ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

Adrenocortical Steroids, Determination of. E. Heftmann and D. F. Johnson. (*Analyt. Chem.*, 1954, **26**, 519.) A method for the separation of 6 active adrenocortical hormones by partition chromatography on silicic acid columns is presented. The method of preparation of the column is given, partition taking place between the stationary water phase and a mobile petroleum ether-dichloromethane phase which contained increasing proportions of dichloromethane, the adrenocortical steroids being eluted in the order of increasing polarity. Details are given for the separation of the steroids deoxycorticosterone, dihydrocorticosterone, cortisone, hydrocortisone and corticosterones B and S; identification in the eluates was by the sulphuric acid test and by ultra-violet absorption assay of the fractions. The separation of steroids was automatic, using a fraction collector. Small amounts of adrenocortical steroids could be determined in the presence of a large excess of other adrenal steroids. R. E. S.

Amino-acids, Determination of. J. F. Roland and A. M. Gross. (*Analyt. Chem.*, 1954, **26**, 502.) A simple method, employing monodimensional paper chromatography, is given for the resolution of 16 amino-acids with two solvent systems. 2-Butanol-3 per cent. ammonia (3 to 1) provided good resolution of the amino-acids lysine, arginine, alanine, proline, tyrosine, valine, methionine, *iso*leucine, leucine, and phenylalanine as individual entities in 48 hours; aspartic-glutamic-cystine, serine-glycine, and histidine-threonine were resolved according to the method of Block (*Analyt. Chem.*, 1950, **22**, 1327) using 72 per cent. phenol. Additional systems are described specially for the resolution of histidine and tryptophan. Measurement of the maximum colour density of the individual spots on the chromatograms was found to be satisfactory for most amino-acids, although high results were usually obtained for lysine, arginine, aspartic and glutamic acids; more accurate results were obtained by the area density procedure. Determination by the method, of the amino-acid composition of β-lactoglobulin were found to agree with reported values. The method was also used for the identification of μg. quantities of peptides separated by paper chromatography. R. E. S.

Cadmium and Magnesium, Determination of, with Disodium Ethylenediaminetetra-acetate. E. G. Brown and T. J. Hayes. (*Analyst*, 1954, **79**, 220.) The simultaneous determination of cadmium and magnesium by titration with a solution of disodium dihydrogen ethylenediaminetetra-acetate containing zinc sulphate is described. Initial attempts at the titration of a cadmium sulphate solution at *p*H 6·8 with disodium ethylenediaminetetra-acetate with Solochrome Black W.D.F.A. as indicator were unsuccessful since the addition of disodium ethylenediaminetetra-acetate solution did not give a definite end-point change from purple to pure blue; titrations in both maleic acid, sodium maleate buffer, ammonium acetate buffer solutions and at various *p*H values between 7·5 and 8·0 were also unsatisfactory. It was found that a mixture of zinc and cadmium sulphates could be quantitatively titrated to a sharp Solochrome Black end-point at *p*H 6·8, the final titration representing the sum of the

two metals; the result was confirmed for several molecular ratios of zinc and cadmium, including one with a very small proportion of zinc to cadmium. It was also found possible to determine cadmium and magnesium on the same solution by titration first at *p*H 6·8 (cadmium) and then at *p*H 10 (magnesium) by the use of this disodium zinc ethylenediaminetetra-acetate reagent, provided that the molecular ratio of magnesium to cadmium was not greater than unity. A mechanism for the reaction is advanced based on the assumption that the cadmium chelate is more stable than the zinc chelate, free cadmium ions displacing zinc ions from the zinc chelate. R. E. S.

Glycerol, Colorimetric Determination of. H. D. Reese and M. B. Williams. (*Analyt. Chem.*, 1954, **26**, 568.) Glycerol solutions (1 to 13,000 μg. per ml.) are mixed with a quantity of standard potassium dichromate solution and sulphuric acid is added. After heating for 5 minutes in a boiling water bath the reaction mixture is diluted to a known volume, an aliquot is added to a sulphuric acid/*s*-diphenylcarbazide mixture and the resulting product again diluted to volume. The light absorption, determined at 540 mμ, is then measured within 10 minutes and the amount of glycerol obtained from calibration curves previously obtained. The wide range of glycerol concentrations which can be analysed by this colorimetric method necessitates several dichromate reagents, the concentrations of which are given. Blank determinations are variable and should be repeated from time to time. A table is given showing the results of 100 analyses by the method. R. E. S.

