perfusion has to be repeated will be influenced by the speed with which the liver develops the capacity to excrete bilirubin.

Because of the underlying hepatic deficit in the newborn baby the importance of using recently drawn blood for transfusion is stressed.

The significance of the large amounts of direct-reacting bile pigment that have been shown to occur in the plasma of some cases of haemolytic disease is discussed.

This study has been made possible by the close co-operation of Miss M. Ashforth in following the clinical condition of the infants and in securing specimens for analysis. She has also been responsible for most of the exchange transfusions. I am grateful to Dr. A. White Franklin for opportunities of studying infants under his care. The serological and haematological examinations have been supervised by Dr. John Murray. Specimens from the Hammersmith Hospital have been obtained with the help of Professor J. McClure Browne and Dr. J. Dean. I am also grateful to P. G. Cole, C. R. J. Ruthven, and S. Bebbington for skilled laboratory assistance, and to Dr. John Murray, Dr. A. E. Claireaux, and Dr. Barbara H. Billing for frequent discussions and suggestions.

REFERENCES

Allen, F. H., jun., Diamond, L. K., and Vaughan, V. C. (1950). *Amer. J. Dis. Child.*, **80**, 779.
Armitage, P., and Mollison, P. L. (1953). *J. Obstet. Gynaec. Brit. Emp.*, **60**, 605.
Aschoff, L (1924). *Lectures on Pathology*, p. 243. Hoeber, New York.
Billing, B. H. (1955). *J. clin. Path.* In press.
—— Cole, P. G., and Lathe, G. H. (1954). *British Medical Journal*, **2**, 1263.
British Medical Journal, 1954, **1**, 692.
Claireaux, A. E. (1950). *Arch. Dis. Childh.*, **25**, 61.
—— Cole, P. G., and Lathe, G. H. (1953). *Lancet*, **2**, 1226.
Cole, P. G., and Lathe, G. H. (1953). *J. clin. Path.*, **6**, 99.
—— —— and Billing, B. H. (1954). *Biochem. J.*, **57**, 514.
Crosse, V. M., Davies, B. S., and Gerrard, J. (1954). *Lancet*, **2**, 91.
Hsia, D. Y. Y. (1953). *Amer. J. Dis. Child.*, **86**, 484.
—— Allen, F. H., jun., Diamond, L. K., and Gellis, S. S. (1953). *J. Pediat.*, **42**, 277.
—— —— Gellis, S. S., and Diamond, L. K. (1952). *New Engl. J. Med.*, **247**, 668.
—— Patterson, P., Allen, F. H., jun., Diamond, L. K., and Gellis, S. S. (1952). *Pediatrics*, **10**, 243.
King, E. J. (1951). *Micro-Analysis in Medical Biochemistry*, 2nd ed. Churchill, London.
Lathe, G. H. (1954). *Biochemical Society Symposia*, No. 12, p. 34. Cambridge Univ. Press.
Malloy, H. T., and Evelyn, K. A. (1937). *J. biol. Chem.*, **119**, 481.
Mollison, P. L., and Cutbush, M. (1954). In *Recent Advances in Pediatrics*, edited by D. Gairdner, p. 110. Churchill, London.
Watson, H. B., Crosse, V. M., and Hatchuel, W. L. F. (1954). *British Medical Journal*, **1**, 679.

