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.) *Correction*: In the abstract on page 519 of this Journal the statement that " results are up to 50 per cent. too high " is incorrect, and is due to a misreading of the heading of the table in the original paper. The whole of the last sentence of this abstract should be deleted. C. H. H.

Alkaloids, Partition Chromatography of. R. Munier and M. Macheboeuf. (*Bull. Soc. Chim. biol.*, 1949, **31**, 1144.) Partition chromatography of various alkaloids and alkaloidal bases has been studied; the technique is applicable if widely differing conditions of *p*H and development are used. In developing the spots obtained on filter-paper strip chromatograms, various reagents were tried. Ultra-violet light was useful and out of 44 alkaloids studied, cinchonine, quinidine, quinine, cinchonidine, narcotine, cotarnine, hydrastinine, boldine, berberine, corynantheine, chelidonine, papaverine, and piperine were detectable in amounts of less than 20μg.; iodine vapour could be used for mescaline, hordenine and ephedrine; iodine in potassium iodide solution gave a brown colour with many alkaloids. Dragendorff's reagent detected 0·2μg. of hyoscyamine and larger amounts of berberine, yohimbine, trigonelline, theobromine, theophylline, nicotinamide and betaine, although caffeine only showed in amounts of 50μg.; nicotine, sparteine, hydrastinine and cotarnine were red while the colour of the other alkaloids ranged from yellow to orange with this reagent. Potassium iodoplatinate showed up spots due to yohimbine, ephedrine, hydrastinine, trigonelline, hordenine, and nicotinamide in quantities from 10 to 20μg. Phosphomolybdic acid treatment followed by washing with water and reduction with stannous chloride solution was useful in detecting 20μg. of cicutine and mescaline although betaine, trigonelline, caffeine, theobromine, theophylline and nicotinamide gave negative results; phosphomolybdic acid solution alone showed up caffeine, theobromine, theophylline and trigonelline. A description of a chromatographic technique similar to that of Consden, Gordon and Martin is given; using this method boldine, sparteine, berberine, chelonidine, hydrastinine and cotarnine were run as bases dissolved in 20μg. amounts in chloroform; for the solvent phase, toluene, glycol, monochlorhydrin and ammonia were used. Caffeine, theobromine, theophylline, trigonelline and ephedrine could also be separated in an alkaline medium. Morphine, thebaine and codeine were run in acid medium as the free base while other examples are given of alkaloids run in acid medium as the salt. Detailed conditions of procedure are given together with diagrammatic representations of the developed chromatograms. R. E. S

Digitalis Glycosides ; Modified Bell and Krantz Method for the Assay of. E. E. Kennedy. (*J. Amer. pharm. Ass., Sci. Ed.*, 1950, **39**, 25.) The following method is applicable to the assay of digitoxin, digoxin and lanatoside C. 10ml. of a methyl alcoholic solution of the glycoside containing about 0·4mg./ml. is mixed with 15ml. of picrate reagent and allowed to stand for exactly 30

minutes. The optical density of the mixture is read on a suitable spectrophotometer using 1-cm. cells at 495mμ and the amount of glycoside calculated from the standard graph. A blank consisting of a mixture of 10ml. of methyl alcohol and 15ml. of picrate reagent is used as a comparison solution. The picrate reagent is prepared by dissolving 1g. of trinitrophenol in 15ml. of methyl alcohol, adding 20ml. of a 10 per cent. solution of tetra-ethylammonium hydroxide and diluting to a 100ml. with water ; it should be freshly prepared. The standard graph is prepared by measuring the optical densities of solutions containing 0·2, 0·4, 0·6 and 0·8mg. of the appropriate reference standard in 10ml. of methyl alcohol treated in the same manner as the test solution. By reading the optical density at 495mμ instead of 525mμ the sensitivity of the method is increased two and a half times. The accuracy of the method is within 2 per cent. of the amount of glycoside present. G. R. K.

Fat Analysis; A Micro-method based on the Formation of Monolayer Films. K. K. Jones. (*Science,* 1950, **111,** 9.) Droplets of piston oil are placed on the cleaned surface of 0·3 per cent. sulphuric acid contained in a glass dish coated with hard paraffin, until the colour of the surface is green. The fat to be estimated is extracted from the original material and used as a solution in light petroleum. An aliquot portion of this solution is placed by means of a capillary pipette on the centre of the oil surface. The light petroleum evaporates, and the fat spreads against the piston oil until equilibrium is established. The area occupied by the fat is measured, and is a sensitive criterion of the amount of fat present; the conversion factor depends upon the constitution of the fat under examination.

G. R. K.

Imidazoline Derivatives, Identity Reaction of. H. Laubie. (*Bull. Trav. Soc. Pharm., Bordeaux,* 1950, **88,** 65.) To 1 ml. of a solution containing about 1 μg. of the compound, add 0.3 ml. of 5 per cent. solution of sodium nitroprusside and 0·5 ml. of N sodium hydroxide, then buffer the solution by the addition of 1 g. of sodium bicarbonate. After a few minutes the brownish-green colour changes to a violet. It has been shown that penicillin, at *p*H2, gives rise to a compound containing an imidazol nucleus; this compound however gives only a weak orange red colour after several hours. G. M.

Iodine and Bromine in Organic Compounds, Determination of. O. Michel and G. Deltour. (*Bull. Soc. Chim. biol.,* 1949, **31,** 1125.) A technique is described which allows the determination of from 100 to 500 μg. of iodine, and from 50 to 500 μg. of bromine simultaneously in an organic compound, with an approximate error of ±4 per cent. To the organic substance, containing about 200 μg. of iodine, is added a small amount of sodium arsenite solution and the resulting mixture is heated to redness in a nickel crucible. On cooling the residue is dissolved quantitatively in 10 ml. amounts of warm distilled water, transferred to a suitable vessel and acidified with 5N sulphuric acid to congo red. 1 ml. of sodium nitrite solution (5 per cent.) is added and the resulting product is extracted with 5, 3 and 2ml. quantities of carbon disulphide. The carbon disulphide solution is separated, centrifuged to free from suspended material, and the depth of the violet colour is measured on a suitable spectrophotometer using as comparison solution a blank prepared in the same way as the test solution but without the iodine. In the case of compounds containing bromine and iodine the colour

due to bromine does not interfere with the above procedure. The estimation of bromine in compounds containing bromine and iodine follows the method of Leipert and Watzlawek (*Hoppe-Seyl. Z.*, 1934, **226,** 108) in which the substance is heated for 12 hours in a sealed tube at 100°C. with 5N sulphuric acid; the solution resulting from this method is divided into two parts. One part gives the total bromine following the method of Leipert and Watzlawek and includes some of the iodine; the other part is used for a determination of the iodine by the sodium arsenite method. The iodine result obtained in the second estimation is subtracted from the result (bromine plus iodine) obtained in the first estimation, to give the true bromine content. Recovery experiments on di-iodotyrosine, dibromotyrosine and known mixtures of these two compounds gave satisfactory results. R. E. S.

