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Abstract
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RES MEDICA

THE ROYAL MEDICAL SOCIETY

226th Session

THE SOCIETY

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THE APPEAL

The future of the Society has been affected by several important developments during the year.

The Society was informed early in the session that the Midlothian County Council has speeded up its plans, and now intends to acquire the present Hall by compulsory purchase within two years' time. Their previous scheme had envisaged our removal in about ten years.

With the co-operation of the University, plans are in hand for the Royal Medical Society to build a completely autonomous New Hall on the site of the proposed Student Amenities Centre. It is welcome news that work will start on clearing this site earlier than had been anticipated—probably in 1965. The estimated cost of such a building is not as high as had been feared, and it also seems likely the value of the present hall will prove to be higher than at first thought.

Thus although the need for new premises has become more urgent during the session, the prospect of obtaining a new hall has become brighter, provided the necessary financial support is received.

NEW LAWS

Next session the triennial meeting to review the laws of the Society falls due. As a preparatory measure, a committee was appointed in February to suggest ways of improving the laws, particularly with a view to attracting more members. In a preliminary report, the committee suggested that business meetings similar to the present 1st. private business should be held on only three evenings each term, so that the first hour of the other meetings could be used for the discussion of topics of interest to preclinical as well as clinical medical students.

Such a change would necessitate considerable streamlining of the Society's procedure, to enable business matters to be completed in the much shorter time available. With this in view, the committee produced a revised version of the laws incorporating the proposed changes, together with a number of time-saving alterations to the procedure for the election of members, fellows, etc. Provision is also made for the election of a Private Business Committee to arrange business for the early part of each meeting, and to share some of the duties of the over-worked Public Business Committee.

At the final 2nd Private Business of the session it was unanimously decided that the revised laws should be brought into effect with the force of regulations for an experimental period from the start of next session until February 1964, when the whole position will be reviewed at the statutory triennial meeting.

THE PHARMACOLOGY OF SOME HYPOTENSIVE DRUGS

The arterial blood pressure is controlled by the autonomic nervous system. Information about the level of arterial pressure is obtained from the receptors in the aortic arch and carotid sinus together with those situated in the heart. Generalised arteriolar constriction increases the total peripheral resistance and hence the blood pressure; conversely arteriolar dilation results in a fall in blood pressure. Normally peripheral arteriolar constriction is brought about by release of noradrenaline and adrenaline from sympathetic nerve endings, or by the release of adrenaline from the adrenal medulla. The same mechanism is responsible for increase in vasomotor tone and, in part, for the mechanism responsible for increase in heart rate. The anatomical pathways for these reflexes are :

(a) Carotid sinus.
(b) Hypothalmus, midbrain and spinal chord.
(c) Sympathetic ganglia.
(d) Sympathetic post ganglionic nerve.
(e) Peripheral adrenergic receptors.

Many drugs acting on the central nervous system cause a fall in blood pressure; even sleep induces such a change. Rises in blood pressure in stress and emotion are reduced or abolished by tranquilisers, e.g. chlorpromazine or sedatives such as barbiturates. Meprobamate is thought to cause block of spinal interneurones and also has a hypotensive effect. A more active analogue, membutamate was discovered. This drug causes a fall in blood pressure in the renal hypertensive rabbit. In man it has a hypotensive effect lasting six hours. It does not alter the cardiac output or cause any obvious haemodynamic changes. In crossed circulation experiments in the dog, where one limb was

isolated except for a connection by the sciatic nerve, a significant increase in the blood flow in the isolated limb following a membutate injection was observed. This suggests that the prime site of action is in the central nervous system, but its place in therapy, if any, has not yet been determined.

Another drug of particular interest belonging to the tranquilliser group is reserpine. Adrenaline, noradrenaline and often 5 hydroxy-tryptamine occur in granules in the brain, sympathetic nerve endings and chromaffin tissues. These are probably associated with A.T.P. The A.T.P. occurring at these sites has been shown by radio-tracer experiments to be far less labile than that occurring in other tissues. The ratio of A.T.P. to catecholamine approximates to 1 : 4.

Brodie, in 1956, showed that reserpine depleted the brain of serotonin and suggested the probability of it having its main effect via central mechanisms. Later Maxwell showed that the drug also depletes the brain of catechol amines. Carbeau and his co-workers then showed that reserpine causes adrenaline and noradrenaline depletion in the nerve endings, and also that it has a direct relaxing effect on smooth muscle. Reserpine, unlike chlorpromazine, does not decrease sympathetic activity passing into the ganglion. Thus it is no longer certain that the hypotensive action of reserpine is central.