Quaternary Ammonium Compounds and Certain Tertiary Amines, Volumetric Determination of. E. D. Carkhuff and W. F. Boyd. (*J. Amer. pharm. Ass., Sci. Ed.*, 1954, **43**, 240.) Small quantities of quaternary ammonium salts and tertiary amines may be estimated by titration with sodium lauryl sulphate or dioctyl sodium sulphosuccinate solution in the presence of sulphuric acid and chloroform. The method is rapid and may be applied to samples containing about 0·025 per cent. of cetylpyridinium chloride, β-diethyl 1-*cyclo*hexyl*cyclo*hexanecarboxylate hydrochloride (dicyclomine hydrochloride), etc. A solution of 1·2 g. of sodium lauryl sulphate in 1000 ml. of water is standardised against the compound undergoing analysis, for example, as follows. Mix 20 ml. of dicyclomine hydrochloride solution with 10 ml. of water, 5 ml. of dilute sulphuric acid, 20 ml. of chloroform and 1 ml. of methyl yellow indicator solution, and shake vigorously. Titrate with sodium lauryl sulphate solution shaking after each addition until the chloroform layer develops the first orange tint. The sample for assay, equivalent to 10 to 25 mg. of dicyclomine hydrochloride is then similarly titrated. Aqueous solutions containing 10 mg. in 50 ml., or chloroform solutions containing 10 mg. in not more than 30 ml. may be assayed, but accuracy is difficult to maintain at greater dilutions. G. B.

Yohimbine, in the Presence of Other Alkaloids, Determination of. C. Stainier and C. Lupière. (*J. Pharm. Belg.*, 1954, **36**, 3.) The following method depends upon the hydrolysis of yohimbine and precipitation of the resulting yohimbic acid with reineckate. Tablets containing phenobarbitone, papaverine hydrochloride, ergotoxine ethanesulphonate, atropine sulphate and yohimbine hydrochloride were shaken with water and chloroform to remove phenobarbitone. The aqueous liquid was extracted with chloroform in the presence of sodium carbonate, and the chloroform solutions, containing yohimbine,

evaporated. The residue was dissolved in ethanol and heated with 0·5 N ethanolic potassium hydroxide under a reflux condenser for 30 minutes, evaporated *in vacuo*, and the residue dissolved in water, extracted with chloroform to remove other alkaloids, neutralised and treated with sulphuric acid and ammonium reineckate. After allowing to stand overnight, the precipitate was filtered off, dissolved in acetone, and the optical density determined at 525 mμ. From this figure the quantity of yohimbine in the tablets was calculated.

G. B.

ESSENTIAL OILS

Essential Oils, Auto-oxidation of. L-E. Fryklöf. (*Farm Revy.*, 1954, **53**, 317, 361.) For the determination of peroxides in essential oils, 1·00 g. of the oil, in a stoppered flask, is dissolved in 20 ml. of citric acid reagent (10 g. of citric acid dissolved in 60 ml. of tertiary butanol and diluted with 35 ml. of carbon tetrachloride). Air is removed by passing carbon dioxide, and then 1 ml. of saturated sodium iodide solution is added. After standing for 20 minutes in the dark, 50 ml. of water is added and the iodine is titrated with 0·01 N. thiosulphate. Results are calculated to a peroxide value, representing the number of ml. of thiosulphate solution equivalent to 1 g. of the sample. Comparative tests under conditions of accelerated oxidation showed the following results for a number of oils.