Phenolphthalein in Mineral Oil Emulsion, Determination of. A. T. Warner, J. E. Logun and R. L. Thatcher. (*J. Amer. pharm. Ass., Sci. Ed.*, 1950, **39,** 10.) About 10 ml. of the emulsion is shaken with two 30-ml. and four 20-ml. quantities of a 25 per cent. solution of sodium chloride containing 0·25 per cent. of hydrochloric acid. The aqueous layers are filtered, the filter paper washed and placed in a 500-ml. flask, to which is added the oily layer from the separating funnel, previously mixed with 30 ml. of sodium hydroxide solution. The funnel is washed with water and the washings are also added to the flask followed by 50 ml. of 0·1N iodine. The flask is stoppered and shaken until the mixture becomes white with a greenish-yellow tint, when 15ml. of hydrochloric acid is added and the excess of iodine titrated with 0·1N sodium thiosulphate ; each ml. of 0·1N sodium thiosulphate is equivalent to 0·003979g. of phenolphthalein. G. R. K.

Water in Glycols and Glycerol, Determination of. C. B. Jordan and V. O. Hatch. (*Anal. Chem.*, 1950, **22,** 177.) A method is described for determining the percentage of water in samples or solutions of glycols and glycerol, based on reflux distillation and salting out and using *n*-butyl alcohol as the refluxing medium, since it forms an azeotrope with water but not with glycol or glycerol and is capable of breaking any hydrates formed in aqueous glycol solutions. The sample under test is placed in a flask fitted with a side-inlet for a thermometer and a Dean and Stark (Barrett type) receiver trap with a water condenser having a calcium chloride tube inserted at the top; *n*-butyl alcohol (b.pt. 238° to 243°F.) is added and the flask is heated slowly until boiling is steady. For samples containing large percentages of water it is necessary to withdraw small portions of water from the trap at regular intervals; after 2·5 hours refluxing the volume of the lower layer in the trap is checked at 20 minute intervals and if there is no visible change in volume the water layer is withdrawn and the heating is increased up to a temperature 3°F. below the boiling point of the butyl alcohol. All the butyl alcohol and water now distilled from the flask is mixed in a measuring cylinder, the volume is recorded, anhydrous potassium carbonate is added and the volume of the top butyl alcohol layer is noted; further potassium carbonate is added until there is no increase in the volume of the alcoholic layer; this volume subtracted from the total distillate volume gives the amount of water present. For aqueous mixtures of glycols or polyhydric alcohols of unknown boiling-point the above procedure can be used with modification; after the 2·5-hour refluxing, or at the time when no increase in the water layer is noticed, the water layer is removed from the trap, the distillation is continued to 350°F., the whole of the liquid is withdrawn from the trap and salted out as

before. 40 samples of known composition, varying in water content from 1 to 95 per cent., were analysed with a maximum error of 0·5ml. on 100ml. quantities. The method was applicable to antifreeze solutions, mixtures of glycols and glycol-ethers and *n*-butyl alcohol and alcohols containing more than 4 carbon atoms. R. E. S.

Yohimbine, Quantitative Reaction for. L. S. Malowan. (*Analyst*, 1950, **75**, 338.) Dimethylaminobenzaldehyde gives coloured compounds with a series of indole derivatives in the presence of mineral acids which can be transformed to blue compounds in the presence of weak oxidants such as hydrogen peroxide or nitrous acid; yohimbine also gives this reaction. Dissolve a small amount of the alkaloid in about 1 ml. of concentrated hydrochloric acid. Add 4 drops of a 2 per cent. solution of *p*-dimethylaminobenzaldehyde in concentrated hydrochloric acid and warm. Add 2 drops of a 0·05 per cent. solution of sodium nitrite to the colourless test liquid. In the presence of yohimbine, a deep violet-blue ring appears after a short time and on shaking gently the whole solution becomes deep blue. 1 mg. of yohimbine gives a distinct reaction and tablets containing yohimbine can be treated in the same way, with the same result. R. E. S.

ORGANIC CHEMISTRY

Aldehydes, Direct Chlorination of. H. Guinot and G. Tabuteau. (*C.R. Acad. Sci., Paris*, 1950, **231**, 234.) Aliphatic aldehydes can be chlorinated, with a good yield of α-derivatives, by the direct action of chlorine in strongly hydrochloric acid solution. Under these conditions the oxidising action of the chlorine is greatly reduced, while substitution proceeds at a low temperature, thus avoiding condensation reactions. With acetaldehyde at a concentration of 4·5N, and 7N hydrochloric acid, formation of monochloracetaldehyde occurs at 18° to 20°C. In order to obtain the dichlorinated product a temperature of 35° to 40°C. is necessary, while, to obtain chloral, the temperature must be raised first to 80°C., the reaction being finished at 90°C. under reflux. The same method may also be applied to paraldehyde, yields of more than 90 per cent. of the various chloracetaldehydes being obtained. The reaction mixture may be separated either by fractionation at reduced pressure, or by extraction with ether. With *n*. propionaldehyde, a temperature of 15°C. gives the monochlorinated product; 30°C. gives α-dichloropropionic aldehyde. No further substitution is attained even at the boiling-point of the mixture. With *iso*propionic aldehyde, 20° to 25°C. gives the mono-derivatives, but no higher derivatives are obtained. G. M.

Curcumin and Curcuminoids. T. Pavolini, F. Gambarin and A. M. Grinzato. (*Ann. Chim. applic., Roma*, 1950, **40**, 280.) Curcumin, the yellow principle from turmeric, can be prepared by fusing acetylacetone with vanillic aldehyde and boric anhydride. The purified product melts at 178° to 180°C. A brown substance which the authors call curcumin brown is also obtained. Made in this way the product gives the characteristic red colour with boric acid and sodium hydroxide, whereas when the condensation is carried out with hydrochloric acid as in Heller's method α and β *iso*-curcumins are obtained which do not give colours with boric acid. Curcumin proper is the keto-enolic form while the *iso*-curcumins are the di-ketonic and di-enolic forms, there are also *cis* and *trans* forms known as rubro-curcumin and

