after the toxin administration. On an average, the content of serotonin and noradrenaline in pooled brains was about 50 per cent of that of the controls. *Shigella shigae* thus causes a considerable depletion of catecholamines in the brain.

29 Excretion of Vanilmandelic Acid by Psychiatric Patients as Related to Drug Therapy. I. MUNKVAD and A. RANDRUP (Denmark).

The demonstration that several psychopharmaca affect brain amines, seems to furnish a clue for further studies on the modes of action of these drugs. Measurement of the influence of the drugs upon the excretion of the amines and their metabolites in urine may thus be of interest, as this could give some information on the direct or indirect influence of the drugs upon the production and the ways of metabolism of the amines. As it is also possible to measure the urinary excretion products in the clinical situation, we have chosen this procedure for studying the mode of action of some drugs in psychiatric patients.

In earlier publications from this hospital the effect of reserpine and of iproniazid upon adrenaline and noradrenaline excretion was reported. This work has now been extended by measurements of vanilmandelic acid, the oxidized excretion product of these two amines. The vanilmandelic acid is isolated by high voltage electrophoresis at pH 3 and measured colorimetrically. The effects of chlorpromazine (in varying doses), reserpine and tetrabenazine is studied.

30 Suppression by Iproniazide of the Antagonistic Action of Reserpine on Amphetamine "Group Toxicity". B. N. HALPERN and C. BARACCO-DRUDI (France).

Reserpine is known to reduce the "group toxicity" of amphetamine in mice, as does chlorpromazine. It has been found in this laboratory that treatment with iproniazide suppresses the effect of reserpine and raises the amphetamine "group toxicity" in reserpine-treated animals to the level of the controls.

The time interval between the injection of iproniazide and reserpine is an essential factor. In our experiments, iproniazide is injected first, followed by the injection of reserpine, while DL benzedrine is administered, in all cases, 4 hr after reserpine. No inversion of the action of reserpine is observed, if the interval iproniazide-reserpine is less than 4 hr. The inversion is regularly observed during the time interval 4–36 hr.

The effect of chlorpromazine is not affected by pretreatment with iproniazide. The mechanism of the inversion by iproniazide of the action of reserpine on the "group toxicity" of amphetamine in relation with the cerebral metabolism of aromatic amines will be discussed.

31 Studies on the Mechanism of Uptake of Catecholamines by Isolated Brain Tissues. E. O. TITUS and H. J. DENGLER (U.S.A.).

Norepinephrine-^{3}H (NE) in slices of cat cerebral cortex incubated with 5 mμg/ml of the labelled amine in Krebs bicarbonate approaches a steady state concentration approximately 4 times that in the medium after 45–60 min. The uptake mechanism, which operates against a concentration gradient and becomes saturated at levels near 100 mμg/ml may be an active transport. It does not function at 0°C and like active transport of 5-hydroxytryptamine in platelets is inhibited by reserpine and cardiac glycosides. Since administration of 3 mg/kg of phenyl α-methylprophylhydrazine (JB 516) 24 hr before the experiment or preincubation of brain slices in 10^{-6} M JB 516 is without effect on uptake, this amine oxidase inhibitor is used to minimize NE breakdown during transport studies. After 45 min incubations, 70 per cent of the isotope in the medium is NE (determined chromotographically). Isotope emerging from the slice in the steady state is accounted for by the following percentages: NE, 42; epinephrine, 2; normetanephrine 35; acidic products of amine oxidase, 19. Corresponding percentages from slices without JB 516 are: 13·6, 10·7, 6·2 and 70·2, respectively. Since 80 to 90 per cent of endogenous NE does not exchange with isotopic NE in 2 hr, NE taken up by the transport mechanism must equilibrate very slowly or not at all with the stored NE in isolated slices. The data suggest existence of at least two intracellular pools of NE.

32a Teneur en Nor-Adrenaline du Tissu Cerebral d'Animaux soumis a l'action de l'Aminodipropionitrile. M. BEAUVALLET et J. FUGAZZA (France).

En 1952, Delay *et al.* ont constaté que l'aminodipropionitrile:HN = $(CH_2\text{-}CH_2\text{-}CN)_2$ (I.D.P.N.) provoque chez la souris une agitation motrice permanente; l'animal présente une activité généralisée avec forte tendance à tourner en rond.

Les rats soumis à l'injection du même produit réagissent de façon voisine, présentant des troubles de la coordination motrice avec perte d'équilibre.

Dans ce travail, nous avons recherché la teneur en nor-adrénaline du tissu cérébral du rat et de la souris avant et après l'injection d'I.D.P.N.

Les premières expériences ont été faites sur des rats de race Wistar de 60–100 g; 3 groupes de 6 femelles et 1 groupe de 6 mâles reçoivent deux injections intrapéritonéales d'I.D.P.N. à 48 heures d'intervalle. Le tissu cérébral est prélevé dès l'apparition du syndrome excito-moteur. En même temps on prélève le cerveau d'un animal normal de même portée, de même sexe et de même poids.

Les résultats que nous avons obtenus montrent que la teneur en nor-adrénaline du tissu cérébral du rat mâle ou femelle soumis à l'action de l'I.D.P.N. est très voisine de celle de l'animal normal.

