ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ALKALOIDS

Atidine, a New Diterpene Alkaloid from *Aconitum heterophyllum*. S. W. Pelletier. (*Chem. Ind.*, 1956, 1016.) The strongly basic alkaloid fraction from the roots of *Aconitum heterophyllum* was chromatographed on alumina and after the removal of atisine from the column with benzene, benzene-methanol (50:1) was used as the eluant and yielded heavy prisms m.p. 176 to 181°. An analytical sample ($C_{22}H_{33}NO_3$) showed m.p. 182·5 to 183·5° $[\alpha]_D^{29} - 47°$ (*c*, 1·7 in $CHCl_3$) pKa 7·53; the hydrochloride crystallised from acetone as prisms, m.p. 204 to 215°. The sample (atidine) had an infra-red spectrum (in KBr) which indicated the presence of –OH, >C=O, >C=CH_2 and C–Me. It formed an amorphous diacetate, and a crystalline diacetate hydrochloride m.p. 182 to 190°. Treatment of atidine with hydroxylamine acetate gave an amorphous oxime. Reduction of atidine with sodium borohydride in 80 per cent methanol afforded an amorphous dihydroderivative which gave an infra-red spectrum devoid of carbonyl absorption. Catalytic reduction gave an amorphous tetrahydroderivative, pKa 8·47, which could be oxidised with lead tetra-acetate to form glyoxal, demonstrating the presence of an ethanol-amine system. The data indicate a pentacyclic, tertiary base of the dihydroatisine type containing a carbonyl group in a six-membered ring. A. H. B.

ANALYTICAL

Barbituric Acid Derivatives, Microscopic and X-ray Diffraction Methods for the Identification of. W. G. Penprase and J. A. Biles. (*J. Amer. pharm. Ass., Sci. Ed.*, 1956, **45**, 585.) For the identification of barbiturates when only small specimens were available, a sample was dissolved in water with the aid of sodium hydroxide and the solution filtered and acidified with dilute sulphuric acid. After the addition of sodium bicarbonate (to prevent extraction of salicylates) the solution was extracted with ether, the ether evaporated and the residue recrystallised from dilute ethanol. Crystals were obtained by recrystallisation from water or strong solution of ammonia, or by sublimation on a microscope slide, and examined under the microscope; photographs illustrating the crystalline habits of the various barbiturates are provided for comparison. The melting point was determined by the Kofler melting point apparatus. Crystallisation from various solvents, fusion and sublimation provide a basis for the rapid identification of barbituric acid derivatives, except for quinalbarbitone, which does not crystallise readily under the usual conditions. Purified samples of barbiturates were finely ground and submitted to X-ray diffraction analysis. The d-distances are reported, and may be used as further evidence for the identification of these compounds. G. B.

Digitalis, Chemical Assay of. H. Knöchel. (*Pharmazie*, 1956, **11**, 378.) The author considers digitoxin the most pharmacologically active component of digitalis. Since gitoxin and digitoxin both give the same extinction when assayed by the Soos method, whereas there is considerable difference in the

extinction when determined according to the method of Howland, it is possible by combining these two methods to determine the digitoxin, and details of the method are given. This includes a hot extraction procedure in which the extracting water is passed through a steam-heated condenser before reaching the drug, so that extraction occurs at about 80 to 90°. The method may also be used for determination of the active glycosides of *D. lanata*. G. M.

Morphine in Individual Poppy Capsules, Determination of. S. Pfeifer. (*Pharmazie*, 1956, **11**, 387.) About 0·2 g. of the finely powdered dried material is rubbed down with 1 ml. of water and, after 15 minutes, treated with 5 g. of "acid" aluminium oxide. The resulting powder is eluted with water, about 20 ml. being collected. This is treated with 1 ml. of ammonia (10 per cent NH_3) and 0·2 g. of ammonium chloride, and extracted twice with 20 ml. portions of chloroform—*iso*propyl alcohol (3 + 1), then once with 10 ml. The chloroformic solution is evaporated to dryness and the residue is taken up in 5 ml. of chloroform, then extracted with 15 ml. of 0·1N hydrochloric acid: 5 ml. of this solution is mixed with 2 ml. of 1 per cent solution of sodium nitrite and shaken for 15 seconds. After exactly 15 minutes 3 ml. of ammonia (10 per cent) is added and then 2·5 ml. of water. After a further 5 minutes the colour is measured (Filter S47). A further 5 ml. of the acid solution is heated for 5 minutes on the water bath with 4·5 ml. of water and 3 ml. of ammonia: this used as a comparison solution and compensation for narcotoline. G. M.

Reserpine, Determination of. C. R. Szalkowski and W. J. Mader. (*J. Amer. pharm. Ass., Sci. Ed.*, 1956, **45**, 613.) A rapid method for the determination of reserpine depends on the formation of a greenish-yellow colour when an ethanolic solution of reserpine is treated with dilute sulphuric acid and sodium nitrite. A sample containing 0·05 to 0·1 mg. of reserpine dissolved in 5 ml. of methanol is mixed with 3 ml. of 0·5N sulphuric acid and 2 ml. of a 0·3 per cent solution of sodium nitrite. After the solution has been allowed to stand for 1 hour, the light absorption at 390 mμ is measured against a compensating blank, consisting of 5 ml. of methanol, 3 ml. of 0·5N sulphuric acid and 2 ml. of water. At the same time, experiments are carried out using known quantities of a standard preparation of reserpine, and the reserpine content of the sample is calculated by comparison. The green colour is given by reserpic acid, methyl reserpate and rescinnamine in addition to reserpine, but alstonine, rauwolscine, sarpagine, raunescine, deserpidine and yohimbine do not interfere. For the assay of reserpine tablets, citric acid solution is added to the powdered tablets. The material is extracted with chloroform, and, after washing with sodium bicarbonate solution, the chloroform solution is evaporated and the residue assayed as above. The extraction process is satisfactory in the presence of acetylsalicylic acid, amphetamine and caffeine, but hydrallazine, mannitol hexanitrate, phenacetin and theophylline inhibit the formation of the colour. In the assay of reserpine tablets, good agreement was obtained between this method and assays by phase solubility analysis and ultra-violet absorption methods. G. B.

Sodium Tetraphenylboron in the Identification and Isolation of Alkaloids. W. E. Scott, H. M. Doukas and P. S. Schaffer. (*J. Amer. pharm. Ass., Sci. Ed.*, 1956, **45**, 568.) Sodium tetraphenylboron derivatives were prepared from 21 alkaloids and in all cases the reagent was at least as effective as Mayer's reagent for detecting the alkaloids. In the concentrations used in the test, Mayer's

reagent failed to detect ephedrine, solanine, tomatidine, tomatine, *N*-acetyltomatine and betaine, all of which gave a turbidity with sodium tetraphenylboron. When using sodium tetraphenylboron as a reagent for alkaloids, potassium and ammonium ions must be absent. In the recommended method, 20 mg. of alkaloid is dissolved in 15 ml. of water and 6 drops of glacial acetic acid. The solution is heated to 70° and 0·1M sodium tetraphenylboron is added until no further precipitation occurs. The alkaloids may be regenerated by adding a 5 per cent solution of sodium hydroxide to the acetone or ethanolic solution, heating on a water bath for 15 minutes, removing the solvent and extracting with chloroform. The melting points of the sodium tetraphenylboron derivatives of 21 alkaloids are reported. G. B.