roso-cyanin. By the same reaction the authors have prepared similar compounds from other aromatic aldehydes, which they call curcuminoids. From piperonylic aldehyde, dipiperonylacriloymethane (m.pt. 190° to 195°C.); from cinnamic aldehyde, dicinnamylacriloylmethane (m.pt. 189° to 190°C.), from benzoylacetone and vanillic aldehyde, benzoylfuroylmethane (m.pt. 152°C.); from cinnamoylacetone and vanillic aldehyde, cinnamoylferuloylmethane (m.pt. 137° to 140°C.); from acetylacetone and salicylic aldehyde, dicumaroylmethane in very small yield. H. D.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Adrenal Cortical Hormones, Synthetic Analogues of. G. P. Hager and R. M. Burgison. (*J. Amer. pharm. Ass., Sci. Ed.*, 1950, **39**, 7.) 4 : 4′-bis-(Acetoxyacetyl)-$\alpha\alpha'$-diethylstilbene, $(CH_3.CO.O.CH_2.CO.C_6H_4.C(C_2H_5) :)_2$, was prepared from *p*-bromopropiophenone in the following way. *p*-Bromopropiophenone was converted to the hydrazone by heating with 85 per cent. hydrazine hydrate, with simultaneous removal of water, and the hydrazone oxidised with freshly precipitated mercuric oxide to *p*-bromophenyl ethyl diazomethane, which was converted to 4 : 4-dibromo-$\alpha\alpha'$-diethylstilbene by treatment with sulphur dioxide and heating the sulphone so formed. The *trans* and *cis* isomers of 4 : 4′-dibromo-$\alpha\alpha'$-diethylstilbene were obtained separately in yields of 52 and 16·8 per cent. respectively. The *trans* isomer was converted by way of the dicyanide, dicarboxylic acid, and di-acid chloride to the diazoacetyl compound, which was finally treated with glacial acetic acid and acetic anhydride to give the required product in 34 per cent. yield. G. R. K.

Chloromycetin, and Serine Derivatives, Analagous action of. C. Mentzer, P. Meunier, L. Molho-Lacroix and D. Billet. (*Bull. Soc. Chim. Biol.*, 1950, **32**, 55.) Chloromycetin may be considered as a derivative of *d*-serine, and it has already been shown that *d*-serine (but not *l*-serine) retards the growth of *E. coli*, while *l*-aspartic acid increases this inhibitory action and aminoacetic acid or dl-alanine annul it. The authors have now shown that similar effects are observed with chloromycetin as with *dl*-serine. *dl*-Phenylserine also has an inhibitory action on *E. coli*, but its behaviour in presence of the other amino acids indicates that its biological action is farther removed from that of chloromycetin than is that of *dl*-serine itself. G. M.

Dihydrostreptomycin Base, Crystalline. H. W. Rhodehamel Jr., S. L. McCormick and S. F. Kern. (*Science*, 1950, **111**, 233.) Dihydrostreptomycin base may be obtained by treatment of relatively pure dihydrostreptomycin sulphate with a strongly basic ion-exchange resin (for example, Amberlite IRA-400) or by titration with barium hydroxide solution to *p*H 12, and precipitation from the aqueous solution with acetone. The oily precipitate gradually crystallises in needles with some tendency to cluster in rosettes. Analysis for elements is in agreement with the formula $C_{21}H_{41}O_{12}N_7,H_2O$, and the product has the following characters:—chars at 240°C. and turns black without melting up to 300°C., *p*H of a 1 per cent. aqueous solution, 12 and biological potency (against *E. coli* by a turbidimetric test), 922 μg. per mg. G. B.

Sodium Azide Preservation of Blocking-type Rh Antiserum. M. Jayne. H. C. Batson and M. Brown. (*J. Lab. clin. Med.*, 1950, **35**, 988.) A study is reported of the preservative effects of sodium azide on unfortified and bovine albumin-fortified blocking-type D(Rh_0) anti-serum stored at refrigerator and room temperatures, and 37°C. over a period of 72 weeks. Sodium azide in a concentration of 0·1 per cent. was found to exert no deleterious effect on the blocking-type antibody and to be a satisfactory bacteriostatic agent in both unfortified and albumin-fortified serum specimens. The agglutinative activity of albumin-fortified serum specimens was much less affected by bacterial contaminants, temperature and time of storage than was that of unfortified samples. S. L. W.

BIOCHEMICAL ANALYSIS

Amino-Acids, Paper Chromatographic Identification of. E. M. Gal and D. M. Greenberg. (*Proc. Soc. exp. Biol. N.Y.*, 1949, **71**, 88.) The amino-acids examined were DL-valine, DL-leucine, and DL-phenylalanine and their *N*-ethyl, *N*-isopropyl, *N*-propyl and *N*-phenyl derivatives. They were separated in 25 μg. quantities with phenol-water and collidine-water solvents. After the solvent had reached a 20-cm. liquid front (within 20 hours), the paper strips were air-dried and examined by ultra-violet light, when the unsubstituted amino-acids showed as faint blue spots and the *N*-substituted derivatives as absorbing non-emitting spots. After treatment with a 0·15 per cent. ninhydrin solution in saturated butyl alcohol-water, all the acids responded although the spots given by the *N*-substituted acids were much less intense in colour than those given by the corresponding unsubstituted acids. Colour intensity and R_F values could be correlated with the rate of hydrolysis of the substituted and with the steric arrangement. During drying, the *N*-phenyl derivatives, which were very soluble in the solvents used, were lost from the papers.
G. R. K.

Aureomycin in Blood and Urine, Estimation of. A. Saltzman. (*J. Lab. clin. Med.*, 1950, **35**, 123.) The antibiotic is separated from interfering substances by adsorption on a column of Decalso, which is washed with limited amounts of distilled water, ethyl alcohol and then air dried. Elution is performed with hot 5 per cent. sodium carbonate solution. In alkaline solutions, aureomycin fluoresces a bright blue under ultra-violet light. The fluorescence of the aureomycin in the eluate is directly measured in a fluorophotometer. The procedure requires only 1ml. of serum which need not be sterile. The sensitivity of the method (0·5 to 10 μg./ml.) is adequate for the usual range of serum values as found by microbiological methods. While the latter have better sensitivity, their accuracy, especially in the upper range, is somewhat less. Similar values are obtained by the application of both methods to blood and urine. The specificity of the procedure was tested with common drugs and with uræmic blood and no interference was found. S. L. W.

Chloromycetin in Serum or Plasma, Colorimetric Determination of. S. P. Bessman and S. Stevens. (*J. Lab. clin. Med.*, 1950, **35**, 129.) A microcolorimetric method is described for the determination of chloromycetin in 1 ml. samples of serum, based on the reduction of the aryl nitro group with stannous chloride, and subsequent diazotisation and coupling to produce a red complex. The method is about 4 times as sensitive as the method of Glazko and co-workers and has the advantages that the entire reaction can be carried

out in the colorimeter tube, no dilution is necessary, no filtration or centrifugation is required to remove the reducing agent, and adenine does not interfere with the determination. A comparison of the values for sera determination by this method and by microbiological methods indicates reasonable agreement, within the limits of error of the microbiological methods. S. L. W.

