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VAN DIE REDAKSIE

AKUTE LEUKEMIE

Vir meer as 'n volle eeu nadat Rudolf Virchow vir die eerste maal die naam ‚leukemie' aan sy gevalle van *Weisses Blut* gegee het, het dit die verbeelding van die mensdom aangegryp. Leke word altyd geboei deur die verhaal van die Skone en die Gedrog—in hierdie geval jeug wat deur 'n noodlottige siekte geteister word—en daar is baie min takke van die wetenskap wat nie by die soektog na 'n bevredigende geneesmiddel betrokke was nie. Inderdaad, leukemie het nog nooit opgehou om die wetenskaplike se aandag aan te gryp nie. As die konsentrasiepunt van hematologie, het dit onlangs egter 'n nuwe belangrikheid aangeneem aangesien die toename in voorkoms daarvan gedurende die afgelope 25 jaar slegs deur kroonslagaartrombose en longkanker oortref is. In 1931 is dit gesertifiseer dat 685 persone in Engeland en Wallis aan leukemie gesterf het: in 1955 was die getal 2,224—'n drievoudige toename in voorkoms. Terselfdertyd het die spits van sterfgevalle daardeur veroorsaak, na ouer mense verskuif (45-75). Dit skyn of die siekte meer dikwels by stedelinge as by plattelanders voorkom, meer dikwels by die rykes as by die armes, meer dikwels—in Amerika in elk geval—by blankes as by nie-blankes.

By hersiening van 'n reeks van 570 gevalle en by bespreking van die huidige begrip van die siekte, het R. Bodley Scott onlangs verklaar dat dit tans, deur middel van nuwer metodes, moontlik is om die mees akute gang van leukemie vir 'n rukkie te stuit.[1] Alhoewel hierdie aanspraak glad nie nuut is nie, kan 'n klein bietjie aanmoediging geput word uit Scott se samevatting in die 1957-Lettsomiaanse lesing oor die jongste vooruitgang op die gebied van leukemie. Dit bly nog, sê hy, 'n hardnekkig noodlottige siekte. Afgesien van die metode van behandeling, sterf die meeste gevalle binne 2 jaar nadat die siekte gediagnoseer is. Hierdie neerdrukkende vooruitsig is geneig om pogings om 'n afname in die siekte te verkry, te ontmoedig; soos almal weet, is hierdie afname altyd net van kortstondige duur. Scott veroordeel egter ten sterkste die nihilistiese benadering as 'n onverdedigbare standpunt; behalwe dat dit 'n ondeurdringbare versperring in die weg van terapeutiese vooruitgang plaas, ontmoedig dit die pasiënt en almal wat met hom te doen het, insluitend sy geneesheer. ‚Selfs 'n paar maande langer om te lewe mag van ontskatbare waarde wees, en dit is die internis se plig om alles in sy vermoë te doen om hierdie tydelike verposing te bewerkstellig.'

Simptomatiese behandeling is waarskynlik nog die internis se beste beleid. In Scott se reeks het 81 gevalle wat simptomaties behandel is, vir 20·2 weke gelewe na die eerste simptome verskyn het, terwyl 63 gevalle, wat bykomende spesifieke preparate (hieronder bespreek) gekry het, vir

EDITORIAL

ACUTE LEUKAEMIA

For the full century or more since Rudolf Virchow first gave the name 'leukaemia' to his cases of *Weisses Blut* the disease has held the fascination of mankind. Lay people are ever drawn by the tale of Beauty and the Beast—in this case youth being mortally afflicted by a fatal disease—and few branches of science have not been involved in the search for a satisfactory remedy. In truth, leukaemia has never ceased to evoke the scientist's attention. Yet recently it has been elevated to a new importance, as the focal point of haematology, for only coronary thrombosis and carcinoma of the lung have exceeded its rise in incidence over the last 25 years. In 1931 685 persons were certified as dying of leukaemia in England and Wales: in 1955 the figure was 2,224—a threefold increase in incidence. At the same time the peak of deaths from it has shifted to older people (45-75). The disease appears to occur more in urban than in rural dwellers, more in the rich than in the poor, more—in America, at any rate—in Whites than in non-Whites.

In reviewing a series of 570 cases and discussing the present understanding of the disease, R. Bodley Scott recently stated that it was now possible, by newer methods, to halt for a while the most acute course of leukaemia.[1] While this claim is by no means new a little encouragement may be taken from Scott's outline in the 1957 Lettsomian lecture of the current therapeutic advances in leukaemia. It remains, he says, a stubbornly fatal condition. Most cases are dead within 2 years of diagnosis, irrespective of the method of treatment. This depressing outcome tends to discourage attempts to procure a remission which all know can never be more than transient. However, Scott vigorously attacks the nihilistic approach as an indefensible standpoint; apart from erecting an impenetrable barrier against therapeutic advance, it demoralizes the patient and all around him, including his medical attendant. 'Even a few more months of life may be immeasurably precious, and it is the physician's duty to do all that is possible to procure this temporary reprieve.'

