LEWERKOMA

'n Redelike benadering tot siektes van die lewer vereis aanhoudende hersiening. Op geen ander orgaan in die liggaam het moderne mediese navorsing so 'n gekonsentreerde en volgehoue aanval gemaak nie. En terwyl ontsaglike boekdele van wetenskaplike gegewens verskyn het, is noue korrelasie met die goedgevestigde en dikwelsaangetrefde kliniese patrone van lewersiekte nooit regtig bereik nie. Dit is nêrens so opvallend soos by die behandeling van hierdie toestande nie, waar dit skyn of die mees spesifieke geneesmiddel waaroor die dokter beskik, nog steeds bed-rus is; op weinig anders kan daar onomwonde aanspraak gemaak word dat dit net so doeltreffend is.

Simptome van geestesgesteldheid en koma is lank reeds as ernstige komplikasies—dikwels laat en teen die einde—van chroniese lewersiekte beskou. Die presiese meganisme van hulle voortbrenging het duister gebly en hul behandeling, simptomaties en grootliks proefondervindelik. Hierdie sogenaamde neuropsigiatriese sindroom is 'n komplikasie van verskillende tipes van lewersiekte en dit is verklaar dat sy voorkoms te wyte is aan die produksie van 'n toksiese stikstofhoudende

HEPATIC COMA

A rational approach to diseases of the liver requires constant revision. Upon no other organ in the body has modern medical research made so concentrated and sustained an attack. And whilst vast volumes of scientific data have appeared, close correlation with the well-established and oft-encountered clinical patterns of liver disease has never really been achieved. This is nowhere so apparent as in the treatment of these conditions, where the most specific remedy in the hands of the physician seems still to be bed rest; little else can be claimed unequivocally to be as efficacious.

Mental symptoms and coma have long been regarded as serious complications—frequently late and terminal —of chronic liver disease. The precise mechanism of their production has remained obscure and their treatment symptomatic and largely empirical. This so-called neuropsychiatric syndrome is a complication of diverse types of liver disease, and its occurrence has been explained as due to the production of a toxic nitro-

stof in die ingewande, wat deur die sieklike lewer in die sirkulasie van die liggaam en in die brein, ingebring word.[1] Voorts is dit aangeneem dat hierdie stof ammonia is, aangesien die bloed-ammonia waardes somtyds verhoog word.[2] Die teorie word gestaaf deur die feit dat lewerkoma by pasiënte met lewersiekte teweeggebring kan word der hulle met 'n dieet ryk aan proteïen of stikstofhoudende stowwe, soos byvoorbeeld ammoniumsoute of ureum, te voed.[3] 'n Grootse bydrae tot die begrip van hierdie belangrike onderwerp, is die onlangse studie deur Sherlock en haar kollegas by die Nagraadse Mediese Skool te Hammersmith, Londen, en die nuwe behoudende terapeutiese kursus wat vir die neuropsigiatriese sindroom aanbeveel is.[4] Die perke van die konvensionele betekenis van die term ‚lewerkoma' is aansienlik wyer gemaak, sodat die neuropsigiatriese sindroom enige kleiner variasie van bewussyn en neurologiese tekens, so wel as onopwekbare gevalle van koma, insluit. Tipies wisselend en hervattend—tot so 'n mate dat ‚herstel' sinoniem is met ‚geskik om huistoe gestuur te word'—word die sindroom omskryf as ‚die progressiewe belemmering van emosionele beheer en intellek, terwyl die pasiënt van bewusteloosheid na koma gaan.' Die klassieke ontlastingsruik, foetor hepaticus, is gedurig aan die asem van gevalle van dreigende koma te bespeur.[5]

Die Hammersmith reeks bestaan uit 66 opeenvolgende gevalle van lewersiekte wat deur ‚lewerkoma' bemoeilik was—dit is met laboratorium-, histologiese en lykskouingshulp oortuigend bewys dat almal sieklike lewers gehad het wat vir die kliniese eienskappe verantwoordelik was. Van hierdie 66 gevalle was 13, pasiënte met chroniese virus-lewerontsteking, 34 met akute lewersirrose, 13 met chroniese lewersirrose, en die oorblywende 6 het uit 'n kliniese mengsel (karsinoom, lewernekrose, ens.) bestaan.