An analogue of reserpine, syrosingopine, in which the trimethoxy phenyl group is replaced by a dimethoxy-propyl phenyl group, has been synthesised. It was found that 25 mgms of syrosingopine depletes the peripheral nerve endings at catechol amines whilst 800 mgms. are needed before depletion of central catechol amines takes place. At the lower dose level syrosingopine has a hypotensive but not sedative effect. Tetrabenasine depletes central catechol amines but not peripheral amines and does not have a hypotensive action. It is, therefore, probable that the sedative action of reserpine can be regarded as distinct from the hypotensive and to be the result of central action. The peripheral action of reserpine is depletion of catecheol amines at the nerve endings with consequent hypotension. It has been shown that if catechol amine content of the nerve ending falls below 10% of the normal level transmission to the effector organ ceases. Dopa has been shown to be taken up rapidly by the reserpinised animals and converted to noradrenaline. However, on analysis, the noradrenaline was found only in the intracellular sap suggesting that the depletion is a result of interference in the storage mechanisms.

Just lately some new hypotensive drugs acting on the post-ganglionic nerve have been discovered. Bretylium tosylate was originally introduced by Bourra. This drug when given intravenously in the cat first causes pilocrection, rise in blood pressure and other sympathomimetic effects. Later it causes hypo tension. Bretylium does not cause depletion at the nerve ending but neither does it block transmission at the ganglia. It does not, in any way, antagonise the effect of reserpine. Bretylium, in high concentrations has been shown to act as a local anaesthetic. It is now thought that it acts by blocking transmission at the nerve terminals resulting in a failure to release noradrenaline.

Another drug recently introduced and acting on the postsynaptic nerve is guanethidine. Chemically the drug is unusual, it contains an eight membered ring and a guanide group. The drug causes depletion of catechol amines in the nerve endings but not in the adrenal medulla or the brain. It also has some ganglion blocking activity. Like bretylium; guanethidine has some sympathomimetic activity but whether this is due to release of noradrenaline or a direct action of the drug is unknown. This drug in no way inhibits the action of injected noradrenaline or angiotonin implying that the point of

action is before the effector site. Transmission has been shown to be depressed at the ganglion but not sufficiently to account for the hypotensive effect. Similarily post ganglionic stimulation did not cause contraction of the smooth muscle effector organ. In certain preparations guanethidine has been shown to enhance the action of acetyl choline. Now on Burn's theory of adrenergic mechanisms the post synaptic nerve is cholinergic and causes the release of noradrenaline from peripheral stores. Thus the story of an action similar to acetyl choline or facilitation of acteyl choline would fit in well with this theory. On the other hand there is no direct proof that the implementation of acetyl choline action has any connection with the hypotensive action. Another possibility is that guanethidine has some action on the storage of catechol amines in the nerve ending. There is no proof that the mode of action is depression of conduction or interference in the synthesis of catechol amines.

Another hypotensive drug, Alpha methyl dopa, has been recently introduced. It has been shown to decrease the excretion products of tyrosine and tryptophane metabolism. It also reduces the stores of catechol amines in the heart and brain. It is thought that it acts as a competitive inhibitor of dopa decarboxylase and, hence, antagonises the formation of adrenaline and noradrenaline. However, after catechol amine depletion following alpha methyl dopa treatment the dopa decarboxylase activity has been shown to recover before the effects of the drug on blood pressure have worn off. Thus one has to postulate either a very slow turnover rate in the formation of the catechol amines, which seems most unlikely, or that competitive inhibition is only part of the story. Perhaps, as with reserpine, there is some interference with the storage mechanism.

BOOK REVIEW

THE CHILD AND HIS SYMPTOMS—A PSYCHOSOMATIC APPROACH by John Apley and Ronald MacKeith. published by Blackwell Scientific Publications, Oxford, at 25s.

"In illness the whole person is involved and, in trying to understand why he is ill at the time and in the way he is ill, it is logical to look at the whole person, body and mind. This is the comprehensive, psychosomatic approach."

Thus opens the preface of this book and thus it is well titled "The Child AND His Symptoms".

The reader must not be put off by regarding this book as only another esoteric account of the ins and outs of child psychiatry. On the contrary, Drs. Apley and MacKeith go to considerable length to put their "psychosomatic approach" into perspective with the simpler and more obvious diagnoses of organic disease.

As is implied by the title this book is mainly concerned with the common symptoms with which a child may present in the doctor's consulting room. Fourteen out of the twenty-three chapters are devoted to the discussion of one such symptom or group of symptoms, topics covered range from respiratory symptoms and recurrent pain to tics and feeding disorders. The two opening chapters are introductory and briefly explain what the authors mean by the term psychosomatic medicine. There are two excellent chapters on handicaps of various types and their effects on parent, sibling and child. The last four chapters are devoted to the discussion of the old subject of the doctor - patient relationship. There is nothing startlingly new in these chapters but there are several useful practical tips to be garnered.

The book is concisely written and is eminently readable to anyone remotely interested in paediatric medicine. The stress is naturally put upon the psychosomatic causes of symptoms but the authors back up their claims with brief, well chosen histories and some most interesting statistics. There are few illustrations, of any form, since these are hardly necessary. The book is well produced in a clear and simple fashion and includes a very adequate index and list of references.

Its price possibly places it outside the financial reach of the average student. However the time taken to read it would be well spent by anyone contemplating a career in general practice and certainly by the budding paediatrician.

N.A.B.