Heparin Assay, a new Technique for. D. C. McGoon. (*J. Lab. clin. Med.*, 1950, **35**, 111.) This method consists of testing short, heparin-induced prolongations of the clotting-time of recalcified citrated human blood with an accurate end-point which determines an incipient degree of clotting. This is made possible by employing a specially constructed hour-glass tube. These tubes are 17 cm. in length, with an inside diameter of 1 cm. At 7·5 cm. from each end an hour-glass constriction commences, narrowing at the centre to an inside diameter of 1 mm. In the centre of each half of the tube there is a small air-vent. These tubes are secured, the bottom openings corked, in a tilt rack which holds 10 tubes, air vents all facing in one direction. Tubes 1 and 10 are used as controls and 1 ml. of saline solution placed in each. Tubes 2 and 9 are used to determine clotting-time of blood containing a heparin solution of known concentration, say, 1 ml. of a normal saline dilution containing approximately 0·45 to 0·50 unit of heparin /ml. Tubes 3 to 8 are used to determine clotting-times of blood containing 6 different dilutions of the unknown heparin solution, and differing approximately 2 to 3 per cent. in concentration. 0·5 ml. of 1 per cent. solution of calcium chloride is added to each tube ; 1 ml. of blood is then added to each tube at nearly the same instant. The top openings of the tubes are then immediately stoppered and the tubes inverted 3 times, as rapidly as the blood solution will flow from one end to the other. The tubes are then inverted every 15 seconds. After from $3\frac{1}{2}$ to 5 minutes the controls will suddenly stop flowing. If 15 seconds intervene between the two controls the longer is considered the control clotting-time ; if 30 seconds, their average. As the remaining tubes clot the time is recorded. From these data, the beginning time is subtracted from the time of clotting, and thus the clotting-time is calculated. The prolongation of clotting-time is then calculated by subtracting the control clotting-time from the actual clotting-time of the heparinised blood, and these values are recorded. The test should be repeated 3 times and the average values plotted on a graph. S. L. W.

Œstrogens Natural, Polarographic Estimation of. C. Heusghem. (*Bull. Soc. Chim. biol.*, 1949, **31**, 1114.) A new method is given for the polarographic estimation of three natural œstrogens. In working out the details of the method a study has been made of the conditions necessary for the formation of the nitroso-derivatives of œstrone, œstradiol and œstriol and the solutions necessary for the reaction are given. For œstrone 50 to 250μg. in alcoholic solution is evaporated under reduced pressure, a specific reagent (acetic acid, 5; sulphuric acid, 5; nitric acid, 0·5) is added to produce the nitroso-derivative, the mixture shaken and placed in a thermostat at 35°C. for 30 minutes. The product is diluted with water and made alkaline by the addition of potassium hydroxide solution (20 per cent.), the solution is freed from oxygen by the passage of nitrogen and polarographed from a voltage of −0·3 to −1·05; polarographic curves are given for the various œstrogens. It was found experimentally that polarographic reduction was best carried out in alkaline solution and the strongly acid reaction solution was therefore made alkaline with a small amount of potassium hydroxide; using these conditions the solution obtained for polarographic estimation was stable for several hours. With the technique described, the

estimation is quantitative up to a maximum of 350μg. for œstrone and œstradiol and up to 500μg. for œstriol. Amounts of œstrogen as low as 5 to 20μg. can be determined. R. E. S.

Œstrone, Equilin and Equilenin in Mixture, Colorimetric Determination of. D. Banes. (*J. Amer. pharm. Ass., Sci. Ed.*, 1950, **39**, 37.) Three separate colorimetric determinations are required. One portion of the mixture is treated with dibromoquinonechloroimide in slightly acid solution, when equilenin yields a stable red pigment extractable with chloroform, equilin slowly develops a similar product with approximately half the intensity, and œstrone gives practically no colour. A second portion is esterified with benzenesulphonyl chloride and the benzenesulphonates so obtained are treated with the same reagent, when equilin gives a stable violet pigment and equilenin and œstrone do not react. The third portion is heated with a reagent containing phenylsulphonic acid and ferric iron in sulphuric acid, when œstrone gives a deep orange-red colour with a green fluorescence, equilin a blue colour and equilenin an orange-pink colour. From optical density measurements of each determination and of suitable standard solutions of the pure ketosteroids, the composition of the original mixture can be calculated. The method was applied to solutions of the œstrogens in sesame oil, extracts from pregnant mares' urine and commercial preparations. Results showed good agreement with the infra-red spectro-photometric method. G. R. K.

Penicillin in Blood, Micromethod for Assay. G. Hildick-Smith and Mary Fell. (*J. Lab. clin. Med.*, 1949, **34**, 1687.) The method requires 0·2 ml. of blood, which can be conveniently collected from a single puncture wound of the finger using the collecting tube described. The serum is separated by centrifuging and added in diminishing amounts to a series of tubes containing a phenol red dextrose broth. The tubes are inoculated with a suitable culture of any penicillin-sensitive organism and incubated at 37°C. overnight. When the amount of penicillin in the blood is insufficient to inhibit the growth of the organism the dextrose broth becomes acid and changes colour. By running a series of control tubes using a penicillin solution of known strength, the concentration of penicillin in the serum can be readily calculated. Comparison with the results obtained by the Rammelkamp method shows the micromethod to be more accurate ; it has been used successfully for hundreds of routine assays of penicillin levels in body fluids. G. R. K.

Penicillin in Liquids ; the Agar-rope Technique for Estimating. H. W. Julius and W. J. Alsche. (*J. clin. Path.*, 1950, **3**, 51.) A technique is described for the rapid determination (after 2 to 4 hours) of penicillin or other antibiotics in liquids such as serum, body fluids or culture media. Accurately prepared agar discs, mechanically cut from an agar rope, containing heavy inocula of bacteria, are submerged in small quantities of graded dilutions of known, compared with unknown, penicillin-containing fluids. Staphylococci are the most suitable bacteria but the method can be adapted for the use of any other organism sensitive to penicillin. An indicator, such as phenol red, detects normal compared with suppressed bacterial activity. The sensitivity of the method is 0·04 unit/ml. (serum). The quantity of material wanted for the test is 2 ml. (serum of 0·4 unit/ml.) or considerably less. With streptococci the activity can be augmented to 0·01 unit/ml. S. L. W.

Progesterone, Paper Chromatographic Separation and Ultraviolet Analysis of Commercial Preparations of. A. L. Haskins, Jr., A. I. Sherman,

and W. M. Allen. (*J. biol. Chem.*, 1950, **182**, 429.) The preparations consisted of solutions of progesterone in sesame or cottonseed oil. Quantities of 0·005 to 0·1 ml. diluted 10 times with carbon tetrachloride were placed on paper strips and allowed to dry. The strips were developed for 16 to 18 hours with alcohol (80 per cent.) and again allowed to dry. The progesterone was found by the blue colour obtained by immersing one-third of the strip cut lengthwise in a saturated alcoholic solution of *m*-dinitrobenzene, heating until dry, immersing in 5N potassium hydroxide and again drying. Under controlled conditions the R_f was about 0·84. The progesterone was extracted from the remaining two-thirds of the strip by immersing the appropriate parts in 5 ml. of alcohol (95 per cent.), and the resulting solution was submitted to ultraviolet analysis. The amount of progesterone was calculated from the density at 240 mμ. Samples prepared with sesame oil yielded a strongly ultraviolet absorptive factor which interfered with the analysis of progesterone ; a correction factor is given. Deoxycortone acetate and testosterone propionate may be separated from sesame oil in the same manner. They also have a similar absorption band and give the same colour reaction with *m*-dinitrobenzene and potassium hydroxide. Physiological tests are necessary to identify progesterone completely. G. R. K.