Oil	Time, in hours, to attain peroxide value of 5
Turpentine ..	10
Lemon	50
Fennel	220
Lavender ..	330
Peppermint ..	840
Bergamot ..	1000
Anise	1450
Rosemary ..	1500
Clove	3500
Cinnamon ..	6750

With the exception of the first two of these, oxidation makes little change in the physical constants of the oil, although changes in the odour can be observed. Under favourable conditions of storage oxidation was slight, but it was much greater with stock bottles from which material was removed at intervals. Turpentine may be to a considrable extent protected from oxidation by the addition of nordihydroguaiaretic acid, propyl gallate or butyl hydroxyanisate, and the effect of these substances is increased by the addition of 0·01 per cent. of citric acid or ethylenediaminetetra-acetic acid. G. M.

BIOCHEMISTRY

BIOCHEMICAL ANALYSIS

Arsenic in Biological Materials, Determination of. R. J. Evans and S. L. Bandemer. (*Analyt. Chem.*, 1954, **26**, 595.) The material under examination is mixed with saturated magnesium nitrate solution and ashed overnight a

600° C. in a muffle furnace. The ash is dissolved in dilute hydrochloric acid and the arsenic distilled as arsine, which is collected in an iodine solution. The arsenic content of the solution is finally determined by developing the blue molybdenum compound of arsenic and reading the colour at 840 mμ. Good recoveries of arsenic added to egg homogenate and either fresh or dried liver tissue were obtained, and the values were reproducible; the method was also applied to eggs, chicken liver, breast muscle, leg muscle, skin and dried pig tissues. Complete recovery of arsenic on distillation was not obtained, but recovery was constant at 87 to 90 per cent., so that standard curves were prepared by distilling known quantities of arsenic. R. E. S.

Fluorine in Biological Material, Estimation of. P. Venkateswarlu and D. Narayana Rao. (*Analyt. Chem.*, 1954, **26**, 766.) It was found that reliable results on biological materials were obtained if a preliminary sulphuric acid distillation was performed; this was necessary owing to the presence of iron. Silica in plant materials also interfered with fluorine recovery; the interference could be reduced by preliminary distillation of the unashed sample, or by fusion of the lime-ashed sample with sodium hydroxide before distillation of the fluorine from perchloric acid. The use of magnesium oxide as an adsorbent for the fluoride ions (*Analyt Chem.*, 1950, **22**, 441) considerably aided fluoride analysis. R. E. S.

Glycogen in Tissues, Determination of. A. Kemp and A. J. M. Kits van Heijningen. (*Biochem. J.*, 1954, **56**, 646.) A micromethod for the determination of glycogen in tissues is described. The tissue is extracted with a solution of trichloroacetic acid at 100° C. and the glycogen in the extracts is determined, without previous hydrolysis, by the colorimetric method described by Mendel *et al.* (*Biochem. J.*, 1954, **56**, 639). Pure glycogen dissolved readily in the deproteinising solution, but only part of the glycogen could be extracted from the tissues with a cold solution of trichloroacetic acid; all of the glycogen could however be brought into a solution by grinding the tissues with trichloroacetic acid solution and then heating the suspension for 15 minutes at 100° C. Glucose present in the tissues, although usually small, is extracted and determined with the glycogen by this method and procedures are described for the determination of both glycogen and glucose in muscle and liver. Only glucose 1-phosphate of the glycogen metabolites containing a hexose molecule gives the colour reaction. R. E. S.

CHEMOTHERAPY

Germine, Synthetic Hypotensive Esters from. F. L. Weisenborn, J. W. Bolger, D. B. Rosen, L. T. Mann, Jr., L. Johnson and H. L. Holmes (*J. Amer. chem. Soc.*, 1954, **76**, 1792.) A number of synthetic esters of high hypotensive activity were prepared by selective and stepwise esterification of germine. The methods for the preparation of mono-, di-, tri and tetraesters are described. Evidence is presented indicating that direct acylation of germine introduces the acid radicals on the same hydroxyl groups found esterified in the natural di- and tri-esters. All the synthetic tetraesters were essentially inactive, while the triesters of germine were the most active. The results indicated that, four- or five-membered α-branches acid radicals are necessary for appreciable hypotensive activity with the restriction that the over-all dimension of the germine ester molecule lies close to an optimum value. None of the synthetic esters showed a significantly more favourable emetic ratio than the natural ones.

