RELATION BETWEEN DIURETIC AGENTS AND ALDOSTERONE IN CARDIAC AND CIRRHOTIC PATIENTS WITH SODIUM RETENTION

BY

J. PICTON THOMAS,* M.D., M.R.C.P.

AND

FREDERICK C. BARTTER, M.D.

Medical Director

Section on Clinical Endocrinology, National Heart Institute,
National Institutes of Health, Bethesda, Md., U.S.A.

The factors responsible for initial accumulation of oedema or ascites in patients with cirrhosis and cardiac disease still await precise definition, but the available evidence (Duncan *et al.*, 1956; Wolff *et al.*, 1957) suggests that aldosterone plays a secondary, compensatory role in these diseases. Thus excessive secretion of aldosterone is probably induced by a homeostatic mechanism (Bartter *et al.*, 1956), whereby an effective blood volume might be restored by renal retention of salt and water were not this fluid lost from the intravascular space.

Spironolactone ("aldactone") and hydrochlorothiazide, particularly in combination, have been shown to induce a satisfactory diuresis in many of these patients (Morrison, 1960; Gantt, 1960). Their effects, together with those of acetazolamide (Berliner *et al.*, 1951) and the organic mercurial diuretics (Axelrod and Pitts, 1952), may also be used to inquire into the mechanisms of renal tubular reabsorption of sodium.

The present studies were designed to investigate the interaction between aldosterone and these diuretic agents, and to estimate the effects of sodium and potassium loss on homeostasis, as estimated from changes in serum and urinary electrolytes, plasma volume, pulse pressure, and urinary aldosterone. Similar studies were performed with prednisolone and the sympatholytic agents, dibenamine and phenoxybenzamine hydrochloride.

Case Histories

Seven patients were included in this study—three with cirrhosis and ascites, and four with congestive heart failure. They were chosen because their urinary excretion of sodium was less than 5 mEq/day. Brief histories summarize the important features in each case.

Case 1.—A well-built 32-year-old negro man had primary myocardial disease and right heart failure, resulting, over a period of two years, in massive dependent oedema. He had sinus tachycardia with hypotension (blood-pressure 100/80), pulsatile neck veins, a large inactive heart, with a loud third heart sound and a subternal systolic murmur. Oedema extended to the thighs, and ascites produced moderate orthopnoea. Digoxin, 0.5 mg. a day, was given during all metabolic studies.

Case 2.—A 56-year-old woman had had rheumatic heart disease with mitral incompetence and progressive heart failure over a period of 14 years. Her blood-pressure was 155/75; slow fibrillation, enlargement of both ventricles, and a marked systolic thrill and murmur were present, together with a large firm liver, considerable ascites, and some pitting oedema. Digoxin, 0.5–1 mg. a day, was given during all metabolic studies.

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Case 3.—A large 22-year-old man had shown evidence of primary myocardial disease with severe cardiac failure for one year before admission. He had sinus tachycardia and a large inactive heart with a loud third heart sound. His blood-pressure was 118/100. Oedema extended to mid-trunk and marked ascites was present. The electrocardiogram showed an old anterior myocardial infarct. Digitalis was discontinued on admission.

Case 4.—A 47-year-old woman had rheumatic heart disease with dominant aortic and mitral incompetence. Congestive failure had first appeared four years before admission, but was adequately controlled by digitalis and diuretics. Slow fibrillation, marked left ventricular hypertrophy, and multiple valvular lesions were present. Her blood-pressure was 118/60; she had some ascites and peripheral oedema. Digoxin, 0.5 mg. a day, was given during all metabolic studies.

Case 5.—A 42-year-old man had consumed large quantities of alcohol over 20 years. He had developed intractable ascites two months before admission. He was cachectic, with stigmata of cirrhosis and marked ascites. His blood-pressure was 110/70. Hepatic precoma necessitated antibiotic therapy throughout his stay. The serum albumin/globulin ratio was 1.5:3.3, the bilirubin 1.4 mg./100 ml., and the serum creatinine 0.8 mg./100 ml.