Streptomycin, Turbidimetric Assay for, and its Critical Evaluation. E. J. Oswald and L. F. Knudsen. (*J. Amer. pharm. Ass., Sci. Ed.*, 1950, **39**, 61.) A suitable dilution of the unknown preparation is heated in a water-bath at 37°C. for 4 hours with broth previously inoculated with an aqueous suspension of the test organism, *Klebsiella pneumoniæ*, 4 drops of solution of formaldehyde are added and the percentage light transmission read in a photoelectric colorimeter. The potency is then read from a graph prepared by plotting percentage transmission against concentration for a series of dilutions of a standard preparation. The aqueous suspension of the test organism was used as the source of inoculum in an attempt to minimise the day to day variation of the test ; it was found to maintain vitality for 2 weeks when stored in a refrigerator. The factors entering into the test are analysed statistically and a nomograph and formula for calculating the standard error are also given. Comparison of the method with the *B. subtilis* plate assay on about 1,000 samples showed that in general the turbidimetric method gave slightly lower but more precise results. G. R. K.

PHARMACY

NOTES AND FORMULÆ

Chloramphenicol (Chloromycetin). (*New and Nonofficial Remedies; J. Amer. med. Ass.*, 1950, **143**, 813.) Chloramphenicol is D-(−)-threo-1-(*p*-nitrophenyl-2-dichloroacetamido-1 : 3-propanediol ($C_{11}H_{12}Cl_2N_2O_5$). It occurs as a white to greyish-white or yellowish-white crystalline powder, or as needles or elongated plates, slightly soluble in water and freely soluble in alcohol; a saturated aqueous solution has *p*H 4·5 to 7·5. In ethyl acetate it is lævorotatory, but in alcohol dextrorotatory; a solution of 1·25 g. in 15 ml. of absolute alcohol has a specific rotation $[\alpha]_D^{25°C.}$ of + 18·5° ±1·5°. The extinction coefficient $E_{1\text{ cm.}}^{1\text{ per cent.}}$ at 2780 Å is 289 ±9. The identity tests comprise a test for absence of inorganic halides, a test for the presence of organic chlorine and a test for the presence of a nitrophenyl group, which consists of reduction with tin and hydrochloric acid, diazotisation and coupling with β-naphthol, when a brilliant orange precipitate is obtained. The amount of

heavy metals present is equivalent to not more than 25 p.p.m. of lead. Chloramphenicol is assayed by determining the optical density of a 0·002 per cent aqueous solution spectrophotometrically at 2780 Å, compared with water as a blank; it contains 97 to 103 per cent. of chloramphenicol. Large doses may produce nausea and vomiting, otherwise no toxic effects have been observed. The initial dose is 50 to 75 mg./kg. of body-weight by mouth, with subsequent doses of 0·25 to 0·5 g. 2 or 3 hourly. G. R. K.

Chloriodised Oil (Iodochlorol). (*New and Nonofficial Remedies; J. Amer. med. Ass.*, 1950, **142,** 990.) Chloriodised oil is an addition product of arachis oil and iodine monochloride. It is a pale yellow viscous oily liquid with a faint bland taste, almost insoluble in water, slightly soluble in alcohol and freely soluble in benzene, chloroform and ether; refractive index at 25°C, about 1·505, specific gravity, about 1·260, residue on ignition not more than 0·1 per cent. It is assayed by hydrolysing with methyl alcoholic potassium hydroxide, diluting with water, acidifying with hydrochloric acid, extracting with chloroform and titrating the aqueous layer with potassium iodate; chloriodised oil contains 26·5 to 28·5 per cent. of iodine. It is used as a radiopaque agent to assist visualisation of the bronchial tract, genito-urinary tract, soft tissue sinuses, fistulas, etc. G. R. K.

Dymenhydrinate (Dramamine). (*New and Nonofficial Remedies; J. Amer. med. Ass.*, 1950, **143,** 815.) Dimenhydrinate, 2-(benzohydryloxy)-*N*:*N*-dimethylethylamine 8-chlorotheophyllinate ($C_{17}H_{22}ON$, $C_7H_6O_2N_4Cl$) is a white, crystalline, odourless powder, m.pt. 102°C. to 107°C., soluble in alcohol, benzene and chloroform and sparingly soluble in ether and water; a saturated aqueous solution has *p*H 6·8 to 7·3. The base, obtained by treatment with ammonia and extraction with ether, responds to the identity tests for diphenhydramine hydrochloride (N.N.R.). The addition of dilute sulphuric acid to a solution of dimenhydrinate produces a white precipitate of 8-chlorotheophylline, which responds to the following tests: (a) the murexide test (U.S.P.), (b) when fused with sodium peroxide, a solution of the residue in water gives a white precipitate with dilute nitric acid and silver nitrate (distinction from theophylline), and (c) when dissolved in diluted ammonia, it gives a white precipitate of silver 8-chlorotheophylline with silver nitrate. Dimenhydrinate loses not more than 0·1 per cent. of its weight when dried *in vacuo* over phosphorus pentoxide at room temperature for 24 hours; sulphated ash, not more than 0·1 per cent. It contains 53·0 to 53·3 per cent. of diphenhydramine and 44·0 to 47·0 per cent. of 8-chlorotheophylline. It is assayed for diphenhydramine by liberating the base with ammonia, extracting with ether, treating with a known volume of hydrochloric acid and titrating the excess acid with sodium hydroxide. The content of 8-chlorotheophylline is determined by dissolving in water with the aid of ammonia and ammonium nitrate, precipitating the 8-chlorotheophylline as the silver salt by adding silver nitrate, filtering and titrating the excess silver nitrate with ammonium thiocyanate. Dimenhydrinate is a histamine antagonist. It exerts a temporary therapeutic and prophylactic action in motion sickness, particularly in sea-sickness and car-sickness. Dose: 50 to 100 mg. half-an-hour before departure, repeated before meals and at bedtime. The untoward effects are similar to those of diphenhydramine, drowsiness being frequently observed G. R. K.

Fluoro-Iodo X-Ray Contrast Media, Preparation of. S. G. Mittelstaedt and G. L. Jenkins. (*J. Amer. pharm. Ass., Sci. Ed.*, 1950, **39,** 4.) Search was made for an ideal X-Ray contrast medium which gave

clear concise shadows of the required parts, was concentrated and retained for sufficient time in structures such as the kidney or gall bladder and then excreted fairly rapidly without toxic effects. Ease of administration and rapid transport in the body were also required with stability under normal conditions and in the blood stream, and lastly, ease and low cost of production were desired. A number of derivatives were prepared of aromatic hydrocarbons with iodine ortho to fluorine. Those prepared were 3-iodo-4-fluorobenzoic acid and a number of salts of the acid. They all exhibited anæsthetic, hypnotic and analgesic effects. Most of them had low toxicity. Ethyl-3-iodofluorobenzoate and the sodium salt of the free acid were tested for use as contrast media. When used in concentrations necessary to produce a distinct shadow of the gastro-intestinal tract, they proved to be rather irritating. They appeared to be rapidly eliminated.