A. H. B.

PHARMACOGNOSY

***Claviceps purpurea*, Culture of.** A. G. Paul, W. J. Kelleher and A. E. Schwarting. (*J. Amer. pharm. Ass., Sci. Ed.*, 1954, **43**, 205.) A medium containing 2 per cent. of mannitol and 1 per cent. of casein hydrolysate together with mineral material was inoculated from slant cultures of the organism and incubated at 21 to 22° C. on a reciprocal shaker. Sub-cultures were incubated for 72 hours on the shaker, after which solutions of indole, indole and DL-serine, L-tryptophane and α-amino-*N*-methyltryptophane were added. These cultures were incubated for 24 hours. The mycelia were separated centrifugally, washed and incubated on a reciprocal shaker in a solution of the test compound in saline solution. The cultures were freeze-dried and extracted by the U.S. National Formulary method for the determination of total alkaloids of ergot, the extracts being concentrated and analysed chromatographically. Mycelium was separated from the replacement cultures and the filtrate submitted to chromatography on paper, using a mixture of butanol, glacial acetic acid and water (4:1:5). The chromatograms were sprayed with a 2 per cent. solution of *p*-dimethylaminobenzaldehyde in hydrochloric acid which gave a pink colour with indole, and blue with tryptophane and amino-*N*-methyltryptophane. Quantitative determinations of these substances were made spectrophotometrically. The various compounds used, representing several structural moieties of lysergic acid, had no effect on the production of ergot alkaloids in the organism. In the absence of organic material, indole in a solution containing 50 μg./ml. was completely utilised in 24 hours and 25 μg./ml. of tryptophane appeared in the solution. Added L-tryptophane and amino-*N*-methyltryptophane were partially utilised. When the organism was grown on a tryptophane-free medium, it could be shown that growth was significantly inhibited by the addition of tryptophane. G. B.

***Digitalis ferruginea*, A Preliminary Phytochemical Investigation of.** R. M. Appel and O. Gisvold. (*J. Amer. pharm. Ass., Sci. Ed.*, 1954, **43**, 215.) An aqueous extract of the fresh leaves was treated with methyl *iso*butyl ketone. From the aqueous mother liquor, saponin, chiefly tigonin, was extracted in a quantity representing 0·42 per cent. of the weight of the leaves. The methyl *iso*butyl ketone extract was separated into ether-soluble and ether-insoluble fractions. The ether-insoluble material yielded a crystalline glycoside, apparently α-acetyldigoxin. From the ether-soluble fraction, an amorphous glycoside was obtained which appeared to be digitoxin. Attempts to separate a mixture of digoxin, acetyldigoxin and the crystalline and amorphous glycosides obtained from *Digitalis ferruginea*, by the use of paper chromatography with a mixture of methyl *iso*butyl ketone, methanol and water (10:1·8:5) or a constant-boiling mixture of methyl *iso*butyl ketone and water as solvents were not successful. The amorphous glucosides gave a positive reaction in the periodate-benzidine test. G. B.

Rutin, Presence of, in *Rheum* Species. L. Hörhammer and K. Müller. (*Arch. Pharm. Berl.*, 1954, **287**, 126.) In a systematic paper chromatographic examination of the Polygonacæa, the leaves and flowers of all species of *Rheum* examined contained a flavone with an R_F value of 0·35. This was identified as

rutin. The species in question, with yields of rutin obtained from them, are given below

Species	Date of collection	Yield of rutin per cent.
R. emodi	July	0·32
R. officinale	July	1·30
R. palmatum ..	July	3·10
R. pruinosum ht. ..	July	0·61
R. rhaponticum ..	July	0·70
R. ribes	July	—
R. undulatum ..	June	—
R. wittrockii	July	—