Believed to be the only unit of its kind ever to be formed in the British Army, the Parachute Medical Team is described by Dr. J. S. Macdonald in the *Journal of the R.A.M.C.*, January, 1955. It is staffed by personnel of the 16th Independent Parachute Brigade Group and operates in the Middle East. On receiving a signal that an aeroplane has crashed in the desert, the team sets off in a "Valetta" aircraft standing by and fitted out specially for the dropping of men and containers. On finding the crashed aircraft, a suitable dropping zone is sought, a smoke canister thrown out to determine wind speed and direction, and then the medical officer and nursing orderly jump. If they find that further help is needed, they fire a green Very cartridge, and the rest of the team follow—namely, three privates R.A.M.C., and one corporal and two signalmen Royal Signals. (The main duty of one of the signalmen is to carry a radio set down, since this is still the surest way of getting these delicate instruments to the ground intact.) If the first two to jump find they do not need any assistants, they fire a red Very light, and the aircraft drops food and water. The team's task is to give such first-aid treatment as may be required until the R.A.F. ground rescue team can arrive and take them all to safety. The equipment parachuted includes intravenous fluids, splints, morphine, anaesthetics, surgical instruments, antibiotics, and a bivouac tent to provide that most longed-for solace in the desert—shade.

ALDOSTERONE IN URINE OF NORMAL MAN AND OF PATIENTS WITH OEDEMA

ITS INCREASED RECOVERY AFTER HYDROLYSIS WITH ACID AND WITH BETA-GLUCURONIDASE*

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Neutral lipid extracts of acidified urine from patients with the nephrotic syndrome, in heart failure, and in some other oedematous states cause sodium retention and potassium elimination when injected into adrenalectomized rats (Deming and Luetscher, 1950 ; Luetscher *et al.*, 1952 ; Luetscher and Johnson, 1954b ; Chart and Shipley, 1953 ; Singer and Wener, 1953 ; Gordon *et al.*, 1954). The substance responsible for this mineralocorticoid activity has been separated by paper chromatography from urine extracts (Luetscher and Johnson, 1954a). Further work (Luetscher, 1955 ; Luetscher, Neher, and Wettstein, 1954) has shown that this sodium-retaining corticoid is identical with aldosterone (Simpson and Tait, 1953 ; Simpson *et al.*, 1954) in the following ways: (1) its high sodium-retaining potency in bioassay ; (2) its absorption of ultra-violet and of infra-red radiations ; (3) its reducing activity ; (4) its melting point, and (5) the chromatographic mobility of the native substance, of its mono- and di-acetates, and of its oxidation products after treatment with periodate.

Cope and Garcia-Llaurado (1954) found a substance of similar chromatographic behaviour in the urine of a woman suffering from a severe potassium-losing condition. Their extracts of neutral urine from normal men yielded only traces of activity. Luetscher and Axelrad (1954) obtained a much larger yield of aldosterone from normal urine which had stood for a day at *p*H 1. Venning *et al.* (1954) found increased amounts of sodium-retaining substances in urine treated with beta-glucuronidase. Thus the amount of active material extracted depends partly upon the method of hydrolysis. This report compares the yields, after various methods of hydrolysis, from urine of normal subjects on their usual diet and after salt restriction. The present study also includes data on the hydrolysis of urine of patients showing an increased urinary output of sodium-retaining material.

Methods

Urine was immediately stored in a refrigerator without preservative. The total 24-hour specimen was mixed, the volume was recorded, and a small aliquot was set aside for chemical analysis. The remaining urine was frozen and stored at −20° C. until extraction. Immediately before extraction, urine was brought to 20° C. and the *p*H was adjusted as indicated.

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Methods of Hydrolysis.—"Neutral" (N): These extracts were made at once after adjusting the urine to *p*H 6.5 ± 0.1. "Immediate Acid" (A): Urine was extracted within 40 minutes after acidification to *p*H 1. "24-hour Acid" (B): Urine which had already been extracted within 40 minutes at *p*H 1 was then allowed to stand at 20° C. at the same *p*H for 24 hours; it was then re-extracted. "Control for Glucuronidase" (Cg): Urine was adjusted to *p*H 4.8, and 0.02 volume of 5 molar acetate buffer of *p*H 4.8 was added. The specimen was then incubated at 37° C. for the specified time over 50 to 100 ml. of chloroform. The *p*H did not change appreciably during incubation. "Glucuronidase" (G): Specimens were prepared as described for Cg and were incubated with the enzyme (Cohen, 1951). Concentrated beta-glucuronidase prepared from calf spleen (Vio-Bin Corporation, Monticello, Illinois) was used in the first experiments. Subsequently, a solution of purified beta-glucuronidase, derived from beef liver, was obtained from the Warner-Chilcott Laboratories, New York. The activities, measured by the method of Talalay *et al.* (1946), were of the order stated by the makers. The various concentrations and times of incubation at *p*H 4.8 and 37° C. are noted in the tables. When urine was extracted by method A before treatment with glucuronidase, the symbol AG is used.

