ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

Adrenaline, Determination of, in Mixtures. C. O. Björling and H. Hellberg. (*Farm. Revy*, 1950, **49**, 69.) The method described below has been tested for adrenaline in admixture with ephedrine, nupercaine, procaine, tetracaine or xylocaine. 1 to 10 ml. of a solution, containing 10 to 50 μg. of adrenaline hydrochloride, is treated with 0·1 g. of trisodium citrate and passed through a column of alumina in a tube of 5 mm. diameter. The column is washed with 3 ml. of water, then with 10 ml. of alcohol, and finally with 5 ml. of water. This eluate contains the alkaloid or other base. The adrenaline is then recovered by washing the column with 10 ml. of 0·1N hydrochloric acid and 3 to 4 ml. of water. The adrenaline is determined fluorimetrically, with rivanol as standard, using the method of Ehrléns. Although the figures given show that the results are up to 50 per cent. too high, this appears to be due to the limitations of the fluorimetric method, the recovery of adrenaline being apparently quantitative. G. M.

Chlorine and Bromine, Microdetermination of. J. Grodsky. (*Anal. Chem.*, 1949, **21**, 1551.) A method is described for determining halogens in organic compounds by fusing with potassium and titrating the resulting potassium halide with silver nitrate using dichlorofluorescein as indicator; the method can be used for all types of compounds, including volatile liquids. A liquid sample (4 to 20 mg.) is weighed in a weighing capillary, the handle of which is a glass rod, 20 to 25 mm. long, and the capillary end is placed down in the reaction tube; a solid sample is weighed with a long handled weighing stick. About three shavings of potassium each about 1 cu. mm., are cut under ether, dried rapidly with clean tissue, and added to the microsample, using 2 to 5 times as much for semi-microsamples or in the presence of nitrogen or sulphur. The tube is heated at a point about 3 cm. below the open end then drawn to a thick walled capillary and when cool is evacuated and sealed off. The tube is shaken to break the inner capillary containing the liquid sample and is placed for 15 minutes in a furnace preheated to 400°C. When the tube is cool, it is washed, opened by cutting just below the shoulder and 1 ml. of ethyl alcohol is added to destroy excess of potassium and to wash the sides. To carry out the argentimetric titration the solution is transferred through a sintered-glass funnel into a flask containing 5 ml. of 0·01N potassium chloride. The reaction tube is washed four times with hot water containing a drop of nitric acid and the solution in the flask is brought to the boil at a low heat. About 5 mg. of barium carbonate is added to the hot solution, it is acidified if not already acid, and boiling is continued for at least 2 hours with replacement of evaporated water to assure quantitative removal of the hydrogen sulphide; excess of barium carbonate is then carefully added until an undissolved residue of about 50 mg. remains; 1 ml. of dichlorofluorescein indicator and 10 ml. of acetone are added to the cooled solution which is then titrated with 0·01N silver nitrate. R. E. S.

Morphine in Opium, Determination of. J. A. C. van Pinxteren and M. A. G. Smeets. (*Pharm. Weekbl.*, 1950, **85**, 1, 48.) The sources of error of the lime method were investigated. The amount of morphine remaining in the mother liquor was determined by extraction with benzene-butyl alcohol at *p*H 9, and determination as nitrosomorphine. The results showed that the quantity varied considerably with different methods, but was small under favourable circumstances. On the other hand, some abnormal types of opium gave considerably higher figures, so that it is not possible to apply a correction for this error. The amount of calcium carbonate precipitated with the morphine was determined after ashing of the precipitate. This also can lead to an appreciable error, although in those methods in which the morphine is purified before crystallisation it is small. Co-precipitation of other alkaloids may be followed by determining the methoxyl value of the recovered morphine. In the method of Mannich (determination as chlorodinitrophenyl ether) the purity of the product obtained, checked by a determination of methoxy and nitro groups in it, was found to be unsatisfactory. It appears, however, that better results are obtained by this method if the purification of the extract is better. Since Rusting's method gives the purest morphine, although it allows of a considerable loss in the mother liquors, a new combination of the last two methods was developed. 1 g. of morphine is rubbed down with 1 ml. of water, then mixed with 5 ml. of 5 per cent. solution of manganous chloride and 0·5 g. of calcium hydroxide. The mixture is filtered through a crucible 3G3 into a tared flask, being washed through with, in all, 15 ml. of water. During the filtration the residue must not be allowed to become quite dry. The filtrate is treated with 4 ml. of a solution of 20 g. of potassium oxalate and 10 ml. of N potassium hydroxide in 100 ml., and heated for 15 minutes on the water-bath. After cooling, the mixture is filtered on a porcelain filter crucible A_2, the residue on the filter being stirred to speed up filtration. After washing three times with 2 ml. portions of water, the filtrate is made up to 40 g. To this is added 250mg. of 4-chlor-1 : 3-dinitrobenzene dissolved in 30 ml. of acetone. After standing for 3 hours, with occasional shaking, the mixture is filtered through a weighed 3G3 crucible and the crystals are quantitatively transferred to the crucible, washed quickly with 3 × 2 ml. of acetone, then, with 2 × 2 ml. of water, dried at 70° to 80°C., and weighed. The factor 0·632 is used to convert the weight of chlorodinitrophenyl ether to morphine. A method of titrating the ether is also given. G. M.

Pyranisamine Maleate, Spectrophotometric Assay of. L. T. Anderson, W. C. Gakenheimer, C. Rosenblum and E. H. Smith. (*J. Amer. pharm. Ass. Sci. Ed.*, 1949, **38**, 373.) Pyranisamine maleate is obtained by neutralising 1 molecule of the free base *N*-(α-pyridyl)-*N*-(*p*-methoxybenzyl)-*N'*, *N'*-dimethylethylene-diamine with 1 molecule of maleic acid. As a substituted derivative of ethylenediamine, pyranisamine exhibits an ultraviolet absorption spectrum sufficiently intense and characteristic to distinguish it from substances commonly present in pharmaceutical preparations. The spectrum was found to change with acidity and with solvent; in aqueous solution at *p*H values below 5·5, it consisted of 2 bands at 2400 to 2430Å., and 3075 to 3100Å., whereas above *p*H 6 a third band was present at 2215 to 2240Å, probably due to a shift to longer wave lengths of a band existing in acid solutions below 2100Å. The spectra in distilled water and in alcohol (20 per cent.) were practically identical with the curve at *p*H 5·5, but in alcohol-light petroleum solution, three band maxima were

found at 2475, 2850 and 3075 Å. The absorption band most suitable for analytical determination was that *ca.* 2435Å. since the extinction coefficient remained constant at *p*H 4 to 6·5. The same curves were found in alcohol (20 per cent.) and in distilled water (*p*H 5·5), indicating an insensitivity of the spectrum to the presence of alcohol and salts from the buffer mixtures. For all work in water or alcohol (20 per cent.), therefore, an all-over average $E_{1\ cm.}^{1\ per\ cent.}$ of 422 was employed in calculating concentrations of pyranisamine maleate. For solutions in 1 : 1 absolute alcohol-light petroleum, the 2475Å. band with an $E_{1\ cm.}^{1\ per\ cent.}$ of 477 was employed. Methods are given for the determination of pyranisamine maleate in tablets, in elixirs, in anhydrous water-soluble ointments, in anhydrous petrolatum ointments, in aqueous emulsion type ointments and in parenteral solutions. In general the preparation was simply diluted with a suitable solvent before reading the extinction at the specified wave length in a suitable spectrophotometer. In the case of the elixir and the anhydrous petrolatum ointment a previous extraction was performed. R. E. S.