G. M.

PHARMACOLOGY AND THERAPEUTICS

Anticholinergic Agents, Comparative Effects of, on Human Gastric Secretion. J. A. McGowan, Jr. and M. Stanley. (*J. Lab. clin. Med.*, 1954, **43**, 359.) Atropine and 10 quaternary ammonium compounds were compared for their anticholinergic activity in diminishing gastric acid secretion in man. The quaternary compounds tested were methanthelinium, propantheline, oxyphenonium bromide, prantal, Squibb compounds 2963 (dimethylethyl 3-*n*-propyl benzilate ammonium bromide) 3199 (*N*-diethylaminoethyl-*N*-methylbenzilamide methobromide) 2998 (2-hydroxyethyl methylpiperidinium bromide, 1 benzoyl*cyclo*propane carboxylate) 3505 (di*iso*propyl [2-hydroxyethyl] methylammonium bromide, 1-benzoyl*cyclo*propanecarboxylate) 2806 (2-ethyl [1-benzoyl*cyclo*propanecarboxylate] methyldiethyl ammonium bromide) and Roche compound Ro2-3773 (1-methyl-3-benzyloyl-oxyquinuclidinium bromide). The subjects were 134 hospitalized patients, 25 of whom were controls, 43 per cent. of the test group and 48 per cent. of the controls having peptic ulcers, active or healed. The drugs were studied by the double meal technique where a standard meal was followed after 15 minutes by intubation and complete aspiration of gastric contents. The drug was then given orally or parenterally and the meal procedure repeated one hour later. The drugs were also compared by their depression of basal acid secretion in patients with gastric hypersecretion, but the control responses here were more variable than with the double meal method. Achlorhydria was seen only infrequently after large oral doses of the more potent agents, but smaller parenteral doses of most of the drugs achieved this ideal more often. As might be expected, achlorhydria was seen more often in studies on basal secretion. Despite claims to the contrary no drug appeared to have a clear superiority over the others in relation to side effects (xerostomia mydriasis, blurring of vision, and bladder and intestinal dysfunction). The approximate single oral doses which will reduce the basal acid secretion in patients with hypersecretion, or food-stimulated secretion in normals by 20 per cent or more:—Atropine, 1·3 mg.; oxyphenonium, 10 to 25 mg.; Ro2–3773, 10 to 35 mg.; propantheline, 30 to 60 mg.; Squibb 2963, 75 to 125 mg.; methanthelinium and Squibb 3199, 100 to 150 mg.; prantal, Squibb 3505, 2998 and 2806; 400 to 700 mg. G. P.

Cyanocobalamin; Nasal Instillation and Inhalation in Pernicious Anæmia. R. W. Monto and J. W. Rebuck. (*Arch. intern. Med.*, 1954, **93**, 219.) This is a report on the treatment of 12 patients with pernicious anæmia in relapse by both inhalation and nasal instillation of cyanocobalamin. Cyanocobalamin in isotonic sodium chloride solution without a preservative was employed. The maximum hæmopoietic effect was elicited with a solution containing 100 μg. per ml.; 1000μg. in 1/10 ml. by volume of lactose powder was used for administration as a dust. Nasal instillation was performed in 0·5 ml. volume divided between the two nostrils and given in the usual manner of nasal liquid medicaments. In each of the 12 patients a satisfactory hæmatological and clinical response was obtained. Maximum reticulocyte increase occurred between the 8th and 10th days of treatment and varied between 18 and 44 per cent. according to the severity of the anæmia. The bone marrow picture reverted from a megaloblastic arrest to normal erythropoiesis, and the peripheral blood findings reflected this improvement. A single inhalation of 100 μg. of cyanocobalamin in 1 ml. of isotonic sodium chloride solution produced a reticulocyte elevation to 18 per cent. in a patient whose initial erythrocyte count was 1,020,000, and a similar installation effected a reticulocytosis of 37 per cent. in another patient whose original red cell count was 2,880,000. In addition, the condition of 20 patients with pernicious anæmia in remission has been maintained by this therapy for periods varying up to 18 months. S. L. W.