Extraction.—Extracts were made by shaking the hydrolysed urine with four aliquots of chloroform (0.1 volume per volume of urine, but not less than 100 ml. per aliquot). Emulsions were broken by centrifugation.

Alkali Wash.—All chloroform extracts except those designated AU in Table I were cooled to 5° C. and washed twice with cold 0.1 N solution of sodium hydroxide and once with cold distilled water. The combined aqueous washings were acidified and re-extracted with chloroform only in a few instances (Table I). Chloroform was removed under reduced pressure below 40° C. Extracts were stored in 95% ethanol at 0° C.

Chromatography.—The system used was toluene-propylene glycol (Burton *et al.*, 1951). "Fraction E" is that which contains cortisone and aldosterone in this system. In a few instances other systems described by Bush (1952) were also used.

Bioassay.—The method was described by Johnson (1954). Groups of nine adrenalectomized rats were used. Results are expressed as that dose of deoxycortone acetate (D.C.A.) which would produce in the rats an equivalent response in urinary potassium-to-sodium ratio. The 95% confidence limits of this estimate are ±2.15 μg. D.C.A. in a range of dosage from 0 to 10 μg. D.C.A. assayed in a group of nine rats. In all assays the effect on sodium output has also been calculated, and has been found to agree well with the more precise estimates based on potassium-to-sodium ratio. The term "sodium-retaining activity" has been used because this is the predominant effect measured in the bioassay. In those instances in which the test material caused increased excretion of sodium the estimate of dosage as μg. D.C.A. has a minus sign.

The dose of extract given to each rat is a known fraction of the patient's 24-hour urine extract. Each dose is expressed in minutes; for example, 20 minutes is 1/72 of the extract from one day's urine (1,440 minutes).

Effect of pH and Alkali Wash

Extracts made from urine at *p*H 6.5 showed insignificant sodium-retaining activity in a dose of 20 minutes (Table I, N). When the same urine was acidified to *p*H 1 before extraction, significant activity was found in 20-minute doses from two patients (Ro., nephrosis with oedema, extracts AU and A; Ph., cirrhosis with ascites, extract A), but not in the extract from a healthy man (Lj., extracts AU and A). Insignificant difference in activity was noted between active extracts which had been washed with cold dilute sodium hydroxide and water (A) and those extracts which had not been washed (AU). No sodium-retaining material was recovered from re-extraction of the alkali wash. Since washing with alkali removed much pigment and other material from the extract, and thus facilitated handling and chromatography, this procedure has been followed routinely with all extracts.

TABLE I.—*Effect of pH and of Alkali Wash on Sodium-retaining Activity of Urine Extracts. Effect on K/Na Ratio in μg. D.C.A. Equivalent. Dose=20 Minutes*

Subject	Age and Sex	Diagnosis	Extract at *p*H 6·5 (N)	Extract at *p*H 1 (AU)	Extract AU after Alkali Wash (A)	Extract of Alkali Wash
Ro.	4 M	Nephrosis	0·2	8·1	8·2	−0·9
Jo.	2 M	,,	—	8·4	8·3	0
Pe.	4 M	,,	—	1·5	0·2	−0·2
Ph.	48 M	Cirrhosis	1·9	—	3·3	—
Lj.	40 M	Normal	−0·8	−0·1	−4·0	−2·3