Case 6.—A 45-year-old woman had been a chronic alcoholic for many years. Massive ascites had developed two years before admission, and had proved resistant to sodium restriction and diuretics. She was emaciated, with signs of cirrhosis and ascites. Her blood-pressure was 120/80. The serum albumin/globulin ratio was 2.1:3.7, the bilirubin 0.4 mg./100 ml., and the serum creatinine 0.6 mg./100 ml.

Case 7.—A 50-year-old woman was admitted to hospital a year prior to her study for cholecystectomy to terminate a carrier state of *Salmonella typhosa*. Liver biopsy at operation revealed Laennec's cirrhosis, and the patient later developed marked ascites. There were no spider naevi, but a firm liver and marked ascites were present. The albumin/globulin ratio was 2.4:3.3, the serum bilirubin 0.6 mg./100 ml., and the serum creatinine 0.8 mg./100 ml.

Methods

Sedentary activity was permitted within an air-conditioned metabolic unit. Each patient was given a constant diet containing 9 mEq sodium a day and a constant volume of distilled water. Two patients (Cases 2 and 5) were unable to tolerate addition of sodium to their diets, but the remainder received an extra 41 mEq of sodium, as NaCl, to make a daily total of 50 mEq.

Before collections were started, three days were allowed for equilibration. The administration of any diuretic agent was preceded and followed by four "control" days. Urine was collected in 24-hour lots. Each drug was given in divided doses and at constant intervals over the 24-hour period. Body weight was determined daily, and plasma volume and urinary aldosterone were determined for each new regimen. If potassium loss was induced by any drug, an equivalent quantity was returned by mouth, as potassium chloride, before a new agent was administered.

Serum and urinary sodium and potassium were measured by an internal standard (LiCl) flame photometer and creatinine by the method of Bonsnes and Taussky (1945). Analysis of serum, collected under oil for carbon dioxide content, was performed by the method of Van Slyke and Stadie (1921). Plasma volume was determined by a technique described by Thomas and Bartter (1961) which utilizes I-131 human serum

albumin. Urinary aldosterone was determined by the double isotope dilution of Kliman and Peterson (1960).

Results

Comparison was made of the effects of hydrochlorothiazide and of spironolactone, alone and in combination, over four- or eight-day periods in six patients. The results are shown in Tables I and II.

TABLE I.—Effects of Diuretic Agents on Fluid and Electrolyte Balance and Aldosterone

Case No.	Drugs	mg.	Duration (days)	Serum Na (mEq/l.)	Serum K (mEq/l.)	Total Na† Increment (mEq)	K† Increment (mEq)	Plasma Volume (ml.)	Urinary Aldosterone (μg./day)	Weight Change (kg.)
1	HD	200	8	141*	4.5*	1,053	221	3,940*	8.0*	-6.45
	S	400	4	138*	3.5*			3,780*	21.0*	
	HD	200	8	143	4.5	0	0	4,290	33.0	0
2	HD	100	8	132	5.0	15	245	4,150	33.0	-1.49
	S	400	4	134	4.9			4,054	22.5	
	HD	100	8	130	4.5	0	15	4,120	56	-3.65
3	HD	200	4	137	4.0	530	374	5,850	148	
	S	200	4	137	4.5			6,330	20.7	-3.60
	HD	200	4	141	4.2	11	10	6,330	—	+1.22
4	HD	100	4	141	4.4	441	347	4,880	23.3	-2.03
	S	200	4	139	3.0			4,760	15.5	
	HD	100	4	141	4.4	11	42	—	—	-0.56
5	HD	100	4	133	4.8	2	358	2,910	152	0
	S	200	4	129	2.8			3,100	42.3	
	HD	100	4	134	4.8	50	18	—	—	-0.78
6	HD	100	8	141	4.7	387	556	2,684	109	-1.15
	S	200	8	141	2.9			2,606	20.5	
	HD	100	8	145	4.9	1,174	70	2,732	44.5	-3.71
7	HD	100	8	136	4.2	1,635	145	2,462	153	
	S	200	8	145	5.2			2,753	63	-6.96
	P	40	4	135	4.4			2,450	155	

HD = Hydrochlorothiazide. S = Spironolactone. P = Prednisolone.