Symptomatic treatment is still probably the physician's best line. In Scott's series, 81 cases treated symptomatically survived for 20·2 weeks after the first symptom appeared, while 63 cases receiving additional specific preparations

21·7 weke gelewe het. Daar is dus geen rede om optimisties te wees oor hierdie preparate nie, alhoewel Scott waarsku dat hulle nie té ligtelik buite rekening gelaat moet word nie. Die simptomatiese maatreëls word op die beheer van ontstekings en die hemorragiese toestand toegespits. Bloedvergiftiging kom dikwels voor en lokale infeksie van die mond (gewoonlik moniliaal van aard) vereis flinke behandeling met geskikte antibiotika. Weens die hemorragiese neiging behoort hulle egter nie as 'n roetine of voorbehoedende maatreël gebruik te word nie. Die gevaar wat hierdie kenmerk inhou, word getoon deur die feit dat 23 uit 55 pasiënte aan bloeding gesterf het, 14 daarvan aan die binneskedel-soort. Dit is aan die hand gedoen dat die finale noodlottige voorval, na daar vir maande geen bloeding was nie, deur 'n fibrolisien of sirkulerende teenstollingstof, as gevolg van 'n bykomende infeksie, veroorsaak word. Bloedoortapping is nuttig om bloedarmoede te verlig, maar slaag nie daarin om die neiging tot bloeding te beheer nie—bloedplaatjie-oortapping mag van meer nut hiervoor wees, alhoewel die voordeel daaraan verbonde van verbygaande aard is. Dit lyk of bloedoortappings, indien dit intelligent en doelbewus gebruik word, tans die hematoloog se waardevolste wapen is om die leukemiese pasiënt aan die lewe te hou.

Spesifieke middels wat 'n gunstige wending aan die toestand kan verleen, al is dit tydelik, sluit in kortisoon en verskeie antimetaboliete. Kortisoon is vir die eerste keer in 1950 gebruik en dit is bevind dat 'n afname in die siekte (van 6 weke of langer) by ongeveer die helfte van die gevalle verkry kan word. Algehele afname kan by kinders met limfoblastiese leukemie en soms by volwassenes verwag word; die ander seltipes reageer nie so goed nie. Die antimetaboliete wat gebruik word, is dié wat die sintese van nukleïensuur in die liggaam belemmer. Die foliensuurteenwerkers het terapeuties in onbruik geraak, maar hulle het spesifieke heilsame waarde by die behandeling van akute limfoblastiese leukemie by kinders, waar afname van die siekte deur hulle gebruik verkry kan word. Die purien-teenwerkers, waarvan 6-merkaptopurien tans die gewildste is, word meer algemeen gebruik. In Scott se reeks het ongeveer een-derde van die kinders en een-sewende van die volwassenes wat met hierdie stof behandel is, afname van die siekte, wat gemiddeld 3 maande geduur het, getoon. Die aard van die sitologiese soort van die leukemie was van minder belang by die prognose as wat dit by die behandeling met foliensuur was.

Greig *et al.*,[3] in 'n studie van die gebruik van 6-merkaptopurien by akute leukemie, wat hulle in 'n referaat by die laaste Suid-Afrikaanse Mediese Kongres (Pretoria, 1955) aangebied het, het tot die gevolgtrekking gekom dat hierdie purien-teenwerker wel van nut is by die behandeling van akute leukemie (asook by die akute eindstadium van chroniese murgleukemie en by monoblastiese en miëloblastiese leukemie), maar dat die uitwerking daarvan nie altyd dieselfde was nie. Hulle het gevind, dat by die gevalle wat daardeur gebaat het, die smartlike simptome van akute leukemie versag was, en die einde, toe dit aangebreek het, genadig was, daar dit so skielik en soms onverwags gekom het.

1. Scott, R. B. (1957): Lancet, **1**, 1053.
2. Freeman, G. (1952): Blood, **7**, 235.
3. Greig, H. B. W., Metz, J., Laird, M. J., Zentkowsky, D. en Fitzpatrick, M. M. F. (1956): S. Afr. T. Geneesk., **30**, 360.

(discussed below) survived for 21·7 weeks. So there is no cause to be optimistic over these preparations, although Scott warns that they should not be too lightly discounted. The symptomatic measures are directed at controlling infections and the haemorrhagic state. Septicaemia is frequent, and local infection of the mouth (usually monilial in nature) requires brisk treatment with appropriate antibiotics. But these should not be used as a routine or prophylactic measure because of the haemorrhagic tendency. The danger of this feature is shown by the fact that 23 out of 55 patients died of haemorrhage, 14 of the intracranial type. It has been suggested that the final fatal episode, after months of freedom from bleeding, is brought about by a fibrolysin or circulating anticoagulant resulting from a superimposed infection.[2] Blood transfusion is useful in relieving anaemia but fails to control the bleeding tendency—for this, platelet transfusion may be more useful, although its benefit is transient. Intelligently and purposively used, blood transfusion seems at present to be the haematologist's most valuable weapon in keeping the leukaemic patient alive.

