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KALMEERMIDDELS

Die woord ‚kalmeermiddel' is oor die laaste jare gebruik vir sekere soorte sedatiewe wat op die sentrale senuweestelsel inwerk. Daar is beweer dat hulle wat kwaliteit betref voortrefliker is as die barbiturate omdat hulle minder slaperigheid en minder verstandelike dofheid veroorsaak. Moontlik sal dit later blyk dat die verskil nie so groot is as wat dit nou lyk nie. Die middels wat onder hierdie hoof sorteer—soms ook bekend as ataraktiese of frenotropiese middels—behoort aan verskillende chemiese en farmakologiese groepe. Om die saak nog verder te bemoeilik, word verskillende verbindings van hierdie middels geadverteer, byvoorbeeld met 'n estrogeen, prednisolone, of 'n anticholinergiese stof.

Chlorpromazine en sommige van die nuwe ooreenkomstige middels (waarvan daar meer as 1,000 bestaan) sowel as reserpine, is goed bekend en baie doeltreffend. Die behandeling van psigiatriese pasiënte met chlorpromazine is met merkwaardige verbetering beloon, en soms is die reaksies daarop dramaties. Hierdie middel word grootskaals in hospitale vir sielsiekes gebruik.[1, 2] Meprobamate is ook gewild, en sekere ander middels is tans ook beskikbaar. Daar is in werklikheid omtrent 9 ondergeskikte groepe in hierdie klas middel.

Reserpine het 'n sedatiewe werking wat geskik is vir uitgerekte behandeling. Dit is goedkoop en slegs een dosis daagliks hoef toegedien te word. Soos die chlorpromazinegroep werk dit op die sentrale en op die outonomiese senuweestelsels. Dit het baie hoedanighede in gemeen met chlorpromazine; sommige daarvan gunstig en ander ongunstig.

Chlorpromazine is in 1950 sinteties voorberei en sy vinnige opname in die (behandelende) medisyne is goed bekend; nagenoeg 300 referate oor sy farmakologiese aksies is tussen 1954 en 1956 gepubliseer, en die moderne menings insake hierdie middel en ander stowwe wat onder die algemene groep van ‚kalmeermiddels' sorteer word in onlangse artikels bespreek.[3, 4] Dit is vandag moontlik om die aksie en toediening van chlorpromazine taamlik bevredigend te bereken. Die meeste van sy aksies spruit uit selektiewe, omkeerbare, sedatiewe uitwerkings op die sentrale senuweestelsel, wat nou nog moeilik is om uit te lê. Die teorie dat dit op die polisinaptiese retikulêre formasie van die brein inwerk is reeds voorgelê. Die werking van die sentrale outonomiese stelsel word sonder twyfel onderdruk. Die werking van verdowingsmiddels en van die barbiturate word daardeur moontlik gemaak, maar dit is nog nie vasgestel of dit ook met pynstillende middels gebeur nie. Slaperigheid, lusteloosheid, kalmte en onverskilligheid of apatie kan ontstaan en, met groot dosisse, ook motoriese vertraging, ataksie, en 'n Parkinsoniese gelaats-

EDITORIAL

TRANQUILLIZERS

The term tranquillizer has been used in recent years for certain types of central nervous depressants. Claims have been made that they are qualitatively superior to the barbiturates on the grounds that they produce less drowsiness, less mental clouding. This distinction may ultimately prove to be less than now seems apparent. The drugs that are being grouped under this heading—sometimes also referred to as ataraxic and phrenotropic drugs—belong to different chemical and pharmacological groups. To complicate matters, various combinations of these drugs, for example with an oestrogen, prednisolone, or an anticholinergic agent, are being advertised.

Chlorpromazine and some recently introduced congeners, of which altogether there are more than 1,000, and reserpine, are well known and most effective. In the treatment of psychiatric patients marked improvement has followed the use of chlorpromazine and sometimes the response is dramatic. The drug is used on a very large scale in the mental hospitals.[1,2] Meprobamate has been popular, and certain others are now available. There are actually about 9 subgroups in this class of drugs.

Reserpine has a tranquillizing action suitable for long-term therapy. It is cheap and a single daily dose can be administered. As with the chlorpromazine group, it has an action on the central nervous system and on the autonomic nervous system. It has numerous properties in common with chlorpromazine, some desirable, others undesirable.