Activity of Various Extracts in Normal Adults on Usual Diet

Luetscher and Johnson (1954b) found that extracts made by method A from the urine of 11 normal men and women on unrestricted diets either showed no significant sodium-retaining activity or promoted the excretion of sodium in adrenalectomized rats (range +0.5 to −7.2 μg., mean −2.8 μg. D.C.A. per 20 minutes of extract). When such extracts were chromatographed in toluene and propylene glycol, fraction E contained no appreciable activity at doses of 33 minutes. Results of further studies in three of these normal adults are included in Table II. When the dose of "fraction E" of the A extract was increased to 167 minutes there was still no activity (Cases Lj., Ab., and Da.). However, extracts made from the same urine by method B contained strong sodium-retaining activity in fraction E at a dose of 167 minutes. Insignificant activity was found in fraction E prepared from one of these urines after incubation with glucuronidase.

Extracts from Adults on Diets Low in Sodium

It has been reported that when normal men reduced their dietary sodium to 11 mEq a day for five days there was consistently an increase in sodium-retaining activity of the A extracts, but the level reached was not high (Luetscher and Johnson, 1954b). In Lj., on his usual diet (Table II), the activity of the A extract was −4.0 μg., and on a low-sodium diet it rose to +1.4 μg. per 20-minute dose, and significant activity appeared in fraction E. In the extract prepared by method B, five times as much aldosterone was found with salt restriction, for on bioassay the effect produced by a dose of 30 minutes was the same as that produced by a dose of 167 minutes when the subject was on his usual diet. Likewise, on salt restriction, glucuronidase released additional sodium-retaining material (extract AG), which appeared in fraction E on chromatography. Since incubation of urine without glucuronidase at *p*H 4.8 and 37° C. for four hours (extract ACg) did not release appreciable sodium-retaining material, it appears that the addition of glucuronidase was responsible for the observed activity in extract AG. Observations on two other normal men (Cases Ab. and Jb., Table II) resemble those in Case Lj.

Activity of Various Extracts in Heart Failure and Hepatic Cirrhosis

Studies were made on urine of three patients in whom congestive heart failure was associated with a marked reduction of sodium excretion (Table III). In Case Bu., extracts A and B contained far more active material than comparable extracts from normal adults on a similar sodium intake, for in doses of only 20 minutes there was highly significant activity. Glucuronidase (AG) released much additional active material, while a smaller but significant yield was obtained from the control (ACg) incubated without glucuronidase at 37° C. and *p*H 4.8 for 24 hours. When

these extracts were chromatographed, activity was found in fraction E in each instance. In Case Ta., similar results were obtained from extracts A and AG. Case Lo. again demonstrates the appearance of much activity after 24 hours at *p*H 1.

Two patients, We. and Ph., had Laennec's cirrhosis with ascites and impaired excretion of sodium (Table III). In both cases, extracts A and B contained strong activity, which could be found in fraction E after chromatography.

Activity of Extracts in Children

Previous studies of four normal children on unrestricted diets showed insignificant activity in A extracts at doses of 20–33 minutes (Luetscher and Johnson, 1954a). Extracts made by method B contained measurable activity when the dose was increased to 167 minutes. When the three methods of hydrolysis were compared in one case (Rg., Table IV), method B released aldosterone in an amount only slightly less than that found in normal adults, but extracts A and G did not contain amounts measurable in the dosages given.

Three children with oedema due to the nephrotic syndrome were studied (Table IV). The A extracts showed strong activity in two cases, while the third was not significantly active. The B extracts were highly active, and so were the fractions E derived from them. Compared with that from a normal child these B extracts from nephrotic children contained much more aldosterone; for on bioassay the effects of doses of 20 and of 33 minutes were greater than that produced by a dose of 167 minutes from the normal child.

In one case (Co.) the substance responsible for the sodium-retaining activity was isolated from extracts prepared by methods A and B. In each instance a corticosteroid indistinguishable from aldosterone was obtained.