Silver, Colorimetric Determination of Small Quantities of. G. Saini. (*Ann. Chim. applic., Roma,* 1950, **40,** 55.) The method is based on the catalytic action of silver ions in the oxidation of manganous ions to permanganic acid by persulphates. The substance containing the silver should be dissolved in nitric acid, sulphuric acid added, and the solution heated until white fumes are evolved, thus removing reducing substances. Phosphates must be removed by precipitation with magnesium in ammoniacal solution. The reagents required are 25 per cent. sulphuric acid, 4 per cent. solution of borax ($Na_2B_4O_7$, $10H_2O$), solid potassium persulphate, 4 per cent. solution of manganous sulphate ($MnSO_4$, H_2O). The author used a Lange colorimeter with a green filter and 100 ml. containers. The solution of silver nitrate used for standardising contains 1·8 μg. of silver per ml. Run the silver solution into a 150 ml. beaker, add 12 ml. of manganous sulphate solution, 6 ml. of diluted sulphuric acid and 10 ml. of borax solution. Heat slowly to 90°C., adding gradually 2 g. of potassium persulphate and boil gently for 5 minutes (not longer). Filter off the precipitated manganese meta-hydroxide through a porous porcelain filter, wash with a little water and make up the filtrate to 150 ml. The water used for washing and making up should be redistilled or contain a trace of persulphate to remove reducing substances. The colour is then read in the colorimeter. The graph of the relation of colour to amount of silver is not a straight line. If 15 ml. of borax solution is used instead of 10 ml., the graph is straight but of lower values. Colourless cations do not interfere, but with coloured cations the standards should contain the same amount of them as is present in the solution to be tested. The method can be used for quantities between 12 μg. and 120 μg. per 100 ml. H. D.

Soft Paraffin, Peroxide in. M. J. Golden. (*J. Amer. pharm. Ass., Sci. Ed.,* 1949, **38,** 301.) A reagent is prepared by dissolving 2 g. of ferrous sulphate in 100 ml. of distilled water and 2 ml. of sulphuric acid, adding 200 ml. of acetone and 100 ml. of 2 per cent. aqueous ammonium thiocyanate, and heating under a reflux condenser with 0·2 g. of iron powder and 6 in. of No. 30 iron wire until the solution is colourless. Samples of soft paraffin are heated at 250°F. 2 ml. quantities are removed at hourly intervals, diluted with mineral oil at 250°F, cooled to 170°F, the reagent added under carbon dioxide, shaken and observed. The peroxide test time is taken as the time of heating of the first 2 ml. quantity which produces a darker pink to red

colour in the above test. A minimum peroxide test time of 2 hours is suggested for soft paraffin for pharmaceutical uses, or for cosmetics. The test can be made quantitative by measuring the transmission of the lower layer with a photoelectric colorimeter and a filter having a mean transmission of 560 mμ, and using heated mineral oil in a blank test. The colorimeter may be calibrated by using mixtures of reagent and hydrogen peroxide, the results being expressed in terms of peroxide, calculated as hydrogen peroxide.

G. B.

Strychnine and Brucine, Chromatographic Separation of. K. B. Jensen and A. B. Svendson. (*Pharm. Acta Helvet.*, 1950, **25,** 31.) Although direct partition of brucine and strychnine, from ether-water, should produce separation of the two alkaloids, the method is not suitable for practical application on account of the speed with which the compounds would pass through the column. The rate of passage can however be reduced by using a buffer solution. Conditions found suitable for separation of the alkaloids were as follows: the supporting phase consisted of 10 g. of kieselguhr, the immobile phase of 3 ml. of 0·2M. phosphate buffer of *p*H 7. The rate of elution was 10 ml. in 2 to 3 minutes. For the assay of nux vomica, the alkaloids were extracted from 30 g. of the drug with 200 g. of ether and 100 g. of chloroform, after the addition of 25 ml. of 10 per cent. solution of sodium carbonate. After shaking for 30 minutes, 50 ml. of water was added, and the ether-chloroform mixture was filtered. The solvent was distilled off, and the residue dissolved in chloroform and mixed with an equal volume of ether to a total volume of 50 ml. The solution was then passed through the column, and eluted with ether. The strychnine in the solution was determined by titration, while the brucine was recovered by elution with chloroform.

G. M.

Sulphates, Insoluble Inorganic, Microscopic Identification of. G. Denigès. (*Bull. Trav. Soc. Pharm., Bordeaux,* 1949, **87,** 101.) To distinguish the sulphates of calcium, barium, strontium and lead, a little of the finely powdered material is placed on a microscope slide with a drop of sulphuric acid, and warmed over a small flame, with stirring, until the acid commences to fume. After cooling, the preparation is covered with a cover glass and examined microscopically. The crystals observed are characteristic for the different sulphates.

G. M.

Sulphonamides, Identification of. C. J. de Wolff. (*Pharm. Weekbl.*, 1949, **84,** 717.) A table for the identification of the chief sulphonamides is based mainly on the following reactions: 1. Diazotisation sometimes gives a yellow colour, which may be so intense that it is easily seen in a 0·05 per cent. solution; 2. Ammonia, following diazotisation, gives a stronger yellow colour with many aromatic derivatives; 3. Insoluble compounds may be formed with formaldehyde; 4. Many sulphonamides react with Nessler's reagent. The complete scheme comprises the following compounds: albucid, cibazol, dagenan, elkosin, irgafen, irgamid, lucosil, marfanil, neo-uliron, percoccide, septazine, septosil soluble, soluseptazine, sulphadiazine, sulphaguanidine, sulphamethazine, sulphanilamide, sulphanilic acid, sulphaphthalidine, sulphasuxidine, uliron, ultraseptyl.