BIOCHEMISTRY

BIOCHEMICAL ANALYSIS

Carbutamide, Determination of. A. Häussler. (*Arzneimitt.-Forsch.*, 1956, **6**, 393.) For determination in urine, 1 ml. of the sample (containing 10 to 100 g.) is mixed with 2 ml. of water and 2 ml. of N hydrochloric acid, and diazotised in the cold with 1 ml. of 0·1 per cent solution of sodium nitrite. After 3 minutes 1 ml. of 0·1 per cent sulphamic acid is added and, after 3 minutes, 3 ml. of a solution containing 2 per cent of potassium guaiacol sulphonate and 10 per cent of sodium carbonate. The absorption at 470 mμ is compared with a standard curve. For determination in serum, 3 ml. is treated with 3 ml. of a mixture of 9 parts of 13 per cent trichloroacetic acid and 1 part of N hydrochloric acid. After standing 10 minutes and centrifuging, 3 ml. of the clear liquid is mixed with 1 ml. of water and 1 ml. of N hydrochloric acid, and the analysis is completed as above. The standards are prepared with serum to which is added known quantities of carbutamide. For faeces, 3 g. is mixed with 3 ml. of water and 3 ml. of the trichloroacetic acid solution. After centrifuging, the liquid is filtered twice and to 3 ml. of the filtrate is treated as above. These determinations show only the non-acetylated compound: the total may be determined after hydrolysis by the usual methods. To distinguish between other compounds which also give a colour in this reaction, a chloroform extract is taken up in hydrochloric acid and the absorption curve determined. Carbutamide shows a maximum at 255 mμ. G. M.

5-Hydroxytryptamine in Brain, Identification and Assay. D. F. Bogdanski, A. Pletscher, B. B. Brodie and S. Udenfriend. (*J. Pharmacol.*, 1956, **117**, 82.) A fluorimetric method for the determination of 5-hydroxytryptamine (5-HT) in brain is described. A spectrophotofluorimeter capable of activating compounds and measuring their fluorescence over the range 250 to 650 mμ was used. The 5-HT content of rat's and rabbit's brain was identified and determined by this method and by countercurrent distribution and subsequent fluorimetric assay. Estimates of brain 5-HT content by these methods correlated well with bioassay on the clam heart. G. P.

Lysergic Acid Diethylamide, Metabolism of. J. Axelrod, R. O. Brady, B. Witkop and E. V. Evarts. (*Nature, Lond.*, 1956, **178**, 143.) The development of a sensitive method for estimation of the hallucinogenic agent, lysergic acid diethylamide (LSD), in biological materials has enabled the study of its distribution and metabolism in the body. The LSD was extracted from a salt-saturated suspension of biological material into heptane containing 2 per

cent *iso*amyl alcohol. It was then returned to dilute hydrochloric acid and after activating at 325 mμ, the fluorescence was measured at 445 mμ in a spectrophotometer. The method was sensitive to as little as 0·001 μg. of LSD. After administration of LSD to a cat the drug was recovered from all tissues, in order of decreasing concentration: bile, plasma, lung, liver, kidney, brain, cerebrospinal fluid, spleen, intestine, muscle and fat. It was calculated from the figures obtained that LSD in man exerts its action at a concentration of 0·0003 μg./g. of brain tissue. The drug was almost completely metabolized in the body, only traces appearing in the urine and faeces. Transformation was by liver microsomal enzymes, mainly to 2-oxylysergic acid. This metabolite was shown to have no effect on transmission through the lateral geniculate nucleus at a dose level ten times that at which LSD produced 80 per cent block. Similarly 300 μg. of 2-oxylysergic acid diethylamide given orally had no psychological effects in human subjects who responded to 30 μg. of LSD.

G. P.

Trichloroethylene, Trichloroacetic Acid and Trichloroethanol in Urine, Determination of. T. A. Seto and M. O. Schultze. (*Analyt. Chem.*, 1956, **28**, 1625.) Advantage is taken of the Fujiwara pyridine-alkali reaction for the determination of these trichloro compounds. This depends upon the formation of a crimson colour formed by heating traces of these compounds with pyridine in strong alkaline solution. Although the reaction is not generally considered to be very specific, methods are given for the direct determination of the above three chloro compounds in urine in the presence of each other, special attention being directed to the need for careful adjustment of alkali concentration and temperature and time of the reaction in each case. For trichloroethanol, preliminary oxidation with chromic oxide was necessary. 0·07 to 0·50 μg. of trichloroethylene could be determined and quantities of 10 to 50 μg. of the other compounds to within about ±10 per cent accuracy.

D. B. C.

PHARMACY

Aminosalicylic Acid, Decomposition of Solutions of. R. F. Rekker and W. T. Nauta. (*Pharm. Weekbl.*, 1956, **91**, 693.) The decomposition of solutions of *p*-aminosalicylic acid at various pH values was followed by observing the changes in absorption spectrum. Below pH 6·3 the decomposition results from decarboxylation, which reaches a maximum at pH 2·7. In addition, long-term storage of strongly acid solutions leads to the development of discoloration. At pH above 6·3 the stability decreases slowly, but without formation of *m*-aminophenol: the brownish discoloration observed in alkaline solution is not identical with that developing in acid solution. It is concluded that solutions of aminosalicylic acid should not be kept at a pH below 6·3, and that the storage of the acid is undesirable unless moisture can be satisfactorily excluded.

G. M.

Senegin, Stability of. P. Finholt. (*Dansk tidsskr. farm.*, Suppl. II, 1956, 92.) A previous determination of the stability of senegin (Schou and Toft Madsen, *Dansk tidsskr. farm.*, 1937, **11**, 153) was based on the haemolytic activity, and indicated that the stability was at a maximum at a pH of 3. Since this investigation did not take into account the sensitivity of the dilute solutions used to diffused daylight, which may lead to a loss of activity of 50 per cent in 1 hour, a new investigation was made. The removal of sugars from senegin was followed iodometrically, and changes in the aglycone by spectrophotometry.

The stability, as determined from the haemolytic activity, is at a maximum at pH 3 to 5, and is very low at pH 10 to 13. In acid media (pH 1) and to some extent in strongly alkaline ones, sugar is split off, while changes in the aglycone occur most rapidly when alkaline. This process also proceeds at the lowest rate at pH 3 to 5. It is the changes in the aglycone in particular which affect the haemolytic activity. G. M.

PHARMACOLOGY AND THERAPEUTICS

Alkyl Sulphonates, Tumour Growth-inhibitory. A. Haddow and W. C. J. Ross. (*Nature, London*, 1956, **177**, 995.) 2-Chloroethyl methanesulphonate inhibited growth in the transplanted Walker rat carcinoma, both in its solid and ascites form. The drug was effective both by a single intraperitoneal injection of 100 mg./kg. in arachis oil or by daily feeding of an aqueous solution (10 mg./rat/day) for the duration of the experiment (13 days). With these doses there appeared to be no significant depression of the bone marrow. The compound had a mutagenic action on *Drosophila melanogaster*, but the mode of action appears to differ from that of other biological alkylating agents such as the sulphur and nitrogen mustards, dimethylsulphonates, diepoxides and polyethyleneimines. The fluorine analogue had similar cytotoxic activity. The hydrogen analogue, ethyl methylsulphonate was noteworthy in that daily oral administration was much more effective than daily injections of the same aqueous solution (20 mg./rat/day). G. P.

