South African Medical Journal: Suid-Afrikaanse Tydskrif vir Geneeskunde

EDITORIAL

WITHDRAWAL SYMPTOMS

The characteristic abstinence syndrome which occurs when morphine is withdrawn from the addict is well known. The emotional and physical dependence of the addict on the drug is revealed by the features that develop, and authorities now agree that there is an organic basis for the syndrome. The character and severity of the syndrome depends on many factors. Although certain features are determined by psychic factors, most of the signs and symptoms represent an imbalance in the homeostatic adaptive mechanisms which developed in the body during the continued use of morphine.[1] Thus the former opinion that the abstinence syndrome is largely psychogenic in origin arising merely from anxiety and terror is no longer tenable.

The fact that the continued use of barbiturates can lead to addiction has been emphasized in recent years, although it has long been recognized in Germany. Primary barbiturate addiction resembles that to morphine in certain respects but is more serious as a medical problem. It has become an alarmingly common condition. In this country the recent promulgation of the Sixth Schedule, a list of potentially harmful drugs, including the barbiturates, has been designed to prevent easy access of the public to these drugs. Most persons addicted to barbiturates suffer from some basic disorder of character or psychoneurosis. Morphine addicts have used these drugs when the alkaloid was not readily obtainable, and in some instances both types of drug have been taken. Severe and even dangerous symptoms have followed the abrupt withdrawal of barbiturates from addicts. In morphine addiction nalorphine has been used for diagnosis since its administration may produce withdrawal symptoms; in this test for addiction it is advisable to obtain the patient's consent in writing, and reliable witnesses should be present.

When phenobarbitone has been used in the treatment of major epilepsy and for some reason it is decided to discontinue the drug great care is required not to stop administration abruptly, because status epilepticus may occur. If another drug such as phenytoin sodium is to be substituted the phenobarbitone dose should be decreased gradually over a week or so until the substituted anticonvulsant drug is exerting its full action. In the treatment of Parkinsonism, too, the same precautions are necessary; treatment with any drug should not be stopped suddenly but the daily dose should be reduced gradually.

Alcohol is an addiction-forming drug for which physical and organic dependence may develop. Some individuals

VAN DIE REDAKSIE

ONTHOUDINGSIMPTOME

Die tipiese terugtrekkingsindroom wat ontstaan wanneer morfien van die verslaafde onthou word, is goed bekend. Die verslaafde pasiënt se emosionele en liggaamlike afhanklikheid van dié middel word ontbloot deur die simptome wat dán ontwikkel, en die gesaghebbendes is dit nou eens dat daar 'n organiese grondslag vir hierdie sindroom is. Die aard en graad van die sindroom hang van velerlei faktore af. Hoewel sekere kenmerke deur psigiese faktore bepaal word, verteenwoordig die meeste van die tekens en simptome 'n wanverhouding in die homeostatiese aanpassende meganismes wat in die liggaam ontwikkel tydens die volhoue gebruik van morfien.[1] Die voormalige mening dat die onthoudingsindroom hoofsaaklik van psigogeniese oorsprong is en bloot uit angs en vrees spruit, is dus vandag nie meer geldig nie.

Daar is in die afgelope jare klem gelê op die feit dat die voortdurende gebruik van die barbiturate na verslawing kan lei, hoewel hierdie feit reeds lankal in Duitsland erken is. Primêre verslawing aan die barbiturate kom in sommige aspekte ooreen met dié van morfienverslawing, maar as mediese probleem is dit ernstiger. Dit het reeds 'n skrikwekkend algemene kondisie geword. In hierdie land is die doelwit van die onlangse promulgasie van die Sesde Bylaag ('n lys van potensieel skadelike middels wat die barbiturate insluit) om dit vir die publiek moeilik te maak om hierdie middels in die hande te kry. Die meeste slagoffers van barbituraatverslawing ly aan die een of ander grondslagtelike versteuring van karakter of psigoneurose. Verslaafdes aan morfien het ook al hierdie middels gebruik wanneer die alkaloïed nie maklik bekombaar was nie, en daar is gevalle waar albei soorte gebruik was. Ernstige en selfs gevaarlike simptome het gevolg wanneer barbiturate plotseling van verslaafdes weerhou word. By morfienverslawing is nalorfien gebruik by die diagnose aangesien die toediening daarvan ook onthoudingsimptome kan veroorsaak; by hierdie toets vir verslawing is dit raadsaam om die pasiënt se skriftelike toestemming te verkry, en betroubare getuies behoort teenwoordig te wees.