G. M.

Sulphonamides, Scheme for Identification of. G. Schallengerg-Heertjes. (*Pharm. Weekbl.*, 1949, **84,** 765.) A preliminary classification is effected by adding 1 drop of a saturated solution of potassium bromate to 10 mg. of the substance dissolved in 1 ml. of 4 N sulphuric acid. The

following appearances are observed:—sulphanilamide, sulphaguanidine, sulphamethazine, violet colour, changing to brownish; sulphathiazole, ultraseptyl, violet colour, changing to dark colour and brown precipitate liquid yellow; uliron, violet colour, then turbidity, later brown precipitate; neo-uliron,

10 mg./0·5N hydrochloric acid	Dragendorff's reagent	Silicotungstic acid	Bouchardat's reagent	Gold chloride	Eder's reagent	Picric acid	Picrolonic acid
Sulphanilamide	−	−	−	−	+	−	−
Sulphaguanidine	−	+	−	−	+	+	+
Sulphamethazine	+	+	+	weak	+	+	−
Sulphathiazole	+	+	+	+	+	+	+
Ultraseptyl	+	+	+	+	+	+	+
Uliron (in 4N sulphuric acid) ...	+	+	+	+	...		
Neo-Uliron	+	+	+	+	+	+	...
Septazine	−	−	−	−	weak	−	−
Sulphadiazine	+	+	+	+	+	−	+
Percoccide	+	+	+	+	+	+	+

rose colour, becoming brownish; septazine, turbidity and blue-violet colour, becoming violet; sulphadiazine, percoccide, yellow colour, becoming reddish-brown to red, turbidity, later brown precipitate; sulphapyridine, elkosin, lucosil, albucid, irgamid sodium, irgafen, sulphasuccidine, yellow to brown colours only. Further reactions are carried out with a series of alkaloidal reagents, as in the table. Identification is confirmed by the microscopic appearance of the crystals formed with various reagents. Photographs of the characteristic crystals are given. G. M.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Polypeptide with High Adrenocorticotrophic Activity. P. Morris and C. J. O. R. Morris. (*Lancet*, 1950, **258**, 117.) By ultrafiltration of pituitary-gland extracts under suitable conditions it is possible to prepare a polypeptide mixture of high adrenocorticotrophic activity. The authors describe the isolation of an apparently single, homogeneous peptide from this mixture by ultrafiltration and iontophoresis. Evidence of homogeneity comes from paper partition chromatography and iontophoresis at *p*H 2·3, 4·0, 6·0 and 8·0. Comparison of the adrenocorticotrophic activity of this substance with that of the Armour standard adrenocorticotrophin preparation No. La-l-a by the adrenal ascorbic acid depletion method shows it to be 8·5 times as active. E. N. I.

Theobromine in Theobromine and Sodium Salicylate, Determination of. C. W. Bell. (*J. Amer. pharm. Ass. Sci. Ed.*, 1949, **38**, 391.) The literature concerning the methods available for this determination is reviewed and an adaptation of Boie's acidimetric method based on the fact that silver nitrate reacts with theobromine to form insoluble silver theobromine with the simultaneous quantitative liberation of nitric acid, which can then be titrated with standard alkali, is recommended. The actual method is as follows. Transfer about 1 g., accurately weighed and previously dried at 110°C. to constant weight, to a 500-ml. flask, add 75 ml. of distilled water and 40 ml. of approximately 0·1N sulphuric acid. Boil for 2 to 3 minutes, washing down the sides of the flask with three 15 ml. quantities of distilled water. Cool quickly to about 40°C. and add 1 ml. of phenol red indicator. Add a slight excess of 0·1N sodium hydroxide to make alkaline and then carefully adjust the *p*H of the solution by adding the minimum amount of

0·1N sulphuric acid to produce a lemon-yellow colour. Add 35 ml. of 0·1N silver nitrate and titrate the liberated nitric acid slowly with 0·1N sodium hydroxide, to the first sign of a bluish red colour, the end-point being approached drop by drop. Each ml. of 0·1N sodium hydroxide is equivalent to 18·017 mg. of theobromine. Ten commercial samples were analysed by the proposed method, by the National Formulary VIII method, and by a modified total nitrogen (Kjeldahl) determination. The present N.F.VIII method gave high results while the acidimetric method gave results which were in close agreement with those calculated from the nitrogen content. It is contended that the acidimetric method is better than the present N.F.VIII method as regards ease of operation, saving of time, and accuracy and precision. R. E. S.

Terramycin, a new Antibiotic. A. C. Finlay. (*Science*, 1949, **111**, 85.) Terramycin is the name given to a crystalline antibiotic obtained from broth cultures of *Streptomyces rimosus*, isolated from soil. Terramycin is amphoteric and forms the crystalline hydrochloride and sodium salt. It has the following properties: m.pt. 185°C. (approx.) with decomposition, $[\alpha]_D^{25°C.}$ – 196° (1·0 per cent. in 0·1N hydrochloric acid), soluble in methyl alcohol, ethyl alcohol, acetone and propylene glycol, and in water to the extent of 0·25 mg./ml. at 25°C.; insoluble in ether and light petroleum. It is stable over long periods in aqueous solutions at about *p*H 2 to 5 at room temperature. It crystallises in several forms, one of which consists of thick hexagonal plates the refractive indices of which are $\alpha = 1{\cdot}636 \pm 0{\cdot}004$, $\beta = 1{\cdot}644 \pm 0{\cdot}004$, $\gamma => 1{\cdot}700$. In 0·1M phosphate buffer (*p*H 4·5) it shows ultra-violet absorption maxima at approx. 247, 275 and 353 mμ; it also shows characteristic absorption in the infra-red region. It has a low degree of toxicity in animals and shows marked activity *in vitro* against a wide variety of organisms. It displays marked chemotherapeutic activity against experimental infections in mice due to *Streptococcus hæmolyticus, Diplococcus pneumoniæ, Klebsiella pneumoniæ, Salmonella typhosa,* and other organisms, and appears to have definite antirickettsial activity in the chick embryo, and, in high concentrations, to inhibit the infection of the chick embryo with the PR8 strain of influenza A virus. S. L. W.

Vitamin B_{12}: Distribution in Natural Materials. U. J. Lewis, U. D. Register, H. T. Thompson and C. A. Elvehjem. (*Proc. Soc. exp. Biol., N.Y.*, 1949, **72**, 479.) The determinations were made by a rat assay process based on the fact that administration of thyroid-active substances increases the requirement of vitamin B_{12}. Figures are given for more than 30 materials. Two samples of yeast autolysate were found to be completely inactive. A sample of dried "slops" from streptomycin production contained at least 22 μg./100 g. Commercial condensed fish solubles contained more than 40 μg./100 g. Beef liver and beef kidney both contained more than 50 μg./100 g. of dry substance. Desiccated sheep rumen contents contained about as much as beef liver and kidney, suggesting the possibility of synthesis of the vitamin within the rumen. Plant materials showed no measurable activity. H. T. B.