Azacyclonol Hydrochloride, An Ataractive Agent, Pharmacological Activity of. B. B. Brown, D. L. Braun and R. G. Feldman. (*J. Pharmacol.*, 1956, **118**, 153.) Azacyclonol hydrochloride (Frenquel) is the 4-isomer of pipradol. In mice it has a low toxicity. Small doses cause a mild depression characterised by decreased spontaneous activity. Lethal doses cause convulsions. Hexobarbitone sleeping time is increased in mice and hypnosis can be re-induced by azacyclonol after the mice are fully awake. In rats low doses produce a peculiar paralysis of the hind legs, depressed spontaneous activity and increased responsiveness to auditory stimuli. Lethal doses cause tremors and death without convulsions. In dogs and cats doses of 25 and 50 mg./kg. cause increased irritability, tremors and inability to rest. Doses of 100 mg./kg. cause the dogs to be in constant motion. In monkeys single oral doses as high as 160 mg./kg. cause no observable changes in behaviour and no signs of toxicity. Azacyclonol antagonises increased coordination activity induced in mice by pipradol, amphetamine, morphine and cocaine and it antagonises morphine induced stimulation in cats. In man intravenous doses promptly relieve LSD-induced psychoses. G. F. S.

Bemegride and Amiphenazole in Allyl*iso*propylbarbituric Acid Poisoning. J. Pedersen. (*Lancet*, 1956, **2**, 965.) In twenty-two cases of poisoning with a barbituric acid derivative, allyl*iso*propylbarbituric acid, bemegride with and without amiphenazole had a good arousing effect. Patients usually reacted within thirty minutes to strong stimuli, reflexes reappeared and in many cases became hyperactive. However, in most cases patients lapsed into coma again after the first injection and a further dose had to be given. Compared with seventy-four control cases bemegride did not curtail the period of unconsciousness or restore consciousness at higher blood levels of barbituric acid.

G. F. S.

Bemegride and Amiphenazole in Respiratory Paresis. C. Clemmesen. (*Lancet*, 1956, **2**, 966.) Treatment of seventy cases of severe barbiturate poisoning with bemegride and amiphenazole are reported. In seven of the cases there was respiratory paralysis with total apnoea. In each of these cases the paresis was abolished and respiration permanently restored to normal shortly after the administration of bemegride and amiphenazole. If only because of their effect in respiratory paralysis which has hitherto been regarded as an extremely serious complication, bemegride and amiphenazole are valuable adjuvants in the treatment of acute barbituric acid poisoning. G. F. S.

Bemegride, Delirious Psychosis and Convulsions due to. J. Kjaer-Larsen. (*Lancet*, 1956, **2**, 967.) During the treatment of fifty acute cases of barbituric acid poisoning with bemegride, return of consciousness was followed by psychosis in fifteen cases. Their onset was from the first to the fourth day after waking. Visual experiences predominated in the form of "black specks", smoke, or fire and in several cases coloured patterns. Auditory hallucinations were less outstanding. There was an impairment of consciousness, deficient orientation and an inability to sleep. The psychotic states persisted for two to six days. The frequency of psychoses was higher after large doses of bemegride. The psychoses resembled intoxication due to mescaline and lysergic acid. Nine of the cases of psychoses occurred among twelve barbiturate addicts, while among thirty-eight non-addicts there were only six cases of psychosis. These psychoses are apparently exogenous reactions provoked by bemegride in barbituric acid addicts. They resemble spontaneous withdrawal psychoses, but there are certain differences. During treatment with bemegride sixteen of the fifty patients developed convulsions, four had from one to eight severe, typical grand-mal seizures and twelve had petit mal. G. F. S.

Bemegride in Barbituric Acid Poisoning. A. Louw and L. M. Sonne. (*Lancet*, 1956, **2**, 961.) In severe cases of barbituric-acid poisoning bemegride (Megimide), stimulated respiration and restored reflex activity, reduced coma and helped to bring about a safe state. It did not shorten the period of coma, hasten elimination of barbituric acid, or cause patients to recover consciousness at a higher blood-level of barbituric acid than normal. Bemegride induced electroencephalographic changes before any clinical effect was seen. The results did not support the hypothesis that bemegride is a true antagonist of barbituric acid, like nalorphine is in morphine poisoning. They suggest that bemegride counteracts barbituric-acid by a central stimulant action. G. F. S.

Brom-lysergic Acid Diethylamide, a Highly Potent 5-Hydroxytryptamine Antagonist. L. Sollero, I. H. Page and G. C. Salmoiraghi. (*J. Pharmacol.*, 1956, **117**, 10.) 2-Brom-(+)-lysergic acid diethylamide (BOL) more effectively antagonised the action of 5-hydroxytryptamine (5-HT) on the isolated uteri of rats and guinea pigs than did (+)-lysergic acid diethylamide (LSD). LSD did not alter the action of 5-HT on guinea pig's ileum and rabbit's duodenum, whereas BOL was a potent antagonist of the spasmogen in these tissues. The actions of the antagonists were relatively specific in that the actions of acetylcholine, histamine, adrenaline and noradrenaline were not affected. These results suggest that the postulation of two types of tryptamine receptors, one type (rat's uterus and rabbit's ear) where LSD is a highly active antagonist of 5-HT and another where LSD is without effect (guinea pig's ileum), is unnecessary; BOL effectively antagonises the action of 5-HT at both receptor sites. G. P.

Bufotenine, Intravenous Injection in Man. H. D. Fabing and J. R. Hawkins. (*Science*, 1956, **123**, 886.) Bufotenine, in doses up to 16 mg., was injected intravenously into four normal healthy male subjects, the injections being made slowly over a three-minute period. Subjective effects similar to those of the hallucinogenic drugs LSD and mescaline were experienced, but the onset of activity was more rapid and the duration of action shorter with the bufotenine. The presence of nystagmus and mydriasis after the administration of bufotenine indicates that part of its action is located in the brainstem. Cardiovascular effects were slight; blood pressure changes were never more than 15 mm. Hg nor pulse rate variation more than 12 beats per minute. The subjects became cyanosed, presumably by a bronchoconstrictor action akin to that of 5-hydroxytryptamine (bufotenine is the *NN*-dimethyl derivative of this amine). 5-Hydroxytryptamine does not, however, induce model psychoses of the type seen with bufotenine. G. P.

Carbutamide, Effect of Different Doses of. G. Mohnike and U. Hagemann. (*Arzneimitt.-Forsch.*, 1956, **6**, 389.) High doses (1 g. or 0·75 g./kg.) of carbutamide administered intravenously to rabbits produce hyperglycaemia, which may be observed 30 minutes after administration. Hyperglycaemic doses are highly toxic, many animals dying with convulsions which were not the result of glycopenia. The increase in blood sugar must be due to mobilisation of liver glycogen, and a decrease in the latter was observed histochemically. Together with the convulsions there were observed brain changes. The toxicity was shown especially by necrotic processes in the tubules of the kidney. The most favourable hypoglycaemic action was observed with small doses (0·25 g./kg. i.v.), and only with these was there any positive relation between dose and blood sugar level. The experimental results do not indicate an insulin-like action, stimulation of the β cells, or inhibition of a facultative antagonist of islet cells. G. M.