Wanneer fenobarbitoon in die behandeling van ernstige epilepsie gebruik word en daar word om die een of ander rede besluit om toediening te staak, moet groot sorg gedra word dat die onttrekking nie skielik geskied nie, aangesien status epilepticus kan voorkom. Indien die fenobarbitoon vervang gaan word deur 'n ander middel soos fenitoïen natrium, moet die dosis van die eersgenoemde geleidelik oor 'n week of langer verminder word totdat die plaasvervangende stuipebestrydende middel sy volle krag uitoefen. Dieselfde voorsorgsmaatreëls behoort toegepas te word by die behandeling van Parkinsonisme; die toediening van enige middel moet nie skielik gestaak word nie, maar die daaglikse dosis moet geleidelik verminder word.

Alkohol is nog 'n middel wat sy slagoffers liggaamlik en organies aan hom kan verslaaf. Sommige mense kan

may be tolerant to this drug and not develop withdrawal symptoms. Sudden deprivation of alcohol in some heavy drinkers may be followed by delirium tremens. Paraldehyde addicts have also experienced delirium tremens.

Much remains to be learned about the value of the numerous drugs reputed to act as tranquillizers. Some may not be very potent but amongst those which are extensively used important pharmacodynamic action does occur, and many toxic features, some of them severe, are being reported. With meprobamate (Milltown, Equanil, Mepavlon) withdrawal of the drug may cause symptoms resembling those of the barbiturate abstinence syndrome, including insomnia, ataxias, hallucinations, confusion, and grand mal seizures.[2,3]

The xanthine beverages are widely used. It appears to be accepted that the withdrawal of caffeine in individuals habituated to it sometimes results in a 'caffeine-withdrawal' headache, relieved by caffeine and of course by analgesic preparations containing caffeine.

Much stress has been laid on the importance of avoiding abrupt withdrawal of certain hormones used in therapy. Thus with corticotrophin (ACTH) the hypertrophied and overactive adrenal cortex, suddenly deprived of its stimulus, may remain inactive and a state like Addison's disease may develop. With cortisone and related analogues the abrupt withdrawal of the steroid at the end of a course of treatment may lead to the development of adrenocortical insufficiency.

Although strictly speaking it is not relevant to the present theme the opportunity may be taken to mention the general principle that in chemotherapy treatment should not be stopped too soon—for example, when the raised temperature has just been reduced to normal level. This introduces the danger of recurrence of the infection, possibly now more resistant to the drug originally exhibited.

1. Goodman, L. S. and Gilman, A. (1955): *The Pharmacological Basis of Therapeutics*. New York: The Macmillan Company.
2. Kincross-Wright, V. J. (1957): S. Afr. Med. J., **31**, 1167.
3. Ewing, J. A. and Haizlip, T. M. (1958): Brit. Med. J., **1**, 160.

hierdie middel verdra en by hulle ontwikkel geen onthoudingsimptome nie. Skielike ontneming van alkohol van party kwaai drinkers kan delirium tremens as gevolg hê. Delirium tremens kom ook by paraldehiedverslaafdes voor.

Ons moet nog baie leer omtrent die waarde van die talryke middels wat na bewering as kalmeermiddels werk. Party van hulle is glo nie baie sterk nie, maar by party wat grootskaals gebruik word kom daar 'n belangrike farmakodinamiese aksie voor; en baie vergiftigende kenmerke, waarvan sommige vry ernstig is, word gerapporteer. By meprobamaat (Milltown, Equanil, Mepavlon) kan terugtrekking van dié middel simptome veroorsaak ooreenkomstig met dié van die barbituraat-onthoudingsindroom, onder meer slapeloosheid, koördinasiesteurings, hallusinasies, verwarring en grand mal-aanvalle.[2,3] Die ksantiendrankies word oral gebruik. Dit word blykbaar aanvaar dat die onthouding van kaffeïen van indiwidue wat daaraan gewoond is, soms gevolg word deur 'n ‚kaffeïen-onthouding'-hoofpyn, wat verlig word deur kaffeïen en natuurlik deur pyndodende preparate wat kaffeïen bevat.

Daar word veel nadruk gelê op hoe belangrik dit is om skielike staking van sekere hormone by behandeling te vermy. Met kortikotrofien (ACTH) byvoorbeeld, kan die hipertrofiese en oor-aktiewe bynierskors onmagtig bly as dit skielik van sy stimuleerder beroof word, en 'n toestand soos Addison se siekte kan ontstaan. Met kortisoon en verwante analoë kan die skielike onthouding van die steroïed aan die einde van 'n behandelingskursus aanleiding gee tot die ontwikkeling van gebrekkige bynierskors-funksie.

Hoewel dit streng gesproke nie betrekking op die huidige onderwerp het nie, kan ons van die geleentheid gebruik maak om melding te maak van die algemene beginsel dat by chemoterapie die behandeling nooit te gou gestaak moet word nie—byvoorbeeld wanneer verhoogde temperatuur so pas na normaal gedaal het. Dit sou die gevaar van opvlamming van die besmetting meebring—'n besmetting wat ná 'n kort behandeling miskien meer weerstand as tevore aan die betrokke middel kan bied.