BIOCHEMICAL ANALYSIS

Citric Acid, Micro-estimation of. H. W. Malherbe and A. D. Bone. (*Biochem. J.*, 1949, **45**, 377.) A method is given for the micro-estimation of citric acid by its conversion into pentabromoacetone. Vanadic acid is used

to replace the normal potassium permanganate oxidation making the method more adaptable and more specific. For quantities of 0·1 to 1·0 mg. of citric acid the solution (5 ml., containing not more than 1 mg. of citric acid) is mixed with 27N sulphuric acid (5 ml.) in a test tube and cooled to room temperature, saturated bromine water (2 ml.) and a 2 per cent. ammonium vanadate solution (3 ml.) being then added. The contents are well mixed, the stoppered tube is left in a water bath at 50°C. for 20 minutes, the tube is again cooled to room temperature and excess of bromine is removed by adding 10 to 12 drops of a 5 per cent. sodium thiosulphate solution. The solution is extracted with 6 ml. of light petroleum, the aqueous layer is blown out with the aid of a wash bottle head, a small amount of anhydrous sodium sulphate is added and the light petroleum extract is decanted off. A 5 ml. portion of the extract is shaken for 1 minute with 10 ml. of sodium sulphide solution (2 per cent.), the coloured aqueous layer is blown on to a funnel fitted with a dry filter-paper, and the absorption of the clear filtrate is measured in a suitable spectrophotometer using sodium sulphide solution as a solvent blank and determining a calibration curve in the usual way. For quantities of 0·02 to 0·2 mg. of citric acid the same procedure is followed except that the volume of the sodium sulphide solution extract is reduced. The calibration graph was a straight line and the standard deviation of an estimation was below 2 per cent.; a large number of substances of similar constitution did not interfere. For cerebro-spinal fluid (range 40 to 80μg./ml.) 1 volume is mixed with 30 per cent. trichloroacetic acid (0·1 vol.), and 1 to 3 ml. of the filtrate is analysed directly without further pre-treatment; for serum or plasma the protein is removed by treatment with 10 per cent. trichloroacetic acid solution; for normal urine no preliminary treatment is necessary and 1 to 5 ml. quantities diluted fivefold give satisfactory readings although protein, if present, must be removed with trichloroacetic acid. Recoveries of added citric acid were quantitative within experimental error. R. E. S.

Glucose, Microdetermination of. J. T. Park and M. J. Johnson. (*J. biol. Chem.*, 1949, **181,** 149.) A sensitive method for the estimation of glucose in quantities of 1 to 9 μg. is described, based on the ferricyanide reduction method. The sample, deproteinised and neutralised if necessary and containing 1 to 9 μg. of glucose, is placed in a test-tube and diluted to volume (1 to 3 ml. as desired); 1 ml. each of carbonate-cyanide solution (5·3 g. of sodium carbonate and 0·65 g. of potassium cyanide per l.) and of ferricyanide solution (0·5 g. of potassium ferricyanide per l.) is added and after mixing the tube is heated in a boiling water-bath for 15 minutes. 5 ml. of ferric iron solution (1·5 g. of ferric ammonium sulphate and 1 g. of Duponol in 1 l. of 0·05 N sulphuric acid) are mixed with the sample after cooling, and after 15 minutes the sample is then read against a reagent blank in a photoelectric colorimeter at 690 mμ., although any wave-length between 650 and 730 mμ. is suitable. Results are calculated after using a pure glucose sample as standard. In the final method adopted the quantities of reagents used were chosen to effect rapid reduction and colour development; without cyanide the reduction is only half completed in 15 minutes, but with 500 μg. or more of potassium cyanide it is complete in less than 15 minutes. The method is reproducible and the precision is such that over 90 per cent. of individual analyses of a known sample fall within 0·2 μg. of the expected result. R. E. S.

Hetrazan in Body Fluids, Estimation of. M. Lubran. (*Nature*, 1949, **164,** 1135.) In the estimation of hetrazan (1-dimethylcarbamyl-4-methyl

piperazine hydrochloride), blood serum or plasma, or other body fluid, is made strongly alkaline with one-fifth of its volume of 10N sodium hydroxide and extracted with twice to 3 times its volume of ethylene dichloride. The ethylene dichloride layer, after separation and filtration, is shaken for a few minutes with one-fifth of its volume (more may be required for urine) of 0·05 per cent. bromothymol blue solution in phosphate buffer at *p*H 7·0. The intensity of the yellow colour in the ethylene dichloride layer is compared with the colour produced by known amounts of hetrazan treated similarly. With low concentrations of hetrazan (1 μg./ml. or less) the ethylene dichloride is extracted with 2 ml. of N. sodium hydroxide and the blue colour compared with a standard, or alternatively a blue colour may be developed in the ethylene dichloride by addition of 0·1N alcoholic potash and sufficient ethyl alcohol to prevent turbidity. Blank values of the order of 1 μg./ml. are obtained with whole blood or with trichloracetic acid treated blood; urine shows a blank value of *ca.* 5 μg./ml. or occasionally, in concentrated urine up to 20 μg./ml. Although not specific for hetrazan the method is sufficiently sensitive to estimate 1 μg./ml. in blood. Results indicate that ingestion of 10 mg./kg. of body-weight of the hydrochloride causes a maximum plasma concentration of *ca.* 5 to 7 μg./ml. in 3 hours, the level falling slowly to zero in 24 hours, during which period about 20 per cent. of the drug is excreted in the urine. R. E. S

Paper Chromatography, Simplified Quantitative Procedures. R. J. Block. (*Proc. Soc. exp. Biol., N.Y.*, 1949, **72,** 337.) Two procedures are described as applied to the determination of amino acids in protein hydrolysates. The first method is based on the finding that the concentration of a coloured substance can be determined with reasonable accuracy from a paper chromatogram by ascertaining the product of the coloured area and the greatest colour density. In the second method the determination is made simply from the maximum colour density obtained on a two dimensional chromatogram. In the application of the first method to the determination of histidine and tyrosine, the substances are separated on the strip by a mixture of *n*-butyl alcohol, 100 parts, and glacial acetic acid, 10 parts, saturated with water. After running the chromatogram in air-tight chambers for 3 hours, the paper is dried, sprayed with diazotised sulphanilamide in butyl alcohol solution, again dried for 5 minutes, and sprayed with saturated sodium carbonate solution. The maximum colour densities are determined by an electronic densitometer and the factors for converting the product, area × colour density, into mg. of the substances are ascertained by submitting weighed amounts of the amino acids to the same procedure. By the second method it is possible to determine 14 amino acids on approximately 0·3 mg. of hydrolysate of a protein with the usual amino acid pattern with an average error of less than 10 per cent. and only 5 hours working time. The hydrolysate is diluted so as to contain about 1·5 to 10·0 millimols of each amino acid per ml. The paper is "spotted" with 0·005 to 0·01 ml. and the constituents separated by two-dimensional chromatography. The first solvent used is water-saturated phenol in an atmosphere of 0·3 per cent. ammonia, with moistened sodium cyanide and coal gas. The sheets are dried overnight before an electric fan and then developed at right angles to the original direction with a mixture of 2:6-lutedine, 55 per cent. v/v, alcohol (95 per cent.), 20 per cent. v/v and water 25 per cent. v/v, in an atmosphere of diethylamine and moistened sodium cyanide. The completed chromatograms are dried and then sprayed with 0·1 to 0·2 per cent. ninhydrin solution and heated to develop the colour. To prepare the standard, mixtures containing