Carbutamide, Effect of, on Blood Sugar Level. G. Mohnike. (*Arzneimitt.-Forsch.*, 1956, **6**, 388.) When administered at a level of 100 mg./kg. to rabbits with meta-alloxan diabetes, carbutamide caused a distinct drop in blood sugar when the sulphonamide content of the blood exceeded 10 mg. per cent. If this dose was given shortly before the administration of insulin, there was a greater drop in blood sugar level than when the insulin alone was given. This effect was marked in the period when the insulin action was especially distinct and when the sulphonamide level of the blood showed its highest value. These observations suggest that carbutamide and related substances increase the effect of the nsulin administered on blood sugar, and it may be assumed that the same applies to the insulin of the body. The actual mechanism is not clear. G. M.

Chlorhexidine in Urology. H. Beeuwkes and H. R. de Vries. (*Lancet*, 1956, **2**, 913.) Chlorhexidine (Hibitane) is of great value as a urological disinfectant. Its antibacterial spectrum covers all the organisms likely to be encountered, its oral and local toxicity is extremely low and in the concentrations used it is non irritant to the mucosa. Chlorhexidine is used in the following way for cystoscopy. The rinsing fluid for the irrigator is a 1 : 10,000 solution in tap water. For bladder irrigation and as the cystoscopy medium the concentration is 1 : 5,000 and for disinfecting the external genitalia 1 : 1,000. The top of the irrigator tube is stored in a 1 per cent solution. The hands of the staff are rubbed with a cream containing 0·5 per cent chlorhexidine hydrochloride. Before the introduction of chlorhexidrine 70 per cent of the urine samples became infected (56 per cent *Ps. pyocyanea*, 10 per cent proteus and 4 per cent *Staph. albus*). After the introduction of chlorhexidine only 8 per cent became infected, all with *Staph. albus*. G. F. S.

Contaminants in Stored Blood. M. G. McEntegart. (*Lancet*, 1956, **2**, 909.) Two fatal transfusion reactions are reported because blood was contaminated with an organism (resembling but not identical with *Klebsiella cloacae*) which grew at 4°. Both bottles of blood were in the third week of storage. The source of the infection was not found, but when the blood-taking equipment was checked bacteria were found in the fluid used to preserve the plastic caps. These did not grow at 4°. Thus the caps are a possible source of contamination and must be sterilised by autoclaving before use. A study of the growth rate of the organism showed that infected blood is unlikely to be dangerous until the third week of storage. The risk of severe reactions of the "infection" type could be very greatly reduced if, before any blood in its third week of storage is issued, a stained film is examined to exclude the presence of bacteria. In cases of severe reactions stained films of the blood should be examined at once. If the blood is infected the patient should be treated at once. Treatment should correct the acute peripheral circulatory failure which develops and the administration of noradrenaline and plasma to maintain the blood pressure should be considered. In the two fatal cases reported the infecting organism was unable to grow at body temperature. It is therefore unlikely that multiplication of bacteria in the body plays any important part in these reactions. G. F. S.

Cortisone Acetate in Status Asthmaticus, Controlled Trial of Effects of. Report to the Medical Research Council by the Subcommittee on Clinical Trials in Asthma. (*Lancet*, 1956, **2**, 803.) A comparison was made at 13 centres of the effectiveness of cortisone with that of antispasmodic drugs in the treatment of status asthmaticus. The trial was made on adult patients admitted to hospital in status asthmaticus who had suffered at least one previous severe attack of asthma and had not previously received cortisone therapy. For the first 24 hours they were given the treatment normally adopted by the physician in charge. This might include adrenaline subcutaneously, aminophylline intravenously, isoprenaline inhalation, oxygen, antibiotics or sedatives. During the first 12 hours endeavour was made to establish the dose of antispasmodic required and this dose was continued during the second 12 hours. Patients still in status asthmaticus at the end of 24 hours were admitted to the trial. In one group the treatment was continued and cortisone acetate was given in addition; in the second group also the treatment was continued but placebo tablets were given in addition. All the patients in the treated group received the same dosage of cortisone. Starting with 350 mg. in divided doses on the first day and ending with 25 mg. in two doses on the 9th day, the total amount administered was 1·25 g. Clinical assessment of each patient was made twice daily. By day 4, 10/15 patients in the treated group no longer had disabling bronchial obstruction whereas only 4/17 in the control group were relieved. This difference was maintained to the end of the 14-day treatment period. 6 patients whose condition caused concern were withdrawn from the trial. 5 who were successfully treated with cortisone or corticotrophin were found to belong to the control group; the sixth patient, who was receiving cortisone, had mitral stenosis and developed signs of cardiac failure on day 6. One patient in the cortisone group died; he had considerable bronchial infection and bronchopneumonia. The smallness of the number of patients admitted to the trial was due to the success of the standard treatment during the first 24 hours and it seems desirable to use antispasmodic drugs except for extremely exhausted and dehydrated patients. Observation of the patients for 3 months after the trial showed that they reverted to their usual asthmatic condition; status asthmaticus recurred in 9/11 in the cortisone group and 7/14 in the control group. H. T. B.

Diphenhydramine, 2-Methyl Derivative of (Mephenamine), Pharmacology of. U. G. Bijlsma, A. F. Harms, A. B. H. Funcke, H. M. Tersteege and W. T. Nauta. (*Arch. int. Pharmacodyn.*, 1956, **106**, 332.) In contrast to the 4-methyl derivative of diphenhydramine, which has greater antihistamine activity than the parent compound, the 2-methyl derivative has much weaker antihistamine effects, but increased anti-acetylcholine activity. The 2-methyl derivative (mephenamine, Disipal, BS 5930) had low acute and semi-chronic toxicity in rats and mice. Clonic spasms were obtained after subcutaneous injection of 40 mg./kg. mephenamine into a normal cat; this action was absent in the thalamic cat. An effect on the diencephalon was observed in thalamic cats (in contrast to decerebrate or spinal cats) after injection of mephenamine into the vertebral artery; an inhibition of the ipsilateral flexor reflex similar to that seen with scopolamine was obtained. The gait of thalamic cats was also altered by both mephenamine and scopolamine, scopolamine being 20 times the more active. A vasodilator action on perfused frog blood vessels and coronary vessels of the isolated mammalian heart was demonstrated. The force of contraction of isolated frog or mammalian hearts was reduced. Atropine-like activity was 1/25th that of atropine on the guinea pig's ileum, 1/350th in inhibiting salivary secretion in rabbits and 1/250th in mydriatic activity in mice. A ganglion-blocking action was not observed. In the nicotine tremor test in rabbits, mephenamine resembled atropine and scopolamine. Surface anaesthesia with the drug was several times greater than that of procaine and conduction anaesthesia about half that of procaine. Mephenamine had no protective effect in an anti-emetic test in pigeons. The drug prolonged barbiturate sleeping-time, but was less potent than diphenhydramine. Clinical reports of the use of the drug in Parkinsonism have been favourable. G. P.