In Case Ro. the fraction E derived from urine incubated with glucuronidase (G) showed strong activity. When this

TABLE II.—*Sodium-Retaining Activity in Various Extracts of Urine from Normal Adults on Usual Diet and on Sodium Restriction*

Subject	Age and Sex	Sodium mEq/day		Method of Hydrolysis	Sodium-retaining Activity μg. D.C.A. Equivalent/Dose	
		Diet	Urine		Extract	Fraction E
Lj.	40 M	Usual	155	Acid (A)	−4·0/20 mins.	0·5/167 mins.
				,, (B)	—	10·3/167 ,,
				Glucuronidase[1] (G)	—	1·9/167 ,,
		11	7	Acid (A)	1·4/20 mins.	2·9/60 ,,
				,, (B)	—	10·5/30 ,,
				Glucuronidase[2] (AG)	5·1/20 mins.	7·0/33 ,,
				,, control (ACg)	−1·9/20 ,,	—
Ab.	28 M	Usual	149	Acid (A)	—	−2·1/167 mins.
				,, (B)	—	6·4/167 ,,
		11	23	,, (A)	—	0·9/130 ,,
				,, (B)	—	7·7/33 ,,
Jb.	31 M	11	2	,, (A)	—	1·6/33 ,,
				Glucuronidase[3] (AG)	—	3·0/33 ,,
Da.	31 F	Usual	74	Acid (A)	—	−0·8/167 ,,
				,, (B)		12·2/167 ,,

[1] Warner-Hudnut 200 units per ml. for 24 hours. [2] Warner-Hudnut 400 units per ml. for 4 hours. [3] Vio-Bin 100 units per ml. for 47 hours.

TABLE III.—*Sodium-Retaining Activity in Extracts of Urine from Patients with Congestive Heart Failure or Hepatic Cirrhosis with Ascites*

Subject	Age and Sex	Diagnosis	Sodium mEq/Day		Method of Hydrolysis	Sodium-retaining Activity μg. D.C.A. Equivalent/Dose	
			Diet	Urine		Extract	Fraction E
Bu.	18 M	Aortic insufficiency	102	4·8	Acid (A)	5·8/20 mins.	4·4/33 mins.
					,, (B)	13·2/20 ,,	10·0/20 ,,
					Glucuronidase[1] (AG)	9·6/20 ,,	6·6/33 ,,
					,, control (ACg)	5·6/20 ,,	4·8/33 ,,
Ta.	41 F	Mitral stenosis	68	1·2	Acid (A)	3·2/20 ,,	3·4/33 ,,
					Glucuronidase[2] (AG)	—	7·4/33 ,,
Lo.	42 M	Aortic stenosis	345	1·8	Acid (A)	—	−2·0/33 ,,
					,, (B)	—	12·6/33 ,,
We.	42 M	Laennec's cirrhosis	85	1·7	,, (A)	8·2/20 mins.	8·2/33 ,,
					,, (B)	—	10·8/33 ,,
Ph.	48 M	,, ,,	51	3·3	,, (A)	3·3/20 mins.	—
					,, (B)	8·0/20 ,,	—

[1] Warner-Hudnut 200 units per ml. for 24 hours. [2] Vio-Bin 85 units per ml. for 69 hours.

TABLE IV.—*Sodium-Retaining Activity in Extracts of Urine from a Normal Child and Three Cases of the Nephrotic Syndrome*

Subject	Age and Sex	Diagnosis	Sodium mEq/Day		Method of Hydrolysis	Sodium-retaining Activity μg. D.C.A. Equivalent/Dose	
			Diet	Urine		Extract	Fraction E
Rg.	4 M	Normal	Usual	49	Acid (A)	0·5/20 mins.	0·8/33 mins.
					,, (B)	—	5·7/167 ,,
					Glucuronidase[1] (G)	—	−0·1/33 ,,
Co.	10 M	Nephrosis	Low	0·8	Acid (A)	8·4/20 mins.	6·3/20 ,,
					,, (B)	10·4/20 ,,	10·8/20 ,,
Ar.	4 M	,,	,,	1·7	,, (A)	1·6/20 ,,	—
					,, (B)	10·3/20 ,,	8·0/33 mins.
Ro.	4 M	,,	,,	0·5	,, (A)	8·2/20 ,,	14·1/33 ,,
					Glucuronidase[2] (AG)	—	15·7/33 ,,
					Glucuronidase[3] (G)	—	5·7/33 ,,
					Acid (A) after (G)	—	13·0/33 ,,