Alle gevalle was behandel asof die ingewandstoksienteorie geldig was, en die volgende terapeutiese program is ingestel. Eerstens is die ingewande van stikstofbevattende stof deur lawemente gesuiwer (wat, so word dit gesê, die pasiënte geriefliker laat voel het), en dan deur die uitsluiting van proteïen uit die dieet, vry gehou. Koolhidraatopname is deur binnemaagse drup (20% glukose) en binneaarse politienbuise (40%) geforseer tot in die koparmaar om trombose in die kleiner are te vermy. Tydelike uitputting van stikstofhoudende proteïen is waarskynlik onskadelik by pasiënte met lewersiekte,[6] en by ‚lewerkoma'—maar slegs by koma—is dit die aangewese behandeling. Later, soos die pasiënt herstel, word klein hoeveelhede proteïen in die dieet ingesluit. Tweedens word chloortetrasiklien (Oureomisien) in volledige terapeutiese dossise toegedien. Eksperimenteel verhoed hierdie antibiotika massiewe lewernekrose by rotte,[7] en dit werk waarskynlik deur sy uitwerking op die organismes van die ingewande. Derdens word faktore wat bekend is om lewerskade te bespoedig—kalmeermiddels ammoniumsoute, ureum, verdowingsmiddels—vermy, en maagdermbloeding, veral van spatare van die slukderm, word deeglik behandel. Nege van Sherlock se 34 gevalle van akute lewersirrose was deur maagdermbloeding bespoedig; samepersing van die slukderm by wyse van 'n ingeslukte buis mag lewensreddend wees.

genous material in the intestines which is introduced through the disordered liver into the systemic circulation and the brain.[1] This toxic substance has further been held to be ammonia, since the blood-ammonia values are sometimes raised.[2] The theory is supported by the fact that hepatic coma can be induced in some patients with liver disease by feeding with a high-protein diet or nitrogenous substances such as ammonium salts or urea.[3] A major contribution to the understanding of this important subject is the recent study by Sherlock and her colleagues at the Postgraduate Medical School at Hammersmith, London, and the novel conservative course of therapy advocated for the neuropsychiatric syndrome.[4] The confines of the conventional meaning of the term 'hepatic coma' are considerably widened, so that the neuropsychiatric syndrome includes any minor variation of consciousness and neurological signs, as well as unrousable cases of coma. Typically fluctuant and recurrent—so much so that 'recovery' is synonymous with 'fit to be discharged home'—the syndrome is defined as 'the progressive impairment of emotional control and intellect, the patient passing from stupor into coma'. The classical faecal smell, foetor hepaticus, is constantly on the breath of cases of impending coma.[5]

The Hammersmith series comprises 66 consecutive cases of liver disease complicated by 'hepatic coma'—all conclusively proved by laboratory, histological or post-mortem aids to possess diseased livers responsible for the clinical features. Of these 66 cases, 13 were patients with acute viral hepatitis, 34 were acute biliary cirrhotics, 13 were chronic biliary cirrhotics, and the remaining 6 comprised a clinical miscellany (carcinoma, liver necrosis, etc.).

All cases were treated as if the intestinal-toxin theory was valid, and the following therapeutic programme was instituted. First, the intestine was cleared of nitrogen-containing material by enemata (which, it is said, made the patients feel more comfortable) and then kept free by the omission of protein from the diet. Carbohydrate was 'pushed' by intragastric drip (20% glucose) and intravenous polythene tubing (40% glucose) into the innominate vein to avoid thrombosis in the smaller veins. Temporary depletion of nitrogenous protein is apparently not harmful in patients with liver disease,[6] and in 'hepatic coma'—but only in coma—it is the treatment indicated. Later on, as the patient recovers, small amounts of protein are included in the diet. Secondly, chlortetracycline (Aureomycin) is administered in full therapeutic doses. Experimentally this antibiotic prevents massive hepatic necrosis in rats,[7] and it probably acts by its effect on the flora of the intestine. Thirdly, factors known to precipitate liver damage—sedatives, ammonium salts, urea, anaesthetics—are avoided, and gastro-intestinal haemorrhage, especially from oesophegeal varices, is vigorously treated. Nine of Sherlock's 34 cases of acute hepatic cirrhosis were precipitated by gastro-intestinal hae-