Diphenhydramine, Enhancement of the Central Nervous System Effects of Strychnine and Pentobarbitone by. J. F. Sherman. (*Science*, 1956, **123**, 1170.) Diphenhydramine given subcutaneously to mice in a dose of 20 mg./kg. increased both the sleeping time with pentobarbitone sodium and the convulsive activity of strychnine. Such a dose of diphenhydramine had no gross effects of its own. Two modes of action were considered. The first entails an inhibition of the metabolic transformation of pentobarbitone and strychnine, similar to an action already described for β-diethylaminoethyl diphenylpropyl acetate hydrochloride (SKF 525-A), to which diphenhydramine is related structurally. An alternative to this is a more direct effect on elements of the central nervous system, the result of which would be an alteration in the levels of neuronal activity; this would then affect the degree of response to either strychnine or the barbiturate. G. P.

5-Hydroxytryptamine-releasing Activity Limited to Rauwolfia Alkaloids with Tranquillizing Action. B. B. Brodie, P. A. Shore and A. Pletscher. (*Science*, 1956, **123**, 992.) Of a number of drugs exerting a tranquillising action, only rauwolfia alkaloids reduced brain 5-hydroxytryptamine (5-HT) levels. Rabbits received the drugs intravenously and were killed four hours later. Their brains were removed as rapidly as possible and 5-HT determined fluorimetrically. In the rauwolfia alkaloid series, only reserpine, rescinnamine and deserpidine induced sedation and caused a significant alteration in brain 5-HT levels. A variety of hypnotics, narcotic analgesics and central nervous stimulants had no effect on brain 5-HT. Chlorpromazine, which resembles reserpine in its potentiation of barbiturate sleeping times, also failed to release 5-HT from the

brain, indicating a more direct action on receptor sites in the brain. Azacyclonol, a new drug currently under investigation in the treatment of psychiatric disorders, also failed to release 5-HT. Lysergic acid diethylamide, which antagonises the central action of reserpine, had no effect on the release of 5-HT from the brain tissues; this supports the idea that LSD inhibits the action of reserpine by blocking the released 5-HT. G. P.

Isoniazid in the Treatment of Lupus Vulgaris. B. Russell and N. A. Thorne. (*Lancet*, 1956, **2**, 808.) 111 patients, ranging in age from 8 to 82 years, suffering from lupus vulgaris for periods of from 6 to 74 years were treated with isoniazid. 8 were treated by mouth and by injection, 1 by injection only and the remaining 108 received the drug by mouth only. 104 patients completed treatment. In nearly all cases the daily dose was either 300 mg. or 400 mg. in divided doses of 100 mg. 6 to 12 months treatment was necessary to clear the lesions, and isoniazid was continued for 14 weeks after apparent clinical clearance. There was complete clinical clearance in 99 patients in an average of 29 weeks, the extremes being 8 weeks and 79 weeks. There were 3 deaths, 2 of them from carcinoma superimposed on long-standing neglected lupus. The skin of the affected areas becomes either normal in colour or slightly pigmented with a reticular pattern and slight atrophy. No serious side-effects were noted. 12 patients had mild side-effects at the commencement of treatment; they included nausea, dyspepsia, indigestion, giddiness and, in one case, anosmia. Treatment had to be abandoned after 23 weeks in the case of a pregnant woman because of nausea; she gave birth to a stillborn anencephalic monster at 39 weeks. The only evidence of the development of resistant strains of tubercle bacilli was in 4 cases who improved at first but failed to clear after prolonged treatment. Relapses have occurred in 11 cases between 8 and 130 weeks after completing treatment. In 4 of these a further course of isoniazid is effecting improvement; in the remainder a cure has been achieved by other treatment. Isoniazid was also effective in a case of tuberculosis verrucosa cutis, in 3 cases of scrofulodermia and in 2 cases of erythema induratum. It was ineffective in a case of lupus miliaris disseminatus faciei. H. T. B.

Mecamylamine, Hypotensive Action of. A. E. Doyle, E. A. Murphy and G. H. Neilson. (*Brit. med. J.*, 1956, **2**, 1209.) Mecamylamine (Inversine, 3-methylamino*iso*camphane) was given to 25 hypertensive patients for 6 to 10 months and to a further 15 patients for 3 to 6 months, the effects being compared with those obtained with subcutaneous or oral pentolinium. The fall in blood pressure was more gradual and more prolonged than that produced by pentolinium whether given by injection or by mouth. A dose sufficient to reduce the systolic blood pressure to 140 to 120 mm. Hg often gave a substantial reduction even 12 hours after the dose was given. Minor changes in dosage were occasionally necessary but no tolerance was observed during up to 10 months' treatment. The action is not usually exerted until one hour after administration and reaches a maximum in 3 to 5 hours; even after intravenous administration the action may not occur for ½ to 1 hour. The effective oral dose of mecamylamine is 1 to 2 times the subcutaneous dose of pentolinium required to produce the same effect. Side effects are mainly those due to parasympathetic blockade with gastrointestinal symptoms predominating; they tend to be less severe but more protracted than those due to pentolinium although constipation is more severe. Persistent nausea occurred in 6 patients and in 2 of these persistant vomiting made it necessary to change to pentolinium. Control of the blood pressure was good in 24/45 patients and side effects were mild, while

in 12/45 good control of blood pressure was accompanied by severe side effects. In 9/45 the side effects made it difficult to establish good control and in 5 of these patients treatment with mecamylamine had to be abandoned. Because of the prolonged effect caution is necessary when there is doubt about the safety of reducing blood pressure, as in coronary ischaemia, cerebral vascular disease and impaired renal function, and parenteral hexamethonium is preferable until the reduction is known to be safe. In general an initial dose of 2·5 mg. twice daily is suggested, increments of 2·5 mg. being added at 3-day intervals until an effective hypotensive dose is obtained; the final dose is usually between 10 mg. and 25 mg. twice daily. Prophylactic routine administration of laxatives is an advantage. H. T. B.

Meprobamate, Controlled Trial of. E. D. West and A. Fernandes da Fonseca. (*Brit. med. J.*, 1956, **2**, 1206.) The value of meprobamate was investigated in a straight trial in psychiatric out-patients and in two other trials in which the compound was compared with an inert tablet and with sodium amylobarbitone respectively. In the straight trial, 151 patients were given doses ranging from 400 mg. twice daily to 800 mg. three times daily with a fourth dose at night. Treatment was continued for up to 4½ months. Meprobamate was noticeably most effective in a group of 62 patients classified as anxious and tense, of whom 36 (58 per cent) improved. Only about 25 per cent of patients with tension headache were relieved. Somatic manifestations of anxiety such as tremor, sweating and tachycardia, and cases of muscle spasm such as spasmodic torticollis and writer's cramp, showed very little change. Patients with difficulty in getting off to sleep and those with undue irritability were particularly helped. Severe anxiety states did not respond so well as mild ones and often side effects such as drowsiness occurred. Some benefit occurred in other groups, for example in reactive depression. No marked effect was noted in patients with endogenous depression or when the compound was used as a premedication for electroconvulsion therapy. Minor improvement occurred in 3 patients with globus hystericus. A slight improvement occurred in some patients with obsessive-compulsive neurosis but motor forms such as compulsive handwashing were unaffected. There were no serious side effects but tiredness occurred and 5 patients had transient urticarial rashes. In the comparison with the inert tablets 13/26 patients were given the placebo and half the meprobamate, the tablets being identical in appearance. At each attendance the alternative substances was substituted. The results showed a statistically significant superiority of meprobamate. In a similar comparison with sodium amylobarbitone, mainly in anxiety and tension states, no marked differences in effectiveness were found but meprobamate often seemed more useful where there was marked irritability. H. T. B.

