorkom, kan ook so 'n uitwerking hê. Sommige pasiënte reageer glad nie, sonder enige voor die hand liggende rede.[2] In elk geval sal 'n kennis van die reaksie op oortapping die chirurg in staat stel om daaropvolgende behandeling te beplan en om verdere dosering te bereken. Plaaslike behandeling is belangrik en moet nooit afgeskeep word nie. Die bloeipunte moet waar moontlik afgebind word, selfs al beteken dit dat dit toegewerk moet word. Wonde moet versigtig verbind word en die verband moet styf op sy plek gehou word sodat dit nie kan skuif en die rou oppervlakte beskadig nie. Rekverbande (*one-way-stretch*), met 'n kussinkie van sponsrubber om die druk meer eweredig te versprei, is baie nuttig. By ernstige gevalle is spesiale spalke, pleisters of beddens soms nodig om die beseerde liggaamsdeel onbeweeglik te hou. Besmetting is gevaarlik aangesien sekondêre bloeding nog meer moeilikheid as die primêre soort kan veroorsaak. Indien die verband om hierdie rede afgehaal moet word, moet AHG-inhoud dadelik weer vermeerder word *voor* daar met die operatiewe prosedures begin word.[1] Indien tande getrek moet word, word afsonderlik voorbereide, deursigtige akriliese spalkies voor die operasie gemaak en hulle oefen 'n sagte druk op die bloedingspunte uit.[3]

As die bloeding nie deur plaaslike maatreëls stopgesit kan word nie, is dit nutteloos en selfs skadelik om die bloeding te probeer beheer deur plaaslik meer druk uit te oefen. As die bloeding voortgaan, moet die bloed toegelaat word om te ontsnap. Oormatige druk op 'n bloeiende tandkas kan miskien net die bloed na die nek of middelvleis afkeer en die pasiënt kan versmoor. Bloed in die spiere van 'n ledemaat kan ischiemiese nekrose veroorsaak. As daar enige tekens hiervan voorkom, moet die steke verwyder word en die druk verlig word. Daar is maar net een manier om hierdie probleem op te los en dit is om die sirkulerende AHG tot op bloedstelpende hoogtes te bring.

Ten slotte: 'n Bloeier se lewe kan daarvan afhang of daar are beskikbaar is vir oortapping. As die diagnose eenmaal deeglik beklink is, is dit nie nodig om elke keer as hy in die hospitaal opgeneem word 'n volledige diagnostiese ondersoek van die stelpingstatus te doen nie. Dik naalde vir aarpunksie kan gevaarlik wees, terwyl ‚cut downs' en daaropvolgende afbind van are 'n hoogs benodigde aar prysgee. Dit is gewoonlik moontlik, met genoeg versigtigheid en geduld, om met 'n dun naald in 'n aar te dring. Selfs as aartrombose na veelvuldige gebruik voorkom, sal die are dikwels 'n ander kanaal vorm, mits hulle nie afgebind was nie, en sal hulle weer beskikbaar wees vir gebruik by een van daardie desperate noodgevalle wat nog maar steeds die lot van die bloeier is.

1. Macfarlane, R. G., Mallam, P. C., Witts, L. J., Bidwell, E.,

still receive the other. Once sensitized, patients probably remain so for life so that these materials should not be used for anything but desparate emergencies. The patients have merely been granted one or perhaps two additional chances; in any case supplies are not readily available. Material derived from human sources has been prepared[5] but is as yet not entirely satisfactory and supplies are likely to be even more limited. It is always advisable to assess the effects of transfusion by estimating the AHG level 15 minutes after the transfusion has been completed. If the level has not risen adequately then either the preparation used has even less AHG than it is reputed to have (most so-called antihaemophilic preparations which are commercially available at the present time fall into this category) or else the patient is responding in an abnormal way. A circulating anticoagulant, not infrequent in haemophilia, may produce this effect. Some patients fail to respond without obvious cause.[2] In any case a knowledge of the response to transfusion will enable the surgeon to plan subsequent treatment and to gauge further dosage. Local treatment is important and should never be neglected. Bleeding points must be secured when possible even if this means putting in a stitch. Wounds must be dressed with care and the dressing kept firmly in place without any movement which might damage raw surfaces. One-way-stretch bandages and sponge rubber padding to distribute pressure evenly are helpful. In serious cases special splints, plasters or beds may be required to immobilize the injured part. Sepsis is dangerous since secondary haemorrhage can be even more troublesome than the primary variety. If dressings are to be disturbed on this account then the AHG level must once again be raised *before* the operative procedures are commenced.[1] When teeth are to be extracted, individually prepared transparent acrylic splints are made before the operation and these exert gentle pressure on the bleeding points.[3]

If local measures fail to stop the bleeding it is useless and harmful to attempt to control the haemorrhage by increasing local pressure. Constant watch must be kept for signs of local tension. If bleeding is continuing then the blood must be allowed to escape. Excessive pressure on a bleeding tooth socket for instance may merely succeed in diverting the blood into the neck and mediastinum and the patient may die of suffocation. Blood in the muscles of the limb may cause ischaemic necrosis. If there are signs of this then the stitches must be removed and the tension relieved. There is only one way to handle this problem and that is to raise the circulating AHG to haemostatic levels.

One final point: The life of a haemophiliac may depend on the availability of veins for transfusion. Once the diagnosis has been adequately established there is little point in performing a full diagnostic work-up of the coagulation status every time the patient is admitted to hospital. Thick needles for venipuncture may be dangerous while 'cut downs' with subsequent tying of veins sacrifice a much-needed vein. With sufficient care and patience it is usually possible to enter a vein with a thin needle. Even if veins should thrombose after repeated use, provided they have not been tied they will often recanalize and become once again available for use in one of those desperate emergencies which are still the lot of the haemophiliac.

1. Macfarlane, R. G., Mallam, P. C., Witts, L. J., Bidwell, E.,

Biggs, R., Fraenkel, G. J., Honey, G. E. en Taylor, K. B. (1957): Lancet, **2,** 251.
2. Biggs, R. (1957): *Ibid.*, **2,** 311.
3. Wishart, C., Annand Smith, C., Honey, G. E. en Taylor, K. B. (1957): *Ibid.*, **2,** 363.
4. Hicks, N. D. en Pitney, W. R. (1957): Brit. J. Haemat., **3,** 227.
5. Kekwick, R. A. en Wolf, P. (1957): Lancet, **1,** 647.

Biggs, R., Fraenkel, G. J., Honey, G. E. and Taylor, K. B. (1957): Lancet, **2,** 251.
2. Biggs, R. (1957): *Ibid.*, **2,** 311.
3. Wishart, C., Annand Smith, C., Honey, G. E. and Taylor, K. B. (1957): *Ibid.*, **2,** 363.
4. Hicks, N. D. and Pitney, W. R. (1957): Brit. J. Haemat., **3,** 227.
5. Kekwick, R. A. and Wolf, P. (1957): Lancet, **1,** 647.