Folic Acid, Danger of Polypharmaceutical Preparations Containing. C. P. Lowther. (*Brit. med. J.*, 1954, **1**, 564.) A woman aged 46 complained of stiffness of her knees and after various treatments had been tried it was found that the hæmoglobin level was 48 per cent. The administration of iron was recommended and a preparation containing iron and folic acid with vitamin B and liver extract in capsule form was prescribed. Considerable improvement in the patient's condition occurred but, 3 months later, on examination after 10 days in hospital following a fall she was found to have a spastic paraplegia and eventually subacute combined degeneration of the cord was diagnosed. Anahæmin, 4 ml. on alternate days, and cytamen, 100 μg. daily, brought about rapid hæmatological and neurological improvement although the patient had still a very slight ataxia when last seen. The inclusion of folic acid in polypharmaceutical preparations is condemned on four grounds. It temporarily improves the blood picture and subacute combined degeneration of the cord is likely to be misdiagnosed since it rarely occurs without anæmia. The relief of the general symptoms of pernicious anæmia reassures both patient and doctor and masks the deterioration of the nervous system. Folic acid deficiency occurs infrequently and is not needed in multivitamin or iron preparations. It is still uncertain whether folic acid actually precipitates cord degeneration. H. T. B.

Gastric Secretory Function, Tubeless Method. H. M. Pollard, A. Carballo and R. J. Bolt. (*J. Lab. clin. Med.*, 1954, **43**, 340.) In a series of studies on the determination of gastric secretory function in man, the authors have re-examined the method introduced by Segal *et al.* (*Proc. Soc. exp. Biol., N.Y.*, 1950, **74**, 218) which depends upon the release of quinine in the stomach from the quininium salt of a cation-exchange resin, diagnex; the quinine is absorbed from the small intestine, approximately one-third being excreted in the urine. Determination of this urinary quinine was then made using the ether-sulphuric acid method of Kelsey and Geiling. For the test the patients were fasted overnight and the fasting urine collected. A further urine sample was collected one hour

after giving 250 mg. caffeine sodium benzoate in water. 2 g. of the quininium resin compound was then given in water and urine collected after one and two hours. These two samples were analysed and the second-hour sample results compared with the conventional gastric analysis involving intubation and histamine stimulation of secretion. The test was very reliable for the detection of achlorhydria, but was not quantitative enough for routine gastric acid determinations. In the 76 patients who underwent the tests, there was some degree of correlation between disease state and urinary quininium, duodenal ulceration being associated with hypersecretion of acid and gastric ulceration, with normal or low secretion. Gastric carcinoma was attended by low normal or anacidity and pernicious anæmia by persistent achlorhydria. The test is much simpler than uropepsin determination and is particularly useful where psychogenic or organic illness precludes the use of gastric intubation. Also, in patients with partial gastrectomies and gastro-enterostomies the intubation methods is unreliable whereas there is no loss of accuracy of the quinine method. As a diagnostic aid the usefulness of the test is limited except where a negative result is sought. The analysis of the second-hour sample would seem unnecessary except in such cases and would further simplify the test. G. P.

Lead Poisoning, Monocalcium Disodium Ethylenediaminetetra-acetate in. H. L. Hardy, H. B. Elkins, B. P. W. Ruotolo, J. Quinby and W. H. Baker (*J. Amer. med. Ass.*, 1954, **154**, 1171.) Monocalcium disodium ethylenediamine tetra-acetate (calcium versenate), a chelating agent forming unionised complexes with heavy metals, was tried in 3 patients with chronic lead intoxication. The compound was administered daily for 5 to 7 days by intravenous injection during 2 hours in doses of 3 to 4 g. dissolved in 450 to 600 ml. of 5 per cent. aqueous dextrose solution. The urinary excretion of lead and of coproporphyrin was determined before and during treatment. In each patient the urinary excretion of lead was about 30 times greater during treatment, and there was a decrease in coproporphyrin excretion. When treatment was stopped, lead excretion returned to pre-treatment values; coproporphyrin excretion continued to decrease in 2 of the patients but increased in the third until after a second course of calcium versenate. Before treatment all the patients were anæmic, with stippled cells, increased resistance of the red cells to hypotonic sodium chloride and increased mechanical fragility. The treatment resulted in a rise in the hæmoglobin level and disappearance of abnormalities in the cells. No untoward effects were observed. H. T. B.