Chlorpromazine was synthesized in 1950 and its rapid introduction into medicine is well known; close on 300 papers dealing with its pharmacological actions were published between 1954 and 1956, and current views on this and other drugs in the 'tranquillizer' groups have been published in more recent articles.[3,4] A fairly satisfactory evaluation of its actions and applications is now possible. Most of the actions are due to selective reversible depressant effects on the central nervous system, which remain difficult to explain. It has been suggested that it acts on the polysynaptic reticular formation of the brain. Central autonomic nervous activity is certainly inhibited. The actions of anaesthetics and of barbiturates are potentiated, but it is not yet established whether this happens with analgesics.

uitdrukking. Die pasiënt kan maklik gewek word, selfs al slaap hy. Hy raak onverskillig teenoor sy omgewing; angs verdwyn. Dit blyk dat chlorpromazine 'n kragtige sedatief is wat die hoër sentra vry laat met die vermoë tot volgehoue aandag en konsentrasie. Die reaksies varieer egter opvallend veel tussen verskillende mense. Die middel het ook ander uitwerkings waarvan party baie belangrik is; as voorbeelde dien die uitwerking op die hart en bloedvate en die interessante meganismes wat die veranderings in bloeddruk en bloedstroming teweegbring, en die uitwerkings op die gestreepte spiere en op die braakmeganisme. Daar is 'n paar vergiftigende effekte waarvan ons deeglik bewus is; lewerbeskadiging en bloedveranderings is die gevaarlikste. Dit blyk dat 'n paar van dié middels gewoontevormend kan wees.

'n Paar voorbeelde van die nuutste middels in die chlorpromazine-groep verdien melding. Promazine is minder kragtig en neem langer om te begin werk as chlorpromazine; dit word nie aanbeveel vir chroniese geestelike afwykings nie. Asetielpromazine is omtrent tweemaal sterker as chlorpromazine. Mepazine se anticholinergiese aksie veroorsaak newe-aksies. Perphenazine is kragtig maar, soos die ander middels, veroorsaak dit ook newe-uitwerkings. Prochlorperazine is ook kragtig, veral as 'n braak-teenmiddel.

Meprobamate verskil chemies en farmakologies van reserpine en die chlorpromazine-reeks. Sy mees spesifieke neurofarmakologiese aksie is die onderdrukking van polisinaptiese rugmurgreflekse en 'n uitwerking op die talamus. Dit het betreklik min invloed by ernstige sielsiektes, maar dit word beweer dat dit bekommernis en spanning verlig en ongevoeligheid teenoor uitwendige prikkels meebring. Slaperigheid, bewing, swak koördinasie, purpura en moontlik verslawing en die onttrekkingsimptome is reeds aan hierdie middel gewyt.

Benactyzine het benewens sy sedatiewe aksie ook anticholinergiese en papaverien-agtige uitwerkings. Hydroxyzine het 'n ligte uitwerking en is reeds gebruik by neurotiese pasiënte wat nog op die been is, en ook by angsvolle en oorprikkelbare kinders. Ectylurea kom in hierdie opsigte daarmee ooreen.

Nog meer ‚kalmeermiddels' word vandag bemark, waaroor die beskikbare inligting nog onvolledig is. Dit blyk dat party van hierdie middels op 'n gejaagde en onbeheerde wyse aan die mediese beroep aangebied is. Daar is baie en noukeurige werk nodig om die krag en moontlik toksiese hoedanighede van hierdie groep middels vas te stel en om uit te vind by watter siektes hulle waardevol is.

1. Ginsburg, M. (1957): S. Afr. T. Geneesk., **31**, 175.
2. Van die Redaksie (1957): *Ibid.*, **31**, 161.
3. Pennes, H. H. (1957): Bull. N.Y. Acad. Med., **33**, 81.
4. Gold, M. I. en Stone, H. H. (1957): Anesthesiology, **18**, 357.

Drowsiness, listlessness, calmness and apathy may be produced, and with large doses motor retardation, ataxia and Parkinsonian facies. Subjects are easily awakened even if asleep. They become indifferent to their surroundings, free from anxiety. Chlorpromazine appears to be a powerful sedative leaving the higher centres with the capacity for sustained attention and concentration. Individual responses, however, are strikingly variable. The drug possesses other actions, some of them very important; for example, the effects on the heart and blood vessels and the interesting mechanisms which produce the alterations in blood pressure and in blood flow, and the actions on striated muscle and on the vomiting mechanism. A number of toxic effects are well recognized, of which the most serious are liver damage and blood disturbances. With certain of these drugs it would appear that habit may be produced.