[1] Vio-Bin 100 units per ml. for 48 hours. [2] Vio-Bin 150 units per ml. for 70 hours. [3] Vio-Bin 275 units per ml. for 48 hours.

urine was first extracted after exposure to acid by method A and then incubated with glucuronidase, a very highly active extract was obtained (AG). However, the actual amount of activity in these two glucuronidase extracts cannot be compared, because of the different times of incubation. There were similar amounts of activity in the two "immediate acid" extracts A, and acid A after G, although one was prepared in the usual way and the other after the glucuronidase extract had been made from it. These observations suggest that there are at least two forms of conjugated aldosterone, one form being more readily hydrolysed by acid, and the other by glucuronidase.

Discussion

There are obviously two separate factors which affect the activity of urinary extracts. These are the method of hydrolysis and the amount of active material present in the urine.

Effects of Methods of Hydrolysis on Yield.—In all cases studied, the sodium-retaining activity of the extract increased with time of exposure to strong acid. Negligible activity appeared in extracts of neutral urine. Extracts prepared after 40 minutes at *p*H 1 were more likely to contain active material; while a second extraction after 24 hours' exposure to *p*H 1 regularly produced strongly active material. In one instance incubation at *p*H 4.8 and 37° C. for 24 hours yielded the same amount of activity as brief exposure to *p*H 1 at 20° C. These results parallel the enhanced extraction of glucocorticoids after acidification of urine (Venning *et al.*, 1953). Beta-glucuronidase, prepared from mammalian spleen or liver, released active material in amounts equal to or greater than the initial extract at *p*H 1, but less than the quantity obtained after a day at *p*H 1. Although some of the active material was liberated by the physical conditions rather than by the enzyme, controlled experiments indicate that the beta-glucuronidase was responsible for a part of the yield. These results again resemble the effects of glucuronidase on the release of biologically active glucocorticoids, as described by Venning *et al.* (1953).

Factors Influencing Output in Urine.—The sodium-retaining activity of the various extracts was increased when dietary sodium was reduced or when the presence of disease of the heart, liver, or kidneys was associated with abnormal sodium retention. In all these cases high sodium-retaining activity was associated with low urinary sodium. These findings and other data (Luetscher and Johnson, 1954b) suggest that sodium-retaining activity of urinary extracts reflects the intensity of conservation of sodium by the body; and it appears that the stimulus to conserve sodium can be evoked in health by sodium deprivation, and in some diseases by an as yet ill-defined mechanism.

Identity of Active Material with Aldosterone.—In previous work, cited above, it has been shown that the purified active material obtained from urine in nephrosis has properties identical with those of aldosterone. This finding was confirmed with two extracts from one patient in the present work. In the other subjects, both in health and in disease, the sodium-retaining activity consistently appeared in fraction E on chromatography. Aldosterone is the only known corticosteroid in this fraction which causes sodium retention in the assay used. In several instances fractions have been carried through additional chromatographic systems described by Bush (1952) as B_2, B_5, and C. In each case the active fraction from urine has moved at the same rate as samples of authentic aldosterone, and has shown similar pharmacological properties. For all these reasons it is presumed that the active material is aldosterone in each instance both in normal men and in patients, and when released by brief or prolonged exposure to acid or by glucuronidase.