G. R. K.

Prophenpyridamine (Trimeton). (*New and Nonofficial Remedies; J. Amer. med. Ass.*, 1950, **142**, 817.) Prophenpyridamine is 1-phenyl-1-(2-pyridyl)-3-dimethylaminopropane, $CH(C_6H_5)(C_5H_4N).CH_2.CH_2.N(CH_3)_2$, and occurs as a slightly yellow, oily liquid with an amine-like odour, insoluble in water and soluble in alcohol, benzene, chloroform, ether and dilute acids; b.pt. 135°C. at 0·5 mm. and 181°C. at 13 mm.; refractive index, 1·5519 to 1·5521; specific gravity, 1·0081. It is identified by preparing the dipicrate, which melts at 198° to 204°C., and complies with a test for absence of primary amine. It contains 11·50 to 11·80 per cent. of nitrogen, determined by the Kjeldahl method, and 98·5 to 100·5 per cent. of prophenpyridamine, determined by potentiometric titration with 0·1 N hydrochloric acid. A 0·003 per cent. solution in alcohol exhibits an ultraviolet absorption maximum at 2630 Å ($E_1^{1\ \text{per cent.}}_{\text{cm.}} = 184 \pm 3$), a sharp inflection at 2690 Å and a minimum at 2380 Å. Prophenpyridamine is a histamine antagonist. The average adult dose is 25 to 50 mg.

G. R. K.

PHARMACOLOGY AND THERAPEUTICS

Acetylsalicylic Acid, Effect of Buffering Agents on Absorption of. W. D. Paul, R. L. Dryer and J. I. Routh. (*J. Amer. pharm. Ass., Sci. Ed.*, 1950, **39**, 21.) Two tablets each containing 5g. of acetylsalicylic acid and a buffering agent consisting of a mixture of magnesium carbonate and aluminium dihydroxyaminoacetate were given to each of 238 patients. Subsequently only one patient complained of gastric distress although 22 had experienced ill effects after taking unbuffered acetylsalicylic acid. The effect of buffering on the rate of absorption was investigated by determining the blood salicylate before and 10 and 20 minutes after administration of 10 grains of unbuffered and buffered acetylsalicylic acid to two series of 47 patients. The results indicated that the addition of the buffer doubled the blood salicylate. G. R. K.

Artane in the Treatment of Parkinsonism. B. K. Ellenbogen. (*Lancet*, 1950, **258**, 1034.) Initial results in a series of 12 patients with parkinsonism treated with artane over a period of 3 to 6 weeks suggest that it is a drug of low toxicity and high potency in overcoming mental hebetude, relaxing spasm, and reducing tremor. The initial dose of the drug was 2·5 mg., increased by this amount each day to a total of 12·5 mg. in 5 doses. Where this amount was exceeded no greater improvement was obtained and the patients developed side reactions, such as headache, giddiness, slight

cycloplegia, and dryness of the mouth. The drug does not cause convulsions even with massive doses. Where artane is effective it is so immediately and dramatically; the patient becomes cheerful, alert and more responsive. It was more successful in the post-encephalitic group, controlling oculogyric crises, than in the senile and idiopathic groups. S. L. W.

Emetine and Quaternary Emetine Derivatives, Chemical and Pharmacological Studies on. A. Lasslo and K. K. Kimura. (*J. Amer. pharm. Ass., Sci. Ed.*, 1950, **39**, 43.) *N*-methylemetine-*N* : *N'*-dimethiodide, *N*-methylemetine-*N* : *N'*-diethoethylsulphate and *N*-benzoylemetine-*N'*-ethoethylsulphate were synthesised. The first of these was much less toxic than emetine hydrochloride when given to 28 albino rats ; twice daily intraperitoneal doses of 17·2 mg./kg. for 3 weeks produced no ill effects, and the substance appeared to be excreted unchanged. Lethal doses of the same substance killed by asphyxia in contrast to emetine which kills by direct action on the heart. All 3 quaternary derivatives exhibited curare-like action on the striated muscle of frogs, rabbits and mice. The bisquaternary derivative, *N*-methylemetine-*N* : *N'*-diethoethylsulphate was twice as potent in frogs and mice as *N*-benzoylemetine-*N'*-ethoethylsulphate, which has only one quaternary nitrogen atom, and has approximately one-third the activity of *d*-tubocurarine chloride in rabbits. G. R. K.

Ethylene Glycol Vapour, Chronic Intoxication by. F. M. Troisi. (*Brit. J. indust. Med.*, 1950, **7**, 65.) A description is given of the toxic manifestations caused by inhalation of ethylene glycol vapour in women workers engaged in a process involving the spreading of a mixture of ethylene glycol 40 per cent., boric acid 55 per cent., and ammonia 5 per cent. The mixture was maintained at 105°C. to facilitate application by brush, so that the women were exposed to continuous evolution of the vapour. In 9 out of 38 workers so engaged frequent attacks of sudden loss of consciousness lasting for 5 to 10 minutes occurred, and nystagmus was observed; 5 of these had an absolute lymphocytosis. Among the remaining workers a further 5 cases of nystagmus were discovered, but attacks of loss of consciousness did not occur. Of the 9 most sensitive women, 2 were transferred to another department and the attacks ceased. The remaining workers elected to remain at their occupation and after the installation of a recovery plant the attacks completely disappeared. It is recommended that systematic examination for nystagmus should be carried out among workers in contact with glycols or other solvents of the fatty or aromatic series. H. T. B.

Iron, Intravenously, in the Treatment of Anæmia. A. S. Ramsey. (*Brit. med. J.*, 1950, **1**, 1112.) Intravenous iron therapy is now a practical method of treating microcytic hypochromic anæmia, and is the method of choice for patients unable to tolerate iron orally or in cases of refractory iron-deficiency anæmia. These patients will respond dramatically to intravenous saccharated oxide of iron (reports of 11 cases treated with the proprietary ferrivenin are given). Toxic reactions are avoided when the dosage begins with 100 mg. daily for several days and is then gradually increased to 200 or 300 mg., a full course consisting of not more than 10 injections. Severe toxic reactions occur, however, when attempts are made to replace the requirements of iron by a single intravenous injection. The toxic effects closely resemble the symptoms of paroxysmal hæmoglobinuria caused by cold, and the author suggests as a cause the sudden increased activity of the cells of the reticulo-endothelial system. S. L. W.