A few examples of newer agents in the chlorpromazine group may be mentioned. Promazine is less potent and has slower onset of action than chlorpromazine; it is not recommended for chronic mental disturbances. Acetylpromazine is about twice as potent as chlorpromazine. Mepazine produces side-effects from its anticholinergic action. Perphenazine is potent, but like the others, produces side-effects. Prochlorperazine is potent, especially as an antiemetic.

Meprobamate differs chemically and pharmacologically from reserpine and the chlorpromazine series. Its most specific neuropharmacological action is depression of polysynaptic spinal reflexes and an action on the thalamus. It is relatively ineffective in major mental disorders but is stated to relax anxieties and tensions and to produce indifference to external stimuli. Drowsiness, tremor, incoordination, purpura, possibly addiction and withdrawal symptoms, have been attributed to this drug.

Benactyzine has anticholinergic and papaverine-like actions in addition to a tranquillizing action. Hydroxyzine has a mild action and has been used in ambulatory neurotic subjects as well as in anxious and hyperexcitable children. Ectylurea is similar in these respects.

Still more 'tranquillizers' have been put on the market about which the available information is incomplete. Some of these seem to have been presented to the medical profession in a hurried and uncontrolled manner. Much careful work is needed to determine the potency and toxic potentialities of this group of drugs, and the diseases in which they are of value.

1. Ginsburg, M. (1957): S. Afr. Med. J., **31**, 175.
2. Editorial (1957): *Ibid.*, **31**, 161.
3. Pennes, H. H. (1957): Bull. N.Y. Acad. Med., **33**, 81.
4. Gold, M. I. and Stone, H. H. (1957): Anesthesiology, **18**, 357.

THE ANXIETY NEUROSIS

In these days when so much is being written about anxiety states and so many drugs are being put on the market as anti-anxiety agents to relieve mental and muscular tension and to produce relaxation and peace of mind (ataraxia) it is necessary to be sure in one's own mind of the true meaning of anxiety neurosis, its aetiology, course, and rational treatment. This knowledge is necessary because of the widespread occurrence of this psychoneurosis, and the great emphasis that is being placed in some quarters on the use of tranquillizers for the condition.

The necessity to differentiate psychological illness from organic disease, and the recognition that the symptoms of psychoneurosis may complicate those of organic disease, must constantly be in mind. Anxiety neurosis, hysteria and 'traumatic neurosis' represent the three common psychoneuroses.[1] The anxiety reaction is characteristically found

in intelligent, educated persons. It may occur at any age. It is the most frequently encountered psychoneurosis and fortunately the most amenable to treatment. The patients commonly have a neuropathic inheritance developed in a morbid environment created by their parents. The development of an anxiety neurosis is the culmination of tendencies that always coloured their attitude to circumstances, finally precipitated by some conflict between their individual needs and the reality with which they become faced. Anxiety and fear are followed by mental and physical reactions. Anxiety then becomes transferred from its original cause to the symptoms, which become the cause of anxiety.

The mental symptoms which arise are the outcome of great anxiety, but there is no mental deterioration. Inability to concentrate, irritability, poor memory, loss of sleep, and fear, are some of the features that develop. Pain of unusual nature and discomforts of body sensation may be amongst the complaints. Cardiovascular and gastro-intestinal disturbances and sexual disabilities are also characteristic of the somatic symptoms, but there is no objective evidence of bodily disease. The symptoms engage the patient's attention and he talks of little else. The picture is that of an individual in normal physical health suffering from anxiety and fears which are attributed to mental and physical symptoms.

The majority of cases are amenable to treatment. In its milder forms the condition is common; a short course of treatment is sufficient in many patients, but in the severer cases prolonged therapy may be necessary. In some cases specialist treatment is required, but for very many patients advice from the family doctor should be adequate. Psychological treatment is necessary, and physical remedies are of adjuvant, even of suggestive, value. A careful history and physical examination to rule out the possibility of other conditions, especially depressive psychosis, schizophrenia, early paralysis agitans, and early dementia paralytica, are essential. The patient is best told about the nature of his illness, the absence of somatic disease to account for the symptoms, and the fact that psychological factors are the basis of his illness. The doctor will explain the role of anxiety in the production of the symptoms. Assurance is given that he will get well. Drugs may be used, but if emphasis is placed on them treatment may be defeated by the suggestion that physical factors are really present.

1. Walshe, F. M. R. (1955): *Diseases of the Nervous System.* Edinburgh: Livingstone.