Meprobamate, Toxic Reactions to. H. T. Friedman and W. L. Marmelzat. (*J. Amer. med. Ass.*, 1956, **162**, 628.) Detailed reports are given of 7 cases of severe toxic reactions following administration of meprobamate in therapeutic doses. Five of these were allergic in character, consisting of cutaneous reactions, chiefly purpuric and accompanied by intense itching; in one case one 400-mg. tablet was sufficient to produce the skin lesions without previous exposure. In another case diplopia accompanied by nausea developed following administration of a dose of 800 mg., and in yet another severe diarrhoea, with cramps, gas and watery stools resulted from two doses of 400 mg. In addition to these 7 cases, 3 cases of paradoxical reaction to meprobamate of extreme excitement rather than tranquillisation are recorded. S. L. W.

Morphine Antagonists: Distribution and Excretion of Morphine ^{14}C in the Presence of Nalorphine and 5-Aminoacridine. L. B. Achor and E. M. K. Geiling. (*J. Pharmacol.*, 1956, **117**, 16.) Previous observations have indicated strongly that antagonism of morphine by nalorphine involves changes in the tissue concentrations of morphine. These concentrations were investigated in male white mice using ^{14}C-labelled morphine, 10 mg., before and after the administration of nalorphine 25 mg./kg. or 5-aminoacridine 2·5 mg./kg. (also a morphine-antagonist). The antagonists affected tissue morphine concentration to some degree in all tissues examined, but changes in the liver, kidney, small intestine and urine appeared to be the most significant. Although the control and nalorphine-treated series presented qualitatively similar morphine distribution patterns, the liver concentration in the nalorphine-treated mice decreased more rapidly with time, indicating (*a*) a diversion of significantly larger amounts of morphine from the liver to the urinary system in the unconjugated form and (*b*) facilitation of more rapid conjugation of morphine by the liver. Bladder urine accumulated radioactivity at the same rate in both series, but in the nalorphine-treated mice the urine voided at the end of two hours had approximately the same radioactive content as that of the controls. 5-Aminoacridine was even more active in reversing this antidiuretic action of morphine; other differences in morphine distribution patterns after 5-aminoacridine indicate a mode of action differing from that of nalorphine. The distribution data suggest that both antagonists alter the free/bound morphine ratio in the urine.

G. P.

Neodymium 3-Sulpho*iso*nicotinate and Blood Coagulation. R. B. Hunter and W. Walker. (*Brit. med. J.*, 1956, **2**, 1214.) Although salts of lanthanum, cerium, praseodymium and neodymium are known to prolong the clotting time of blood, most of them are toxic. Neodymium 3-sulpho*iso*nicotinate is a water-soluble salt which prolongs the clotting time in animals without producing toxic effects and its mode of action was investigated. Intravenous administration to dogs, rabbits or mice in a dose of 50 mg./kg. greatly prolongs the clotting time of whole blood. The effect is not reversed by intravenous injection of protamine nor by addition of thrombin, showing that there is no interference with the thrombin-fibrinogen reaction. The one-stage prothrombin time (Quick test) was only moderately prolonged and the two-stage test was normal. The most striking abnormality was gross impairment of the generation of intrinsic blood prothrombin, both the plasma factor and the serum factor concerned being affected. In man the relatively much smaller dose of 250 to 375 mg. intravenously did not prolong the clotting time of whole blood, showing a normal thrombin-fibrinogen reaction. The clotting time of oxalated plasma in the Quick test showed a variable prolongation of 0 to 14 seconds which was corrected by adding aged normal serum, indicating a deficiency of factor VII. Two-stage prothrombin measurements were normal. The impairment of intrinsic blood thromboplastin generation was again striking but the abnormality was found in the patient's serum only. On giving a correspondingly small dose to rabbits, the effects were found to be identical with those in man. The effects in man were not prevented by oral premedication with 50 mg. of vitamin K_1. The effect on thromboplastin generation was investigated in a series of tests using normal serum, Christmas disease serum, and serum from patients treated with phenindione or neodymium. Thromboplastin formation was normal in mixtures of neodymium serum with Christmas serum, or with phenindione serum, but only if the proportions of neodymium serum were respectively below 10 and 2·5 per cent. The addition of normal serum to neodymium serum

was more effective than either of the other additions. Addition of equal parts of phenindione and Christmas sera to neodymium serum was as effective as an addition of normal serum. It appears therefore that neodymium serum contains an inhibitor, weakened by dilution, both of Christmas factor and of factor X. Addition of neodymium to normal serum *in vitro* had this inhibiting effect so that it does not need to be present during clotting to produce its action on those factors. It is possible that neodymium acts by displacing calcium from combination with one or more proteins involved in the reaction but a more probable explanation is its selective combination with plasma proteins.

H. T. B.

New Cholinesterase Inhibitor, Studies on. R. G. Herrmann and R. H. Tust. (*J. Pharmacol.*, 1956, **117**, 75.) The anticholinesterase activity of 4:4′-oxy-bis-(phenacyl-pyridinium) chloride was compared with that of neostigmine *in vitro* on cholinesterase preparations from rat's brain and serum and *in vivo* on brain, serum and salivary gland cholinesterase of the rat. *In vitro* the new drug was one tenth as potent as neostigmine in inhibiting rat brain cholinesterase. Results *in vivo* were similar, but the enzyme-inhibitor complex formed by the new inhibitor was much more readily dissociated than that of neostigmine. In the dog the two anticholinesterases were similar pharmacologically in respect of changes in gut motility, blood pressure and respiration, toxic symptoms and duration of action. Again neostigmine was ten times the more potent. On the rat gastrocnemius muscle preparation the new drug was less effective as an antagonist of tubocurarine, than was neostigmine, but its onset of activity was more rapid. In high dosage a neuromuscular blocking action was seen, which was not seen with neostigmine under similar experimental conditions. G. P.

Phthalylglutamic Imide, a New Sedative. W. Kunz, H. Keller and H. Mückter. (*Arzneimitt.-Forsch.*, 1956, **6**, 426.) *N*-Phthalylimidoglutaric imide (Contergan) has pharmacological properties which suggest that it would be a valuable sedative. The compound melts at 271° (uncorr.), and is only slightly soluble in the usual solvents, but readily soluble in dioxan, dimethylformamide or pyridine. The sedative effect was determined by recording the motility of mice in special cages, and a comparison was made with other sedatives including barbiturates and pentynol. Parenteral and peroral administration were employed, the compound being suspended in water. The onset of the sedative effect was rapid and of long duration, comparable with long term hypnotics. There was no initial excitement or disturbance of co-ordination. Owing to the low solubility it was not possible to determine the toxicity; no side effects were observed with mice, rats, guinea pigs or rabbits. Clinical trials are reported below. G. M.