Summary

The amount of sodium-retaining corticoid that can be extracted from urine by chloroform depends partly on the method of hydrolysis. Of the procedures studied, the greatest yield was obtained from urine after standing for one day at *p*H 1. Smaller quantities were obtained after brief exposure to *p*H 1 or after incubation at 37° C. and *p*H 4.8. Mammalian beta-glucuronidase caused a further release of material. Insignificant activity was found in extracts from urine at *p*H 6.5.

When yields obtained by each method were compared, the sodium-retaining activity of urinary extracts was small but still measurable in health on unrestricted sodium intake. Reduction of dietary sodium was followed by increased sodium-retaining activity. Patients with congestive heart failure, hepatic cirrhosis, or the nephrotic syndrome had a high output of sodium-retaining material when the urinary sodium was low.

In all cases in which urine extracts were chromatographed, sodium-retaining material was found in a single fraction. The active component of this fraction was shown to be aldosterone in one case. It seems highly probable that the sodium-retaining corticoid with similar properties, found in the other cases, was aldosterone.

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References

Burton, R. B., Zaffaroni, A., and Keutmann, E. H. (1951). *J. biol. Chem.*, **188**, 763.
Bush, I. E. (1952). *Biochem. J.*, **50**, 370.
Chart, J. J., and Shipley, E. G. (1953). *J. clin. Invest.*, **32**, 560.
Cohen, S. L. (1951). *J. biol. Chem.*, **192**, 147.
Cope, C. L., and Garcia-Llaurado, J. (1954). *British Medical Journal*, **1**, 1290.
Deming, Q. B., and Luetscher, J. A., jun. (1950). *Proc. Soc. exp. Biol. (N.Y.)*, **73**, 171.
Gordon, E. S., Chart, J. J., Hagedorn, D., and Shipley, E. G. (1954). *Obstet. and Gynec.*, **4**, 39.
Johnson, B. B. (1954). *Endocrinology*, **54**, 196.
Luetscher, J. A., jun. (1955). *Recent Progress in Hormone Research*, **11**. In press.
—— and Axelrad, B. J. (1954). *J. clin. Endocr.*, **14**, 1086.
—— Deming, Q. B., and Johnson, B. B. (1952). *Ciba Foundation Colloquia on Endocrinology*, **4**, 530.
—— and Johnson, B. B. (1954a). *J. clin. Invest.*, **33**, 276.
—— —— (1954b). Ibid., **33**, 1441.
—— Neher, R., and Wettstein, A. (1954). *Experientia (Basel)*, **10**, 456.
Simpson, S. A., and Tait, J. F. (1953). *Memoirs of the Society for Endocrinology*, No. 2, p. 9, Dobson, London.
—— —— Wettstein, A., Neher, R., Euw, J. V., Schindler, O., and Reichstein, T. (1954). *Helv. chim. Acta*, **37**, 1163, 1200.
Singer, B., and Wener, J. (1953). *Amer. Heart J.*, **45**, 795.
Talalay, P., Fishman, W. H., and Huggins, C. (1946). *J. biol. Chem.*, **166**, 757.
Venning, E. H., Carballeira, A., and Dyrenfurth, I. (1954). *J. clin. Endocr.*, **14**, 784.
—— Dyrenfurth, I., and Kazmin, V. E. (1953). *Recent Progress in Hormone Research*, **8**, 27.

In its first annual report since its incorporation, the British Rheumatic Association describes plans for a study in a London borough "to see how many of the bed-ridden, institutionalized, and chair-bound rheumatic people could be equipped for employment in open industry or for independent living in the community." A grant for this work has been received from a charitable trust, and negotiations are proceeding with the Ministry of Health and the London County Council. Other subjects discussed in the report include the association's hostel (Bracken Hill House) for the investigation of industrial workers thought to be suffering from rheumatism; rehabilitation; and the production of a documentary film to teach patients with rheumatism how to help themselves. Last year the association's total income was £3,646, and a deficit of £720 was incurred on the year's working. However, in view of the great activity and change during the year, the honorary treasurer expressed "every confidence that there was no need to be alarmed about the financial situation."