1·25, 2·5, 5·0 and 10·0 millimols/ml. of each amino acid except cystine, tryptophan, proline and hydroxyproline are chromatographed at least 25 times; from the chromatograms the average maximum colour density of *all* the spots is determined by means of the electronic densitometer (the " mean colour density "), and also the average maximum colour density of each amino acid. The latter divided by the former gives the " standard colour ratio " of the individual acids. " Experimental colour ratios " are then determined in the same way for each amino acid on the two dimensional chromatogram of the unknown solution, and these figures divided by the appropriate " standard colour ratios " give " corrected experimental colour ratios " which are proportional to the molar ratios of the amino acids on the chromatogram. If one amino acid can therefore be determined by some other method, or if any acid is known to be absent a weighed quantity can be added to serve as an internal standard, the quantities of each can be ascertained. Methionine, histidine and tyrosine can be determined by specific procedures and thus serve as standards. With 25 replicate chromatograms the average error for a mixture of 14 amino acids simulating β-lactoglobulin was −2 per cent. in one series and −4 per cent. in a second. The method is believed to be applicable to all substances giving colours in paper chromatography.

H. T. B.

Sodium in Biological Fluids, Determination of. G. C. H. Stone and J. W. Goldzieher. (*J. biol. Chem.*, 1949, **181,** (2), 511.) A modification of the previous method (*J. clin. Endocrinol.*, 1949, **9,** 95) based on the Rosenheim-Daehr reaction, in which the uranyl ion in strongly alkaline solution is treated with hydrogen peroxide to produce a complex of intensely reddish yellow colour, is given. The spectrophotometric characteristics of the uranium complex, the influence of temperature on the reaction, the selection of optimum wave-length for measurement, and the accuracy, reproducibility, and recovery obtained were investigated. In the final method 9·0 ml. of 10 per cent. trichloroacetic acid is added to 1·0 ml. of serum, drop by drop, the mixture being shaken and centrifuged. To 1·0 ml. of the protein-free filtrate in a 15 ml. graduated centrifuge tube 6·0 ml. of the uranyl zinc acetate reagent is added. After standing for 20 minutes the tube is centrifuged at high speed for 7 minutes, the supernatant liquid is decanted, and the tube allowed to drain for 1 minute. 5 ml. of the wash reagent is added, the contents of the tube are mixed, and again centrifuged for 7 minutes, decanted and drained. The precipitate is dissolved in a few drops of distilled water and 6 ml. of ammonium carbonate solution is added followed by 1 ml. of 30 per cent. hydrogen peroxide, the volume being adjusted to 15·0 ml. with distilled water. After mixing the solution is examined spectrophotometrically at 460 mμ. as, although the peak absorption occurred below 400 mμ., better precision was obtained at the higher wave-length. As regards stability of the complex ion no detectable change in the colour intensity was observed at varying concentrations after 2 hours; the effect of temperature variation between 20° and 30°C. on the final colour was also negligible. Good recovery was obtained in experiments with known amounts of sodium and the accuracy of the method was considered to be within 1 per cent.

R. E. S.

Streptomycin, Spectrophotometric Method for Determination of. W. Eisenman and C. E. Bricker. (*Anal. Chem.*, 1949, **21,** 1507.) A streptomycin sample (not over 4 ml. in volume and containing between 50

and 2500 units of streptomycin) is pipetted into a glass-stoppered test tube; if the volume of solution taken is less than 4 ml., the sample is diluted with water to this volume. To the solution is added 1 ml. of 5N sodium hydroxide solution and the tube and its contents are heated in a boiling water bath for 3 minutes. After cooling to room temperature and adding 2 ml. of 5N sulphuric acid and 1 ml. of ammonium sulphate, the resulting solution is distilled and a total of 10·0 ml. of distillate is collected. A description of the distillation apparatus, the process being essentially one of steam distillation, is given and a modification in which a slow stream of compressed air is passed through the solution in place of the steam is also quoted. If the sample contains over 500 units of streptomycin, 1·0 ml. of ferric chloride solution (2 g. of $FeCl_3.6H_2O$ in 100 ml. of 2N hydrochloric acid) is added to the distillate and the colour produced is measured at 550 mμ. against 1·0 ml. of the same reagent added to 10·0 ml. of distilled water; if the sample contains less than 500 units, 1·0 ml. of phenol reagent is added to the distillate and the solution is allowed to stand for 1 to 2 minutes before adding 3·0 ml. of 20 per cent. sodium carbonate solution. The optical density of this solution is measured at 775 mμ, against a reagent blank. From calibration curves prepared from known amounts of streptomycin and with both reagents, the number of units of streptomycin in the sample can readily be calculated. Results obtained with several impure solutions which were analysed by the maltol distillation method and by a biological assay method are given. The solutions differed widely in composition and were believed to contain relatively small amounts of mannosidostreptomycin; with one exception the values from the chemical procedure agreed to within less than 10 per cent. with those obtained by the biological method. The slightly higher values from the chemical method were considered to be due either to the presence of a small amount of mannosidostreptomycin or to inaccuracies of the biological method. Several broths of comparatively low activity were examined using both the ferric chloride and phenol reagents, the results with these two reagents agreeing to within 3 per cent. in all cases. If the phenol reagent is used samples with an activity as low as 10 units/ml. can be analysed. R. E. S.