Phthalylglutamic Imide, Clinical Experience with. H. Jung. (*Arzneimitt.-Forsch.*, 1956, **6**, 430.) This new sedative has been tried on more than 300 patients. It may be given to patients with serious liver damage; there was no effect on the blood picture and blood sugar. Side effects resulted from over dosage (drowsiness, vertigo, tremor, constipation) but not with normal doses. Good results were obtained in all types of vegetative dystonia, and in less marked conditions of hyperthyreosis and thyreotoxicosis; and thyreostatic drugs could be discontinued or reduced. Effects in nervous gastric troubles and labile hypertension and bronchial asthma were favourable. G. M.

Pilocereine, a Cactus Alkaloid. C. E. Powell and K. K. Chen. (*J. Amer. pharm. Ass., Sci. Ed.*, 1956, **45**, 559.) Pilocereine, an alkaloid of molecular formula $C_{30}H_{42}O_4N_2$, isolated from *Lophocereus schottii* and *Pachycereus marginatus* was administered intravenously to a series of anaesthetised animals. Pilocereine caused a decrease in the blood pressure of dogs and roosters, and an increase in the case of rats. Small doses administered to cats produced a decrease, followed by an increase in blood pressure. Pilocereine was shown to relieve pituitary-induced spasm in the isolated guinea pig uterus, and adrenaline-induced spasm in the rabbit uterus. Similarly, it relieved methacholine- or histamine-stimulated spasm of the rabbit or guinea pig small intestine. In canaries infected with *Plasmodium relictum*, pilocereine showed an antimalarial action approximately equal to that of quinine. It was shown to be toxic to mice when given intravenously, the LD50 being approximately 52 mg./kg.

G. B.

***n*-Propyl Nitrate, Pharmacological Effects of.** E. F. Murtha, D. E. Stabile and J. H. Wills. (*J. Pharmacol.*, 1956, **118**, 77.) A study of *n*-propyl nitrate, a by-product of the chemical industry, has shown it to be not very toxic, the LD50 in rabbits being 225 mg./kg. Doses of 200 mg./kg. i.v. were fatal to anaesthetised cats or dogs. In anaesthetised dogs intravenous doses of 50 to 250 mg./kg. caused immediate hypotension and arrest of gut activity. The higher doses caused a precipitous fall in blood pressure and respiratory paralysis. Non-lethal doses caused a transient apnoea followed by a persistent hypernoea accompanied by cyanosis. In cats, doses of 100 to 250 mg./kg. i.v. caused death in one minute, but the methaemoglobin values showed only 0 to 4 per cent of the total haemoglobin oxidised to methaemoglobin. In dogs, ECG changes were observed after 30 mg./kg.—including bradycardia, arrhythmia, inverted or widened QRS complex and inverted T-wave and terminal ventricular fibrillation. Contractile studies in the dog heart showed that the contractile force fell to 10 to 15 per cent of normal with a simultaneous fall in systolic pressure. The results suggest that a direct cardio-toxic effect is the cause of the hypotension which may be lethal. Respiratory depression and a direct action on vascular smooth muscle may also play a part. G. F. S.

Rauwolscine, Pharmacological Action of. J. D. Kohli and N. N. De. (*Nature, London*, 1956, **177**, 1182.) Like yohimbine, rauwolscine (α-yohimbine) has local anaesthetic and adrenaline-blocking activity; it lowers the convulsant threshold level to leptazol and has aphrodisiac activity. In guinea pigs a 2 per cent solution of rauwolscine causes complete surface anaesthesia of the cornea which starts 5 to 7 minutes after installation of the drug into the eye and lasts for up to 15 to 20 minutes. By the guinea pig weal method a 2 per cent solution induced local anaesthesia for up to 2 hours, but there was local tissue damage. 10 to 20 mg./kg. injected intraperitoneally into guinea pigs gave signs of psychic excitement and erection in the males. 25 mg./kg. given intraperitoneally to rats lowered the convulsant threshold for leptazol. Adrenaline-blocking activity of rauwolscine was comparable with that of tolazoline on the isolated seminal vesicle of the guinea pig. 12 to 15 mg./kg. injected intravenously in rabbits induced sudden clonic convulsions lasting 2 to 3 minutes, accompanied by increased respiratory rate and followed by sexual excitement; intraperitoneal injection of 20 mg./kg., on the other hand, had no convulsant action, but the other effects appeared in 5 to 10 minutes. G. P.

Reserpine, Antagonists of the Action of, on Smooth Muscle. C. N. Gillis and J. J. Lewis. (*Nature, Lond.*, 1956, **178**, 859.) Since reserpine antagonises non-selectively the contractions of the guinea pig ileum caused by acetylcholine, histamine, serotonin or barium, it is possible that it is affecting the underlying mechanisms connected with the production and utilisation of the energy necessary for the contraction. These mechanisms probably involve the breakdown and resynthesis of carbohydrate through the glycolytic and tricarboxylic acid cycles. Thus an investigation was carried out on the influence of adding known intermediates of carbohydrate metabolism to the isolated ileum of the guinea pig immediately before the addition of the reserpine. The ileum was stimulated by either acetylcholine, histamine, serotonin or barium. All metabolites were tested over a wide dose range. Glucose-1-phosphate, fructose-1 : 6-diphosphate, fructose-6-phosphate, pyruvate, fumarate, succinate and adenosine triphosphate were ineffective as reserpine antagonists. Citrate, *cis*-aconitate, α-keto-glutarate and maleic acid were highly active. Malate and oxalo-acetate had intermediate activity. Removal of calcium from the bath by disodium versenate did not cause antagonism to reserpine. The possibility of release of histamine or acetylcholine by the metabolites was excluded. Since the most active reserpine antagonists are intermediates of the tricarboxylic acid cycle, it seems possible that this is a site of action of the alkaloid. M. M.

Staphylococcal Pneumonia in Adults. W. Hausmann and A. J. Karlish. (*Brit. med. J.*, 1956, **2**, 845.) Eighteen cases of staphylococcal pneumonia in adults are reported to have occurred in a series of 122 consecutive cases of pneumonia admitted to one medical unit in 1952–4. There was no epidemic influenza in the area during that period. The outstanding feature in these cases was the severity of the clinical course and the number of suppurative complications. All of the 18 cases recovered, but only 6 responded to penicillin. Seven responded to oxytetracycline or chlortetracycline, 2 to chloramphenicol, and 2 others to streptomycin. In one man, erythromycin effected a dramatic improvement. There is good evidence that the incidence of staphylococcal pneumonia is growing. A review of the literature in the last 5 years suggests that these cases now constitute from 3 to 10 per cent of all cases of pneumonia admitted to hospital. The average age of the patients is over 50 years and a history of previous chest disease is obtained in at least 40 per cent of cases. The authors conclude that in future staphylococcal infections are likely to present a major problem in the treatment of pneumonia. S. L. W.