Specific agents that can alter the picture for the better, albeit temporarily, include cortisone and several antimetabolites. Cortisone was first used in 1950 and it is found that remission (for 6 weeks or more) can be obtained in about half the cases. Complete remission can be expected in children with lymphoblastic leukaemia and sometimes in adults; the other cell-types do not respond so favourably. The antimetabolites used are those that interfere with the synthesis of nucleic acid in the body. The folic-acid antagonists have now fallen by the therapeutic wayside but they have a specific beneficial value in the treatment of acute lymphoblastic leukaemia in children, where remissions can be obtained by their use. The purine antagonists, of which 6-mercaptopurine has current vogue, are in more general use. In Scott's series about one-third of the children and one-seventh of the adults treated with this substance showed remissions lasting on an average 3 months. The nature of the cytological variety of the leukaemia was less important in the prognosis than it was with folic-acid therapy.

Greig *et al.*,[3] in a study on the use of 6-mercaptopurine in acute leukaemia presented in a paper at the last South African Medical Congress (Pretoria, 1955) concluded that this purine antagonist had a place in the treatment of acute leukaemia (as well as in the acute terminal phase of chronic myelogenous leukemia and in monoblastic and myeloblastic leukaemia) but that it was inconstant in its action. They found that in the cases which benefited the very distressing symptoms of acute leukaemia were mitigated, and the end, when it came, was merciful in being very sudden and sometimes unexpected.

1. Scott, R. B. (1957): Lancet, **1**, 1053.
2. Freeman, G. (1952): Blood, **7**, 235.
3. Greig, H. B. W., Metz, J., Laird, M. J., Zentkowsky, D. and Fitzpatrick, M. M. F. (1956): S. Afr. Med. J., **30**, 360.

MICRODISSECTION OF THE KIDNEY

Microdissection of the kidney allows the scientist to study the nephron in three dimensions throughout the length of each unit and to localize the exact position of pathological lesions. The findings may be correlated with biochemical changes in the patient. Oliver published a classical monograph on the architecture of the kidney in chronic Bright's disease in 1939[1] but new techniques and findings have been reported since then. A recent paper by Darmady and Stranack deals with a study of the nephron by microdissection in a number of conditions,[2] and details are also given of the technique of maceration and of the preparation of an isolated nephron or tubule for study and photography.

In an examination of 53 preparations from persons who had died of anuria caused by a number of aetiological factors but not by known nephrotoxic agents, the microdissection method revealed that in the 'onset phase' (lasting up to 36 hours) many nephrons had focal points of disarrangement of the tubular epithelium and loss of translucency. During the early stages of oliguria or anuria, microdissection once more showed the disarrangement of the tubular epithelium and focal necrosis in varying degree in different nephrons, with certain other changes also present. Ruptures of the tubular wall in all parts of the nephron appear about the middle of the anuric phase, and casts are seen in the lumen in various parts of the nephron, particularly in the lower part, as the disease progresses. In the diuretic phase there is evidence of regeneration, the epithelial pattern of the proximal tubule becoming regular before the distal and collecting tubules. Microdissection clearly shows that there is random distribution of the lesions; some tubules may show rupture of the walls, some may contain multiple casts, while some nephrons may apparently escape.

In 11 cases of Lignac-Fanconi disease (cystinosis) microdissection revealed a structural defect in the renal tubule. In specimens from 8 subjects the proximal tubule was shorter than normal, the first part being replaced by a thin and narrow neck (swan neck); in the 3 others it was also narrower and shorter than normal (hypotrophic).

Examination of biopsy specimens of the kidneys of patients with hyperaldosteronism (Conn's disease) by a number of workers has shown widespread vacuolation of the tubular epithelium. Darmady and Stranack[2] also found intense vacuolation of the renal epithelium, particularly in the proximal but also in the distal tubule, in 4 patients with potassium deficiency (2 associated with an adrenal adenoma and an adrenal carcinoma respectively, and 2 who were cases of Cushing's syndrome with potassium depletion); the vacuolation was not dependent on an increase in the circulating adrenocortical steroids since potassium depletion can apparently alone produce such changes.

Microdissection overcomes certain difficulties and helps to clarify some of the problems encountered in the study of renal pathology.

1. Oliver, J. (1939): *Architecture of the kidney in chronic Bright's disease.* New York: Hoeber.
2. Darmady, E. M. and Stranack, F. (1957): Brit. Med. Bull., **13**, 21.