Vitamin A, Determination of. D. Verhagen and R. W. Parent (*Anal. Chem.*, 1949, **21**, 1584.) A simplified method for the determination of vitamin A in the unsaponifiable fraction of fish liver oils is reported. The oil (0·1 to 0·25 g., depending on potency) is weighed into a test tube, 0·6 ml. of 50 per cent. potassium hydroxide solution and 6 ml. of alcohol are added and the mixture is refluxed on a steam bath under an air condenser for 15 minutes or until the oil is completely dissolved. The condenser is removed and the alcohol evaporated under vacuum with nitrogen. As soon as the solvent is removed about 20 ml. of 1·5 per cent. barium chloride solution saturated with chloroform is added, the mixture is allowed to cool and exactly 20 ml. of water-washed chloroform added. After shaking this mixture thoroughly and centrifuging until the chloroform layer is clear or nearly so (the barium soaps will form a layer at the interface) 10 ml. of the chloroform solution is pipetted into an amber or red volumetric flask. For an ultraviolet absorption determination 0·3 ml. of isopropyl alcohol is added and the mixture is evaporated to dryness under a stream of nitrogen. As soon as the last of the solvent has been removed, the flask is filled to its mark with isopropyl alcohol at room temperature and, if after standing for an additional period of 1 to 2 minutes the solution is cloudy, it is centrifuged.

For a Carr-Price determination a chloroform aliquot may be dried by the addition of a few grains of sodium sulphate and then used directly. When compared with the current method slightly greater recovery and better precision were obtained. It is not thought that the greater recovery was due to failure to remove extraneous absorbing materials as the absorption curves in the range 300 to 350 mμ were essentially identical. R. E. S.

PHARMACOLOGY AND THERAPEUTICS

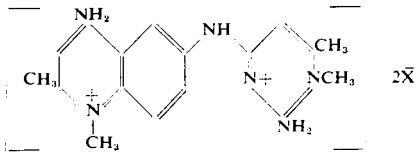
norAdrenaline, Action of. J. H. Burn and D. E. Hutcheon. (*Brit. J. Pharmacol.*, 1949, **4**, 373.) An important difference between the vascular action of noradrenaline and adrenaline is that the former causes constriction whereas the latter causes dilatation of the denervated hind limb of the cat, the difference being in the muscle vessels. Like adrenaline, noradrenaline dilates the coronary vessels of the cat and dog and, in small doses, the intestinal vessels. In the vessels of the rabbit ear the constrictor action of noradrenaline is as easily converted to a dilator action by 2-benzylimidazoline as is that of adrenaline. Denervation increases the action of noradrenaline on the nictitating membrane and on the pupil much more than it increases that of adrenaline. norAdrenaline causes contraction of the spleen *in situ*. It has a smaller constrictor action on renal blood flow than adrenaline; it inhibits intestinal movements recorded by a balloon in the duodenum; it has the same effect as adrenaline on skeletal muscle previously treated with neostigmine; and it has much less effect than adrenaline in dilating the bronchioles. S. L. W.

norAdrenaline; Assay of Substances from the Adrenal Medulla. J. H. Gaddum and F. Lembeck. (*Brit. J. Pharmacol.*, 1949, **4**, 401.) The concentrations of both adrenaline and noradrenaline in a mixture of these drugs can be roughly determined by parallel quantitative assays on the rat uterus and colon. The results may be misleading unless they are analysed statistically. The method used was based on that of Jalon, Bayo and Jalon. Rat's uterus or colon is suspended in a solution of the following composition (g./l): sodium chloride 9, potassium chloride 0·42, calcium chloride 0·06, sodium bicarbonate 0·2, glucose 0·5 at 30°C. Contractions are produced every 2 minutes by a choline ester, and the assay depends on the inhibition of these contractions by adrenaline or noradrenaline. Extracts of cats' adrenals, and plasma collected from the cat's adrenal veins during stimulation of the splanchnic nerves, were both shown to contain some other substance besides adrenaline. The results confirmed that this was noradrenaline and gave an estimate of the amount. S. L. W.

***p*-Aminobenzoic Acid and Thiouracil Compounds, a Comparison of the Anti-thyroid Activity of.** J. F. Goodwin, H. Miller and E. J. Wayne. (*Lancet*, 1949, **257**, 1211.) In a clinical trial of 10 thyrotoxic patients treated with *p*-aminobenzoic acid, 6 did not respond at all and in only one case was full control obtained. When 8 of these patients were treated with the thiouracil compounds, 2 did not respond and full control was obtained in 3 cases. The authors also compared the relative potencies of *p*-aminobenzoic acid and methylthiouracil in humans with normal thyroid function, by means of a tracer dose of radioactive iodine. Results showed that a single dose of 200 to 300 mg. of methylthiouracil was substantially

more effective in reducing the iodine uptake in the normal thyroid than a single dose of 4 g. of *p*-aminobenzoic acid. It is concluded that *p*-aminobenzoic acid has a slight but definite anti-thyroid action in safe dosage (4 g. a day). Other clinical evidence shows potentially serious side effects in larger doses; but to obtain an action comparable to that of the thiouracil group, toxic doses would be needed. E. N. I.

Antrycide, a new Trypanocidal Drug. F. H. S. Curd and D. G. Davey (*Brit. J. Pharmacol.*, 1950, **5**, 25.) Antrycide has the following constitution, where X is an anion :—



Four salts of antrycide have been prepared, the dibromide (m.pt. 316°C.), the dichloride (m.pt. 316°C.), the di-iodide (m.pt. 312°C.), and the dimethylsulphate (m.pt. 265 to 266°C.). They are white crystalline solids. The halides are sparingly soluble in water but the methylsulphate is readily soluble (up to about 33 per cent.). Toxicity, therapeutic and prophylactic experiments were conducted on mice, employing the chloride and the methylsulphate by subcutaneous injection. Absorption of the two salts, after subcutaneous injection, appears to be directly related to their solubility; a suspension of the chloride is absorbed slowly and a solution of the methylsulphate rapidly. A table is given showing the curative properties of antrycide in mice infected with various species of trypanosomes. It is most active against *T. congolense, T. evansi, T. equinum* and *T. equiperdum*. but also exhibits marked activity against *T. brucei, T. rhodesiense* and *T. gambiense*. No activity has been observed against *T. cruzi*. The substance may be used to protect mice for several weeks against *T. congolense*. The prophylactic properties of antrycide are shown to be due for the most part to the establishment of a reservoir of the drug beneath the skin from which absorption takes place slowly, and not to persistence of the drug in the body in the usually accepted sense of the term. S. L. W.

Aspirin, Enteric-coated, Value of. R. H. Talkov, M. W. Ropes and W. Bauer. (*New Engl. J. Med.*, 1950, **242**, 19.) On the administration of freshly prepared enteric-coated aspirin tablets to 32 patients, the analgesic effect was equal to that of ordinary aspirin, and the onset of action was only slightly delayed. Its use is specially indicated where ingestion of ordinary aspirin, in regular dosage, gives rise to gastric symptoms of local origin. Substitution by enteric-coated aspirin causes these symptoms to disappear. It is of value when maximal doses are required to control pain and in patients suffering with peptic ulcers and hæmorrhagic gastritis. E. N. I.