Die Hammersmith resultate is beslis beter as dié wat by enige vorige reeks van gevalle van lewerkoma verkry is. Van die 39 gevalle (58%) wat herstel het, was 21 in diep koma; in die besonder, het 6 van die 13 gevalle van virus-lewerontsteking herstel. Die reekse wat voorheen gerapporteer is, toon aansienlik hoër sterftesyfers (die aantal gevalle wat herstel het, soos deur Sherlock aangegee, word tussen hakies gewys): Foulk *et al.*, lewersirrose 52 (5); Katz en Ducci, virus-lewerontsteking 1,000 (*nul*); Stokes *et al.*, virus-lewerontsteking 23 (2); McDermott *et al.*, poortaarsirrose 20 (4). Die hoër sterftesyfers wat hier opgeteken is, mag te wyte wees aan verwarring oor die definisie van ‚lewerkoma', wat hierdie navorsers miskien tot die beskrywing van bewustelose pasiënte beperk, en wat Sherlock *et al.* op 'n meer algemene wyse gebruik. As 'n mens die neuropsigiatriese sindroom na willekeur in ‚voor-bewustelose' en ‚bewustelose' toestande verdeel, sal die prognose van die laasgenoemde tipe van pasiënte natuurlik ernstiger wees. 'n Ander punt is die kliniese erkenning van die vroeë ‚voor-bewustelose' toestand; wanneer begin 'n siek pasiënt ‚belemmering van emosionele en geestesintellek' toon?

1. Kirk, E. (1936): Acta. med. scand., suppl. 77.
2. Bessmann, S. P. en Bessman, A. N. (1955): J. Clin. Invest., **34,** 622.
3. Sherlock, S., Summerskill, W. H. J., White, L. P. en Phear, E. A. (1954): Lancet, **2,** 453.
4. Sherlock, S., Summerskill, W. H. J. en Dawson, A. M. (1956): Lancet, **2,** 689.
5. Sherlock, S. (1956): Practitioner, **177,** 446.
6. Gabuzda, G. J. en Davidson, C. S. (1954): Ann. N.Y. Acad. Sci., **57,** 776.
7. Gyorgy, P., Stokes, J., Smith, W. H. en Goldblatt, H. (1950): Amer. J. Med. Sci., **200,** 6.

morrhage; oesophageal compression by means of a swallowed tube may be life-saving.

The Hammersmith results are distinctly better than those obtained in any previous series of cases of liver coma. Of the 39 cases (58%) that recovered, 21 had been in deep coma; in particular, 6 of the 13 cases of viral hepatitis recovered. The previous series reported showed considerably higher mortality figures (the number of cases that recovered, as quoted by Sherlock are shown in parenthesis): Foulk *et al.*, hepatic cirrhosis 52 (5); Katz and Ducci, viral hepatitis 1,000 (*nil*); Stokes *et al.*, viral hepatitis 23 (2); McDermott *et al.*, portal cirrhosis 20 (4). The higher death-rates recorded here may be due to confusion over the definition of 'hepatic coma', which these workers may confine to the description of unconscious patients and which Sherlock *et al.* use in a more general way. If one arbitrarily divides the neuropsychiatric syndrome into 'pre-unconscious' and 'unconscious' states, the prognosis of the latter type of patient will naturally be graver. Another point is the clinical recognition of the early 'pre-unconscious' state; when does a sick patient begin to show 'impairment of emotional and mental intellect'?

1. Kirk, E. (1936): Acta med. scand., suppl., 77.
2. Bessman, S. P. and Bessman, A. N. (1955): J. Clin. Invest., **34,** 622.
3. Sherlock, S., Summerskill, W. H. J., White, L. P. and Phear, E. A. (1954): Lancet, **2,** 453.
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6. Gabuzda, G. J. and Davidson, C. S. (1954): Ann. N.Y. Acad. Sci., **57,** 776.
7. Gyorgy, P., Stokes, J., Smith, W. H. and Goldblatt, H. (1950): Amer. J. Med. Sci., **220,** 6.