Nous avons trouvé des taux parfois légèrement inférieurs, parfois légèment supérieurs. C'est ainsi que chez les femelles normales la plus grande quantité de nor-adrénaline observée a été de 0·23 μg/g, la plus faible étant de 0·18; chez les femelles injectées, le maximum est de 0·25 et le minimum de 0·16. La moyenne des différentes valeurs obtenues est de 0·22 μg/g chez les rats normaux et de 0·20 μg/g chez les animaux soumis à l'action de l'I.D.P.N.

Une deuxième série d'expériences a été entreprise sur la souris. Comme chez le rat, nous n'avons observé que de faibles variations—augmentation ou baisse—de la teneur en nor-adrénaline du tissu cérébral de la souris tournante.

Les résultats que nous avons obtenus montrent donc que la nor-adrénaline du tissu cérébral ne subit pas de variations importantes lorsque le syndrome excito-moteur se constitue.

32b Nor-Adrenalin Content of the Cerebral Tissue of Animals under the Influence of Aminodipropionitril. M. Beauvallet and J. Fugazza.

In 1952 Delay *et al.* found that aminodipropionitril;$HN = (CH_2\text{-}CH_2\text{-}CN)_2$ (IDPN) causes permanent motor agitation in the mouse; the animal shows generalized activity and a strong tendency to turn in circles.

Rats, submitted to injections of this substance react in a similar way; they show disturbances of motor co-ordination and loss of equilibrium.

In the present investigation we studied the nor-adrenalin content of the brain tissues of rats and mice before and after the injection of I.D.P.N.

The first experiments were performed on rats of the Wistar strain, weighing 60–100 g; 3 groups of 6 females and 1 group of 6 males received 2 intraperitoneal injections of I.D.P.N. at intervals of 48 hr.

The cerebral tissue was removed as soon as the motor-excitation syndrome appeared. At the same time the brain of a normal animal of the same litter, sex and weight was removed.

The results obtained by us show that the nor-adrenalin level in the cerebral tissue of the male or female rat, subjected to the action of I.D.P.N., is similar to that of normal animals. The values obtained were either slightly lower or slightly higher. Thus, the largest amount of nor-adrenalin found in normal females was 0·23 μg/g, the lowest was 0·18; in injected females the maximum was 0·25 and the minimum 0·16. The mean of the different values obtained in normal rats was 0·22 μg/g and in animals which had been given I.D.P.N. it was 0·20 μg/g.

A second series of experiments was carried out with mice. As in rats, only slight variations (increases or decreases) in the nor-adrenalin content of the brain tissues of revolving mice was found.

The results obtained by us show that nor-adrenalin in the cerebral tissues does not undergo any important variations while the motor-excitation syndrome develops.

33 The Effect of Eserine on the Activity of Adrenergic Nerves in the Rat. V. Varagić, R. Lešić, J. Vuco and B. Stamenović (Yugoslavia).

It has been repeatedly found that eserine raises the blood pressure of the rat anaesthetized by urethane (Varagić, 1955; Dirnhuber and Collumbine, 1955; Hornykiewicz and Kobinger, 1956) as well as of the conscious rat (Medaković and Varagić, 1957). Several factors influencing this effect of eserine have been studied. Pretreatment with reserpine regularly abolished the hypertensive response to eserine. The slow intravenous infusion of noradrenaline, L-DOPA and 5-hydroxytryptamine restored the hypertensive effect of eserine only occasionally. Bretylium and choline 2:6-xylyl ether bromide significantly depressed or abolished the hypertensive effect of eserine. Cocaine was found to antagonize the action of bretylium. In doses which depressed the action of eserine bretylium did not inhibit the hypertension due to excitation of medullary centres induced by clamping the common carotid arteries. Pretreatment with *iso*propylisonizid did not antagonize the inhibitory action of reserpine on the hypertensive response to eserine.

Similar results were obtained by recording the electrical activity in the sympathetic fibres in the mid-cervical region. It is concluded that the available evidence indicates that the hypertensive effect of eserine in the rat is due to central activation of adrenergic nervous elements. Liberation of noradrenaline (and adrenaline) from the adrenals and from the blood vessels by eserine does not play a significant role in causing the hypertensive effect of eserine.

34 The Relation between Structure and Central Nervous Action of some Hydrazine Derivatives. A. Spinks and E. H. P. Young (United Kingdom).

About 300 derivatives of hydrazine have been prepared and examined by several biological tests for activity on the central nervous system and particularly for their ability to cause hyperactivity in mice subsequently injected with reserpine. The compounds tested included both straight and branched chain aralkylhydrazines and their acyl derivatives, bis-aralkylhydrazines and aryloxyalkyhlhydrazines. The effect of these structural changes, and especially of nuclear substitution, on biological activity has been studied and some relationships have been observed.

It was found that the most promising compound in respect of activity and low toxicity was α-methylbenzylhydrazine (α-phenylethylhydrazine). Nuclear substitution in this and other classes usually reduced activity, and 3:4-dichloro-substitution of many