Chloramphenicol in Infantile Gastro-enteritis. K. B. Rogers, S. J. Koegler and J. Gerrard. (*Brit. med. J.*, 1949, **2**, 1501.) Previous authors have noted a close correlation between the same serologically specific type of *Bacterium coli* and epidemic infantile gastro-enteritis. The appearance of the organism has been studied in 86 infants under 1 year old, rectal swabs being taken on admission, and 5 days later, also if a case of gastro-enteritis appeared in the ward. The time between first isolation of

the organism and development of gastro-intestinal disturbance was calculated in 17 cases; it varied from 4 to 24 days with an average of 11. In 25 of the 86 infants, isolation of the organism was not followed by gastro-intestinal symptoms; of the remaining 61 infants, 13 died. Pencillin and sulphonamides and streptomycin were virtually without effect, although they helped to control parenteral infections such as otitis media; some infants developed the disease while actually receiving the medicaments. Chloramphenicol gave highly encouraging results. The average time to effect clearance of the organism was 4 days (range 2 to 8 days). In 2 cases, the organism reappeared in 1 and 7 days after cessation of treatment, but it was still sensitive to the drug; this may have been due to reinfection. Dosage was 75 mg./lb. of body weight per day in 6 or 8 divided doses, the material being removed from the capsules and given as a raspberry-flavoured suspension with tragacanth; the initial dose was twice the maintenance dose. The stools occasionally became coloured bright green. Four infants developed dermatitis, but it is not certain that the drug was responsible. No other toxic reactions were noted, blood and urine examinations giving normal results. This particular strain of *Bact. coli* was sensitive to 2 to 4 μg./ml. of antibiotic; no change in sensitivity occurred during treatment. Blood levels of up to 120 μg./ml. were obtained. H. T. B.

Chloromycetin; Antitreponemal Effect in Early Syphilis. M. J. Romansky, S. Olansky, S. R. Taggart and E. D. Robin. (*Science*, 1949, **110,** 639.) A series of 24 patients with early syphilis was treated with oral chloromycetin 30 mg./kg./day for 4, 6 or 8 days. The lesions in all cases showed evidence of initial healing within 24 hours and most of them showed complete healing by the end of the therapy. Quantitative serological tests were performed prior to therapy and at monthly intervals after treatment. There was a rapid decline in the serological titre in most cases at the end of one month following treatment. Chloromycetin seems to promote healing by a different process from penicillin; penicillin produces healing at the periphery of a lesion whereas healing with chloromycetin seems to be initiated from the base. The only toxic or outward reactions noticed with this series were an occasional mild diarrhœa and an occasional complaint of dryness of the mouth. Several patients complained of a generalised aching sensation 48 hours after the beginning of treatment but no fever or eruptions were noted. Since relatively small doses of chloromycetin will cure gonorrhœa, attention should be called to the possible danger of masking the diagnosis of syphilis. S. L. W.

Curarising Activity, Antagonism of Phenolic Substances. G. A. Mogey and P. A. Young (*Brit. J. Pharmacol.*, 1949, **4,** 359.) This investigation was undertaken in view of the finding that the use of *p*-chloro-*m*-cresol as a bacteriostatic agent in solutions of *d*-tubocurarine has an antagonistic action on the curarising activity. Observations on a series of hydroxy-derivatives of benzene showed them to antagonise the action of *d*-tubocurarine on the rat diaphragm. The relative potencies of the members of the series were expressed as the concentration of antagonist which reduced by half the effect of a concentration of *d*-tubocurarine which alone would cause two-thirds paralysis. The following antagonists were investigated: catechol, *p*-chlorophenol, *o*-cresol, *o*-chlorophenol, *m*-cresol, phenol, *p*-cresol, resorcinol, hydroquinone, guaiacol, and phloroglucinol, and it was found that there was a distinct fall of potency down the series in the order indicated, the last three substances being relatively inactive. The antagonism was

shown not to be due to cholinesterase inhibition or alteration of *p*H: neither was it thought to be due to a chemical combination of antagonist with *d*-tubocurarine. The authors suggest that there is attraction between phenols and proteins, causing steric hindrance. S. L. W.

Decamethonium Iodide and Related Compounds, Pharmacological Actions of. W. D. M. Paton and E. J. Zaimis. (*Brit. J. Pharmacol.*, 1949, **4,** 381.) The pharmacological actions of a series of polymethylene bistrimethylammonium salts, containing from 2 to 18 carbon atoms in the polymethylene chain, have been studied chiefly in regard to their activity in blocking neuromuscular transmission. C10 is the most active compound in causing neuromuscular block in the chloralosed cat, but the excitability of nerve and muscle is retained. Unlike *d*-tubocurarine, C10 can produce profound neuromuscular block without causing respiratory paralysis. The compound by mouth has 1/50 to 1/100 of the activity by intravenous injection. The order of decreasing sensitivity is cat, man, rabbit, monkey, mouse, rat, the variation being greater than with *d*-tubocurarine. C5 and C6 are effective antagonists, probably acting by competitive inhibition; previous administration of *d*-tubocurarine also reduces the effect of C10. Ganglionic transmission is blocked particularly by C5 and C6, higher and lower members of the series having a smaller activity. There is a less well-defined maximum for muscarine-like activity and anticholinesterase activity at C12. No member of the series shows any significant atropine-like activity or ability to stimulate autonomic ganglia. H. T. B.

Digitalis Glycosides, Influence of Saponins on Toxicity of. F. Neuwald and G. Zöllner. (*Arch. Pharm., Berl.*, 1950, **283,** 26.) Digitalis leaves, containing about 0·1 per cent. of total glycosides (determined chemically) should have an activity of 2 cat units/g Actually however the value found was about 10 units/g. It has also been observed that the clinical activity of digitalis is only one-fifth that of digitoxin, if doses of equivalent cat units are given. In order to determine whether this difference was due to the effect of digitalis saponins, determinations of M.L.D. were made with and without the addition of saponins in similar proportion to that of the leaf. The administration, both to cats and guinea-pigs, was intravenous. No significant differences were found, either with digitoxin-digitonin or with lanadigin-tigonin. Thus it appears that the toxicity of digitalis glycosides is not increased by the presence of the saponins of the leaf.