2-Methylaminoheptane (Œnethyl), A Study of. F. E. Shaffer and P. K. Knoefel. (*J. Amer. pharm. Ass., Sci. Ed.*, 1950, **39**, 12.) The action of 2-methylaminoheptane was compared with that of deoxyephedrine, by administration orally and parenterally to two normal men and intravenously to an unspecified number of dogs; it was concluded that as a vasopressor agent, 2-methylaminoheptane had one-fifth the activity of deoxyephedrine. Comparative acute lethal toxicity studies on mice, rats and dogs whose numbers are also unspecified revealed that 2-methylaminoheptane had a degree of toxicity similar to that of tuamine (2-aminoheptane) on subcutaneous and intravenous injection. Deoxyephedrine and 2-methylaminoheptane are equally toxic intravenously but the former is more toxic subcutaneously. Chronic toxicity studies indicated that the smallest dose at which a deleterious effect is noted is 23mg./kg. of body weight per animal per day for albino rats although it is possible that this is true only of female animals. G. R. K.

Œstrogens, Further Observations on the Potency of. P. M. F. Bishop, N. A. Richards, D. J. N. Smith and W. L. M. Perry. (*Lancet*, 1950, **258**, 848.) The potencies of ethinylœstradiol and "equine conjugated œstrogen" were compared with the potency of stilbœstrol by giving the œstrogen daily by mouth in 14-day courses to amenorrhœic women and recording whether œstrogen-withdrawal bleeding took place. "Equine conjugated œstrogen" is the name used for an extract of œstrogenic substances from the urine of pregnant mares and consists of a mixture of conjugated œstrogens, including œstrone sulphate. The results of the investigation indicated that ethinylœstradiol was 20 to 25 times as potent as stilbœstrol and "equine conjugated œstrogen" half as potent. With the doses used to induce withdrawal bleeding there were few cases of nausea with ethinylœstradiol and only one with "equine conjugated œstrogen"; at higher dosage levels such as those necessary to produce hæmostasis in functional uterine bleeding, nausea usually developed with ethinylœstradiol and in 2 such patients "equine conjugated œstrogen" produced severe vomiting.

G. R. K.

Pethidine and Amidone (Methadone) Derivatives. P. O. Wolff. (*Bull. World Hlth. Org.*, 1949, **2**, 193.) The analgesic effects of modifications of the pethidine molecule are as follows. *Ester group:* Only the ethyl, *iso*-propyl, allyl and *n*-propyl esters are active. Corresponding amides are inactive, but ketones are more active than esters (for example, 1-methyl-4-*m*-hydroxyphenyl-4-propionylpiperidine, "keto-bemidone"). Acyl derivatives of 4-phenyl-4-hydroxy-1-methylpiperidine are active, especially the propionyl compound. Benzene ring substitution: 2′-methyl substitution increases potency and duration; 3′-acetoxypethidine is similar to pethidine and 3′-methoxypethidine is about half as active. This relationship is comparable with that of morphine, diamorphine and codeine. β-pethidines: *l-N*-nor-β-pethidine has similar antispasmodic properties to pethidine but is less sedative, and produces no noticeable euphoria. *N-group*: *N*-butyl and *N-iso*propyl derivatives are highly active. 3-alkyl substituted pethidines: The following are 4 to 8 times as potent as morphine: *dl-*, *d-* and *l-* 1:3-dimethyl-4-phenyl-4-propionoxypiperidine, and 1-methyl-3-ethyl-4-phenyl-4-propionoxypiperidine. Steric configuration affects the potency of certain derivatives, 3:3-diethyl-2:4-dioxopiperidine gives good or fair sedation, but is suspect of habit forming. The following amidone derivatives have been examined: *l*-amidone, which has about 50 times the analgesic effect of the *d*-compound, and is responsible for the addiction-producing effect of the

dl-substance; *dl*-methadol (6-dimethylamino-4:4-diphenyl-3-heptanol); *dl-iso*-methadone which is an addiction-producing drug; γ-dimethylamine-α:α-diphenylvaleric acid which has an atropine-like effect on the intestine of the anæsthetised dog; 1-dimethylamino-2-methyl-3:3-diphenyl-4-acetoxyheptane, 2-dimethylamino-4:4-diphenyl-5-hexylidene acetylimine, 2-dimethylamino-4:4-diphenyl-5-acetoxyheptane and 2-morpholino-4:4-diphenyl-5-acetoxyheptane which have a high therapeutic index; phenadoxone (6-morpholino-4:4-diphenyl-3-heptanone), a potent analgesic, the most important side effect of which is euphoria, and 6-dimethylamino-4:4-diphenyl-5-methyl-3-hexanone, which is half as active as amidone. It is suggested that all pethidine and amidone derivatives should be controlled legally as habit-forming drugs, restrictions on a particular compound being withdrawn when practice has shown that it does not produce addiction. G. B.

Priscol in Peripheral Vascular Disease. A. H. Douthwaite and T. R. L. Finnegan. (*Brit. med. J.*, 1950, **1**, 869.) The effects of priscol benzyl-imidazoline) were investigated in 10 normal subjects 4 with rheumatoid arthritis, 9 with Raynaud's disease, 24 with intermittent claudication of arteriosclerotic origin, 2 with claudication of thrombo-angiitis obliterans and 6 with arterial tension without claudication. It was found to have a more lasting vasodilator effect than other drugs commonly employed for this purpose, and to have an elective affinity for the smaller arteries and arterioles of the fingers, hands and toes. The best results are to be looked for where the element of spasm is maximal and organic blockage of the lumen is minimal. It is outstandingly successful in the treatment of Raynaud's disease, but the proportion of cases of arteriosclerotic intermittent claudication which benefit from the drug is surprisingly high. It would seem of little value in thrombo-angiitis obliterans or rheumatoid arthritis and should not be used in arterial hypertension. It is relatively non-toxic, but may give rise to pallor, sweating, weakness, palpitation and giddiness. This effect is known as " priscol shock," and it is advisable to test the patients' sensitivity by giving 25 mg. by mouth; if this has no unpleasant effect 50 mg. intravenously may be given. Of the 9 patients with Raynaud's disease 5 remained completely comfortable on a dose of 25 mg. four times a day and 4 by taking occasional doses. S. L. W.

Procaine Penicillin, Aqueous Suspension of. R. I. Cohen. (*Lancet*, 1950, **258**, 622.) In a trial of an aqueous suspension of penicillin G in 30 adult volunteers intramuscular injections caused no pain or discomfort, and there was no swelling or redness at the site of injection. An effective blood penicillin level of over 0·03 unit/ml. was maintained for 24 hours in 27 out of the 30 volunteers after a single intramuscular injection of 300,000 units. The aqueous suspension used contained the stable crystalline procaine salt of penicillin G with less than 1·5 per cent. of suspending agents; the suspended particles in the preparation were nearly all less than 40μ in diameter. Into a " single-dose " vial of aqueous suspension containing 330,000 units of penicillin 1·2 ml. of sterile water was injected and the vial shaken. As much as possible (about 1·5 ml.) was withdrawn into the syringe and the injection made into the triceps muscle at ordinary speed through a No. 14 needle. No difficulty was encountered in giving the injection, and the suspension was still easier to handle if 2 ml. instead of 1·2 ml. of diluent was added. S. L. W.