***iso*Nicotinyl Hydrazides, Toxicity in Pulmonary Tuberculosis.** E. O. Coates, G. L. Brickman and G. M. Meade. (*Arch. intern. Med.*, 1954, **93**, 541.) Results obtained in a series of 77 patients confirm previous reports that iproniazid (*N-iso*nicotinoyl-*N'-iso*propylhydrazine) is considerably more toxic than isoniazid and suggest, in addition, that side-effects are more frequent and more severe when it is given in combination with streptomycin or *p*-aminosalicylic acid. Termination or interruption of therapy, or reduction in dosage because of toxicity, was necessary for 45 per cent. of those receiving iproniazid, and only 9 per cent. of those given isoniazid. A standard dose of 4 mg./kg. was employed for both isoniazid and iproniazid. Therapy was continued for a minimum of 6 months in 41 patients, for from 2 to 6 months in 22 patients, and for less than 2 months (discontinued because of toxicity) in 14 patients. Toxic reactions occurred in two main categories, those related to the autonomic nervous system and those apparently related to the central nervous system and the

peripheral nerves. In the first category were constipation, postural hypotension, dryness of the mouth, urinary difficulties, sweating, impotence, bradycardia, and increasing dyspnœa. In the second category were mental changes, muscular irritability, paræsthesias. Purpura, accompanied by hæmoptysis, occurred in one patient taking isoniazid and two taking iproniazid. A case of toxic encephalitis and one sudden death (ventricular fibrillation) may have been related to therapy with iproniazid. "Withdrawal" symptoms (nightmares, muscular twitchings, and difficulty with micturition) were observed in 64 per cent. of 14 patients in whom iproniazid therapy was abruptly terminated; these were not relieved by substitution of isoniazid . The authors conclude that in spite of some apparent superiority over isoniazid in its benefits upon the symptoms of pulmonary tuberculosis, iproniazid appears too toxic for general use.

S. L. W.

Noradrenaline, Excretion of, in Urine in Hypertension. U. S. von Euler, S. Hellner and A. Purkhold. (*Scand. J. clin. Lab. Invest.*, 1954, **6**, 54.) Estimates of noradrenaline in the urine of 500 cases of hypertension of unknown origin were made. In 60 per cent. of these the noradrenaline content was within normal limits, in 20 per cent. it was not significantly increased above the normal and in the remaining 20 per cent. it was significantly increased. This increased noradrenaline excretion in some cases of essential hypertension may be important in the pathogenesis of the disease. The increase may come from the adrenergic nerves, in particular the vasomotor fibres. M. M.

Plasma Substitutes. W. d'A. Maycock. (*Brit. med. Bull.*, 1953, **10**, 29.) Dextran possesses most of the desirable properties of a plasma substitute. After infusion, molecules small enough to enter the glomerular filtrate are excreted in a few hours; the remainder leave the blood at a uniform decremental rate of about one-third per day and pass into the tissues. It thus disappears from the body almost completely in a short time and no histological changes attributable to it have been observed. Dextran is metabolised but the metabolic process is not known. Dextran solutions have two disadvantages. They are likely to cause rouleaux formation, thus interfering with compatibility tests, and certain individuals are sensitive to dextran and may exhibit severe reactions. Solutions of animal gelatin have been investigated experimentally and clinically. The native gelatin molecules are degraded by autoclaving, the molecular size varying with the time of heating. The solution originally tested (mean mol. wt. about 33,000) gelled at room temperature; the next preparation (mean mol. wt. about 19,000) gelled at 12° to 15° C. Both these forms are rapidly excreted by the kidneys. More recently a polymerised form (oxypolygelatin), with a gelling point of 10° to 13° C., and a fluid gelatin, with a gelling point of 0° to 4° C. have been under trial. All these gelatins are non-antigenic and are free from harmful effects—apart from causing rouleaux formation—but their clinical value in the treatment of oligæmia has not yet been established. The place of polyvidone among the plasma substitutes has still to be determined. It has been shown that it is not metabolised to any significant degree, that molecules with a mol. wt. of less than 25,000 are excreted very rapidly, and that those with mol. wt. between 25,000 and 40,000 are all excreted within a few days. Molecules with weights greater than 110,000 are probably retained in the tissues for a long time, possibly for years. Histological evidence of storage of polyvidone and of certain regressive changes in human tissues many months after administration have been reported. These observations suggest that polyvidone solutions should not contain molecules of greater mol. wt.