G. M.

Digitoxin. Renal Excretion Following Oral Administration. M. Friedman, S. O. Byers, R. Bine, Jr., and C. Bland. (*Proc. Soc. exp. Biol., N.Y.*, 1949, **72,** 468.) The sensitivity of the embryonic duck heart preparation (Bine and Friedman, *Proc. Soc. exp. Biol., N.Y.*, 1948, **69,** 487) to minute amounts of digitalis glycosides in Tyrode's solution and human serum suggested the possibility of determining the urinary excretion of digitoxin. To extract the excreted glycoside, 200 ml. of urine was evaporated to 5 ml. which was absorbed by diatomite and dried. This powder was then extracted with chloroform and the dried chloroformic extract further extracted with ethyl alcohol, the final residue being taken up in Tyrode's solution. By adding known amounts of pure digitoxin to normal urine and extracting as above, it was found that the time of occurrence of the "digitalis effect" in the duck hearts was dependent upon the amount added. Five subjects received 1·2 mg. of digitoxin orally during 6 hours: the

urine was collected and a 200 ml. aliquot assayed. The rate of excretion varied considerably. During the first 24 hours, an average of 87 μg. was excreted (range, 44 to 144 μg.). During the second and third days, the average weights excreted were 55 μg. and 21 μg. respectively, the average total excretion being about 14 per cent. of the amount administered.

H. T. B.

Dimercaprol, Effect of, on Lead Poisoning in Mice. A. B. Anderson. (*Brit. J. Pharmacol.*, 1949, **4**, 348.) Lead acetate marked with a tracer of Pb^{210} (radium D) was given with a low calcium diet to mice, and after varying periods the lead content of the whole animal was determined by chemical analysis and count of β radiation. The lead content of mice which had received 50 mg./kg. of dimercaprol daily, and lead simultaneously for 10 to 14 days, averaged 0·48 mg. Pb/100 g. of mouse, and was significantly lower than that of controls receiving lead alone, which averaged 1·0 mg. Pb/100 g. When lead alone was administered for 8 to 10 days, subsequent treatment with dimercaprol during a recovery period of 1 to 2 weeks had no significant effect on the final lead content. The author concludes that these results provide no indications for the use of dimercaprol in the treatment of chronic lead poisoning.

S. L. W.

Morphine: Response of Duodenum. T. A. Loomis. (*Proc. Soc. exp. Biol., N.Y.*, 1948, **69**, 146.) Although the earliest investigations of the effect of morphine on intestinal muscle suggested that it produced relaxation, more recent investigations using balloon methods have indicated that the drug produces increased pressure and increased movements of various segments. In view of the possibility that erroneous conclusions may be drawn from the results of balloon experiments the action of morphine on a given segment of the duodenum in the intact anæsthetised dog has been investigated by a method giving simultaneous graphic recordings of both circular and longitudinal muscle activity. Circular contractions were recorded by means of a balloon not more than 2 cm. long which when fully expanded would come into contact with about 1 cm. length of intestinal mucosa. This gave no response to longitudinal movements. Longitudinal movements were recorded by the internal organ apparatus of Jackson (Experimental Pharmacology and Therapeutics, C. V. Mosby Co., 1939, page 89). The balloon was inserted in the duodenum through an incision in the stomach under pentobarbital anæsthesia and the Jackson apparatus was sutured to the mucosal surface of the same segment of the duodenum. All injections were given intravenously, the volume being always less than 5 ml. It was found that repeated equal doses of morphine did not produce equivalent responses and only one dose of the drug was therefore given. Doses of 0·01 to 1·0 mg./kg. body weight were used. The smallest dose consistently effective in altering muscular activity was 0·05 mg./kg. In 17 experiments on as many different animals doses of 0·1 mg./kg. elicited a response by the circular muscle in 16 animals but in 13 animals there was either no response by the longitudinal muscle or a decrease in activity. When the dose was increased to 0·5 mg./kg. all the animals showed increased activity of the circular muscle while in 15 there was either no response or decreased activity in the longitudinal muscle. With 1 mg./kg. a decreased activity in the longitudinal muscle was recorded in 5 out of 6 animals. The increased activity consisted of an increased level of tonus with either an increase or no change in the frequency and amplitude of normal spontaneous contractions. Decreased activity consisted of a

decreased level of tonus with either a decrease or no change in the frequency and amplitude. H. T. B.

Thiouracil and Propylthiouracil, Effect of Halides on Action of. R. H. Williams, H. Jaffe and B. Soloman. (*Amer. J. med. Sci.*, 1950, **219**, 1.) Both thiouracil and radioactive iodine have been observed to produce a slower clinical response if the patients have just been treated with potassium iodide for several weeks. It therefore seemed possible that the effectiveness of these treatments might be increased by first reducing the body store of iodine to subnormal levels. The effect of sodium chloride, bromide and fluoride on the goitrogenesis produced in rats by thiouracil and propylthiouracil was therefore investigated, on the hypotheses that non-iodide halides might reduce the body iodine level and that they might antagonise the synthesis of thyroid hormone. Male rats received the halide in their food in weighed amounts; some received thiouracil and propyl-thiouracil in their drinking water, dissolved with the aid of sodium hydroxide. The animals were killed after 12 days and the thyroid glands removed and weighed. All three halides increased goitrogenesis of the uracil compounds, the chloride being least active and the fluoride most active. Concentrations of the uracil compounds too small to produce goitre alone produced it when the halides were given simultaneously, although the latter alone gave no such effect. It is suggested that the action may be due, in part, to competition of the halide anions for reabsorption by the renal tubules, thus increasing the rate of excretion of iodide. On the basis of these experiments, clinical trial with sodium bromide is suggested.

H. T. B.

Vitamin B_{12} and Thyroid Function. E. J. Wayne, A. G. Macgregor and H. Miller. (*Lancet*, 1950, **258**, 327.) Patients receiving liver therapy for pernicious anæmia sometimes develop hyper-thyroidism. On the other hand, if patients receiving thyroid treatment for hypothyroidism develop pernicious anæmia and liver extract is administered, the dose of dried thyroid must be increased. For this reason the existence of a specific antithyroid principle in liver has been postulated and the effect of vitamin B_{12} on thyroid activity was therefore investigated using radioactive iodine. Doses of 60 μg. and 100 μg. respectively of vitamin B_{12} were given to two normal patients when iodine accumulation in their thyroid glands was proceeding at a steady rate. No effect whatever could be demonstrated and it was concluded that in the doses used vitamin B_{12} has no significant influence on thyroid function. H. T. B.

Vitamin C: Effect on Wound Healing. J. R. Penney and B. M. Balfour. (*J. Path. Bact.*, 1949, **61**, 171.) The effects of vitamin C on the healing of wounds was investigated in guinea-pigs. Muscle wounds were inflicted, and, at intervals thereafter, the animals were killed by stunning and bleeding and the wounds examined microscopically. The presence of acid mucopolysaccharide esters was shown by the production of meta-chromasia with toluidine blue. In animals receiving adequate vitamin C, the initial stage of the healing process, consisting of the invasion of the clot by fibroblasts, could be seen in 4 days. As the process continued, there was close correlation between the distribution of newly formed fibres and extracellular metachromasia with toluidine blue. In depleted animals, some slight fibroblastic invasion occurred, but the cells were very abnormal

(*Continued on page 536*)