Sodium Phosphate in Lead Poisoning. C. D. Procter and H. S. Kahn. (*Amer. J. med. Sci.*, 1950, **219**, 316.) It has previously been pointed out that sodium phosphate appears theoretically to have the following

advantages in the treatment of chronic plumbism. It precipitates the lead in its most insoluble form, as $Pb_3(PO_4)_2$; the slight alkalosis may mobilise some of the lead in the bones; the excess of sodium ions disturbs the calcium balance so that calcium, and therefore lead, are drawn from the trabeculæ; mobilisation and detoxification are simultaneous; the buffer action of the phosphate decreases the amount of ionised lead. The authors therefore undertook an investigation of the therapeutic value of sodium phosphate in this condition Clinical diagnosis was confirmed by determination of the urinary excretion of lead during a 24-hour period. The usual dosage was 30 to 60 gr. by mouth 3 times a day for about a week, although in some cases 5 to 10 gr. was given 3 times a day intravenously as a 5 per cent. solution. In all cases the urinary excretion of lead was markedly increased without producing any symptoms and the treatment reduced the 24-hour urinary lead level below about 150 μg./ml. which was regarded as the toxic limit. Sodium phosphate is considered to provide an effective and inexpensive treatment in chronic lead poisoning which is superior to any other form of therapy at present available. H. T. B.

Tubocurarine Iodide, Dimethyl Ether of, as a Curarising Agent in Anæsthesia. H. B. Wilson, H. E. Gordon and A. W. Raffan. (*Brit. med. J.*, 1950, **1**, 1296.) From the use of this curarising agent in 100 cases of major intrathoracic procedures the authors conclude that it is from 2 to $2\frac{1}{2}$ times more potent than *d*-tubocurarine chloride, but that its duration of action on diaphragmatic activity is a little shorter and subsequent doses are required at intervals of 20 to 25 minutes. Clinically, there seems less release of histamine, as evidenced by maintenance of systolic and diastolic blood pressures and ease of inflation of collapsed lung tissues. In no case was there any cause for anxiety referable to the use of the curarising agent, neither was there any evidence of undue reactions to the drug or to its delayed detoxication. The dosage of the dimethyl tubocurarine employed was of the order of 1 mg./stone, with incremental doses of 3 mg. S. L. W.

Tubocurarine Iodide, Dimethyl Ether of, Pharmacology of. H. O. J. Collier. (*Brit. med. J.*, 1950, **1**, 1293.) Dimethyl tubocurarine is a more effective curarising agent than tubocurarine in the rat, guinea-pig, rabbit and cat, but is less active than tubocurarine in the mouse. In the mouse, rat and rabbit dimethyl tubocurarine is antagonised by neostigmine. Weight for weight it is no more active than tubocurarine in liberating histamine or in blocking autonomic ganglia in the cat. Its repeated administration to the rabbit or rat does not appear to give rise to increased sensitiveness or tolerance. Dimethyl tubocurarine has been successfully administered to the rat with ether and with thiopentone. A combination of dimethyl tubocurarine and ether has a greater effect than either separately. From the experimental evidence it seems likely that dimethyl tubocurarine can be used with success in man in association with an anæsthetic, though it would appear that in man its action is of slightly shorter duration than that of tubocurarine. It depresses the respiration relatively less than *d*-tubocurarine or decamethonium iodide. S. L. W.

BACTERIOLOGY AND CLINICAL TESTS

Antiobiotics, *in vitro* Sensitivity of *Bacillus proteus* and *Pseudomonas æruginosa* to. P. F. Frank, C. Wilcox and M. Finland. (*J. Lab. clin. Med.*, 1950, **35**, 205.) Experiments similar to those described for coli-

form organisms, were carried out. For *B. proteus*, chloramphenicol and penicillin were most effective, rather high concentrations of streptomycin or aureomycin were required for inhibition of growth and polymixin, aerosporin and bacitracin were ineffective. 28 per cent. of strains were resistant to penicillin, and 11 per cent. to streptomycin. For *Ps. æruginosa* the following is the order of decreasing activity :—aerosporin, polymixin, streptomycin, aureomycin and chloramphenicol. Bacitracin and penicillin were not effective. 14 per cent. of strains were resistant to streptomycin. G. B.

Antibiotics, *in vitro* Sensitivity of Coliform Bacilli to. P. F. Frank, C. Wilcox and M. Finland. (*J. Lab. clin. Med.*, 1950, **35**, 188.) A number of strains of *Escherichia co'i, Aerobacter aerogenes* and *Klebsiella pneumoniæ* were cultured from patients with active infectious processes. Routine tests for sensitivity to the antibiotics were carried out by a tube dilution method. When several strains of the same organism were tested simultaneously against all the antibiotics, a plate dilution method was used. Polymixin and aerosporin were most active against all three species, aureomycin and chloramphenicol being somewhat less effective. Streptomycin was as effective as chloramphenicol against two-thirds of the strains, the remaining strains being less sensitive. A higher concentration of penicillin was required for inhibition, and bacitracin was practically ineffective. 16 per cent. of the strains of *E. coli*, 24 per cent. of the strains of *A. aerogenes* and 9 per cent. of those of *K. pneumoniæ* were resistant to streptomycin. *K. penumoniæ* was the most sensitive and *A. aerogenes* the most resistant to the antibiotics. G. B.

Ethylene Oxide for Sterilisation. A. T. Wilson, and P. Bruno. (*J. exp. Med.*, 1950, **91**, 449.) Ethylene oxide gas has been used widely in industry as a sterilising agent and the authors have investigated the use of liquid ethylene oxide as a sterilising agent for bacteriological broth, milk and serum in cases where heat or filtration cannot be used. The liquid vapourises at 10·7°C.; it is kept in a stoppered bottle in the cold and measured by a chilled pipette or syringe, the latter being preferable because the substance is toxic. It was found that ethylene oxide destroys a number of Gram-positive and Gram-negative organisms, aerobic and anaerobic spore-forming bacilli, fungi, and vaccinia virus, including organisms present in culture media contaminated with floor-sweepings, fæces, throat-washings and soil. No organisms were encountered which withstood the action of 1 volume per cent. of liquid ethylene oxide in the culture medium, and 0·5 per cent. is often adequate. The time required to effect sterilisation depended on the amount of ethylene oxide used. 0·5 per cent. sterilised milk contaminated with a Group A streptococcus in 4 hours, and broth inoculated with the same organism in 6 hours. 24 hours after culture media were subjected to treatment with the liquid, they again became fully capable of supporting bacterial growth. Sterilisation of media by ethylene oxide is accompanied by a rise in *p*H which may necessitate adjustment with sterile acid to recover optimal conditions for bacterial growth. A mixture of ethylene oxide and broth was toxic to mice for 6 hours, after which toxicity disappeared rapidly even on repeated intraperitoneal inoculation. The substance combines slowly with water to form ethylene glycol and with many acids. It also reacts with carboxyl, amino, sulphydryl and phenolic groups but no evidence of interference with any essential growth factors was obtained. H. T. B.