than 60,000 to 70,000, the majority having a mol. wt. of 25,000 to 40,000. The retention of such a solution in the blood stream would be short-lived; it is estimated that in the normovalæmic patient the plasma volume expansion would be only 50 to 60 per cent. of the infused volume after 6 hours and only about 30 to 35 per cent. after 12 hours. Since all plasma substitutes fail in one way or another to meet all the requirements and until it is known what importance should be attached to their lack of many of the properties of plasma, they should be used cautiously, though they have an important part to play where transfusion services are lacking, in national emergencies, and during the temporary absence of blood or plasma. S. L. W.

Primidone, Clinical Evaluation of. D. Sciarra, S. Carter, C. I. Vicale and H. H. Merritt. (*J. Amer. med. Ass.*, 1954, **154**, 827.) Primidone (5-phenyl-5-ethylhexahydropyrimidine-4-6-dione), an anticonvulsant drug closely related to phenobarbitone, was administered to 121 patients with one or more types of convulsive seizures. The ages of the patients ranged from 5 to 71 years, the majority being between 20 and 40. All seizure types were represented, but grand mal predominated. In every case primidone was added to the medicaments that the patients were already receiving. The drug was administered in tablets of 0·25 g., the usual starting dose being 250 mg. daily. This was increased by one tablet daily at approximately weekly intervals to the point of therapeutic or toxic effect. The therapeutic effects could be evaluated in 72 of the 121 patients; this group was followed for periods ranging from 1 to 18 months. The period of observation was 1 to 11 months for 28 patients and 12 to 18 months for 44 patients. In the remaining 49 patients it was not possible to evaluate the anticonvulsant effect accurately, owing to toxic reactions or because follow-up data were inadequate. The attacks were entirely controlled in 7 patients (10 per cent.), reduced in frequency in 31 (43 per cent.), and unchanged in 34 (47 per cent.). The greatest benefit occurred when the seizures were of the grand mal, psychomotor, minor or focal types; no improvement was noted in any of the patients with petit mal. Side effects occurred in 65 of the 79 patients, but none was serious. Drowsiness and ataxia were the two most frequent symptoms and made it necessary to discontinue the administration of primidone in 25 patients. In a third of the patients side-effects developed with a daily dose of 0·75 g. or less, and two-thirds of the patients manifested side-effects with a daily dose of 1·25 g. or less. In the remainder the toxic manifestations appeared when the daily dose exceeded 1·25 g. S. L. W.

Vitamin K as Antagonist to Anticoagulants. T. Hilden and O. Munck. (*Scand. J. clin. Lab. Invest.*, 1953, **5**, 361). The purpose of this study was to examine the effect of synthetic vitamin K, menadione, on dicoumarol, ethyl biscoumacetate and phenylindanedione under uniform conditions. The examinations were made on three groups of 8 patients undergoing treatment with one or other of these anticoagulants. Before the vitamin K experiments were made it was ensured that the prothrombin concentrations were at fairly constant concentrations. The menadione was given in a dose of 100 mg. by mouth, in one series of experiments, and in the same dose by intramuscular injection in a second series. Administration of the maintenance dose of the anticoagulant was continued while vitamin K was administered. Menadione was shown to exert an equally potent effect, whether given by mouth or intramuscularly, on all the anticoagulants employed, though the effect varies considerably from one person to another. Vitamin K_1, administered by mouth in a similar dosage, was also found to exert a uniform effect on the three anticoagulants, though its effect was more pronounced than that of menadione. S. L. W.