***Staphylococcus aureus*, Transmission of.** R. Hare and C. G. A. Thomas. (*Brit. med. J.*, 1956, **2**, 840.) Experiments carried out with nasal carriers of *Staphylococcus aureus* suggest that this organism is not transported from person to person by droplets or droplet nuclei but by an indirect route. The first step is the transport of the staphylococci by hand, handkerchiefs or any object coming into contact with the noses to the skin, clothing, bedding, and other objects within the immediate vicinity of the carrier. The second step is the release of the organism into the atmosphere, which may result from friction and dislodgment of dried particles from the skin or hair, from the spattering of water droplets while washing, or from shaking of the clothing during activity. The third step involves the transport of these infected particles by air currents to other individuals. In this way the organisms may reach the anterior nares of normal persons to produce the carrier state in them, or they may reach highly susceptible tissues such as the conjunctiva of the newborn infant, or open wounds in operating theatres, to produce in due course post-operative infection. There

is evidence that some carriers can contaminate the atmosphere in their neighbourhood with much larger numbers of *Staph. aureus* than the majority of carriers. Such persons wearing a sterile gown over their ordinary underclothing may cause potentially dangerous degrees of air contamination during activity; even when wearing a complete set of sterile operating clothes large numbers of *Staph. aureus* may still be detectable in the surrounding atmosphere. Such carriers are probably more dangerous in the hospital environment than members of the staff suffering from a minor degree of skin sepsis. S. L. W.

Substance P, Neurotropic Effects of. U. S. von Euler and B. Pernow. (*Acta physiol. scand.*, 1956, **36**, 265.) Intracisternal or intraventricular (IIIrd ventricle) injection of substance P, a biologically active polypeptide occurring in extracts of brain and intestine, caused increased rate and depth of respiration in anaesthetised cats and rabbits; there was a variable effect on blood pressure, usually a transient moderate fall, followed by a small rise. Diuresis was little affected by the intraventricular injections, while intravenous injection had a slight antidiuretic effect. In the cat, intravenous injection had no consistent effect on serial carotid occlusion tests; nor was transmission through the superior cervical ganglion altered. Large intravenous doses depressed the amplitude of respiration. Introduction of the polypeptide into one of the lateral ventricles of the cat, through a permanent cannula, caused an increase in depth and rate of respiration. Behaviour was also affected, the animals showing lack of spontaneity of movement, except for occasional vigorous tail movements. Aggressive tendencies were induced in one normally docile animal. These central neurotropic actions bear some resemblance to those of acetylcholine and nicotine, although the drugs differ in several other respects. G. P.

Sulphonamide Hypoglycaemic Agents, *In Vitro* Studies of. M. Vaughan. (*Science*, 1956, **123**, 885.) It has been suggested that a possible mode of action of the sulphonamide hypoglycaemic agents, *N*-*p*-aminobenzenesulphonyl-*N'*-*n*-butyl urea (carbutamide, BZ55), and *N*-toluenesulphonyl-*N'*-*n*-butyl urea (tolbutamide), is through some direct effect on the reactions involved in the conversion of liver glycogen to blood sugar. In this connection, neither carbutamide nor tolbutamide had any inhibitory activity against rat liver insulinase, ruling out an indirect effect of the drugs through hyperinsulism of this type. Nor did tolbutamide interfere with the conversion of liver glycogen to blood sugar at the level of glucose-6-phosphatase. However, the increased release of glucose from rat and rabbit liver slices incubated with adrenaline or Glucagon was markedly diminished by the addition of tolbutamide. If, as has been suggested, adrenaline and Glucagon act by promoting phosphorylase reactivation by phosphokinase, then tolbutamide may decrease this by inhibiting phosphokinase. G. P.

Tetracycline and Chlortetracycline in Pneumonia. Report from the City General Hospital, Sheffield. (*Brit. med. J.*, 1956, **2**, 1146.) Thirty-two patients were treated with tetracycline and 24 with chlortetracycline in a controlled trial of the two antibiotics in clinical pneumonia. The dosage was 0·5 g. orally six-hourly for 3 days, followed by 0·25 g. six-hourly in either case. Three desperately ill patients received initial intravenous administration (0·5 g.) of one or other of the drugs. The patients given tetracycline were slightly older and more of them had lobar consolidation and a positive blood culture than those given chlortetracycline; otherwise the two groups were comparable. In most cases

(ABSTRACT *continued on page* 272.)

Gathercoal and Wirth's PHARMACOGNOSY. Third Edition by Edward P. Claus. Pp. 731 (including 307 illustrations and Index). Henry Kimpton, London, 1956. 93s. 6d.

The presentation of the subject matter of this book reflects a change in emphasis which is being accepted in the United States of America and to some extent in this country, stress being laid on the chemistry of crude drugs rather than on their morphology or taxonomy. Monographs on crude drugs are found in chapters devoted to Carbohydrates, Glycosides, Tannins, Fixed Oils, Fats and Waxes, Volatile Oils, Resins, Alkaloids, Endocrine Products, Vitamins, Enzymes, and Proteins. The taxonomical classification of previous editions is relegated to a short but adequate appendix. Macroscopical and microscopical descriptions of crude drugs are inadequate, the reader being referred throughout to the United States Pharmacopeia and the American National Formulary. For some drugs no descriptive matter is included, for others macroscopical characters only are given, while for yet others the microscopical features of the powdered drug only are described. However, the book is freely illustrated with drawings, photographs and photomicrographs, many of them excellent, though in most magnification is not stated. The key for the identification of powders suffers the defect of inflexibility and in some instances gives misleading information, such as the absence of sclereids from cardamom seed and the presence of lignified tissue in rhubarb. The introduction gives a clear outline of the scope of Pharmacognosy, but the quantitative microscopy of powdered drugs merits more prominence, and the section on chromatography would have benefited by the inclusion of examples. There is a good general account of the cultivation of drug plants, and of the collection and preparation for the market, although details for individual drugs are lacking. The chemical constituents of drugs and the characters of many of the isolated pure principles receive adequate treatment. Fuller accounts could have been given of digitalis, rauwolfia and senna leaf in the light of recent work. While specific references to original literature are few, general reading references are quoted for the chemistry of crude drugs, and for the new and useful chapters on Antibiotics, Immunizing Biological Products, Allergens and Pesticides. Another new feature of this edition is that proprietary products, some available in Britain, are named under the crude drugs from which they are derived. The nomenclature would benefit by the use of a uniform system and adherence to convention. The text is almost free from spelling mistakes and is reasonably well indexed. Presentation has been improved by standardising the size of print, and the quality of paper and the binding are excellent. This is a very comprehensive work with few omissions, and both student and drug analyst will find it a useful reference book.

FRANCIS FISH.

(ABSTRACT *continued from page* 270.)

the pneumonia was pneumococcal and about half the patients in each group had chronic chest disease. The results show that both antibiotics were equally effective in the treatment of bacterial pneumonia. Deaths were few (3 with tetracycline; 2 with chlortetracycline) and were confined to elderly patients with serious complicating diseases. The incidence of side-effects, mostly mild, was about 30 per cent with each antibiotic. This does not confirm the reported lower toxicity of tetracycline. The only serious complication followed tetracycline therapy, namely, one case each of staphylococcus enteritis, pulmonary moniliasis, and aspergillosis; in the last case the patient died. S. L. W.