* Each vertical pair of figures indicates the value before and after treatment.
† Total sodium and potassium increment represents the difference between periods of therapy and pretreatment control.

TABLE II.—Influence of Spironolactone and SC 8109. An Analogue of Spironolactone on Fluid and Electrolyte Balance and Aldosterone

Case No.	Drug	Dose	Duration in Days	Serum Na (mEq/l.)	Serum K (mEq/l.)	Total Na In-crement (mEq)	Total K In-crement (mEq)	Plasma Volume (ml.)	Urinary Aldosterone (μg./day)	Weight Change (kg.)
4	S	800 mg.	4	141*	4.4*	190	21	4,640	56	-4.16
	S	1,600 mg.	4	136*	4.0*			4,480	75.7	
5	S	1 g.	4	129	3.4	296	0	2,620*	29.4*	-2.20
	S	1 g.	4	134	3.7			2,480*	38.4*	
6	S	1 g.	4	131	4.5	410	0	2,680	124	-3.27
	S	1 g.	4	135	5.2			2,524	82	
7	S	1 g.	4	136	5.1	766	2	2,680	61	-3.28
	S	1 g.	4	139	4.8			2,540	98.5	
8	SC 8109	1 g.	9	143	5.2	1,078	30	2,900	65	-3.15
	SC 8109	1 g.	9	138	6.1			2,700	100	

* See footnote to Table I.

Hydrochlorothiazide.—A marked loss of potassium and a fall in serum potassium were observed in each case, and a satisfactory natriuresis occurred in Cases 1, 3, and 4 (Table I). Case 6 lost potassium in excess of sodium, and no sodium diuresis was observed in Case 2 or Case 5. Except in Case 1, in whom initial values were normal, urinary aldosterone fell in each case. These changes were associated with expansion of plasma volume in Case 3, who lost a large amount of sodium, and in Case 5, who lost none; there was some contraction of plasma volume in Cases 2, 4, and 6. Kaliuresis was most marked on the first two days of drug therapy, and further loss of potassium did not occur even when the dosage of hydrochlorothiazide was increased (Fig. 1).

Hydrochlorothiazide and Spironolactone.—In each patient the dose of hydrochlorothiazide that had been given alone was combined with spironolactone in ratios of 1:1 to 1:4 (Table I). Conservation of potassium, with only a slight fall in serum potassium, and enhancement of sodium diuresis were consistently observed; thus Cases 2 and 5 now obtained a good diuresis of sodium with diminished potassium loss. Urinary aldosterone appeared to be governed by the relative changes in serum potassium and plasma volume: aldosterone excretion rose in the two studies (Cases 4 and 6) which showed the least fall in serum potassium, and fell in the others.

Spironolactone.—Spironolactone, given alone, produced minimal sodium loss in the cardiac patients and moderate sodium diuresis in the patient with cirrhosis (Case 5), who received small doses of this drug (Table I). An interesting contrast was observed between the responses of patients with heart disease and those of patients with cirrhosis to larger doses of spironolactone (Fig. 2). The cardiac patients, with the exception of Case 4, showed almost complete resistance to daily doses of 1.6 to 2 g. over three to four days. Abdominal pain and dyspepsia were experienced by each patient on this high dosage. In contrast, the patients with cirrhosis on doses of 1 g. of spironolactone, and Case 4, on doses of 800 to 1,600 mg., showed a marked sodium diuresis

FIG. 1.—Case 6. Effects of hydrochlorothiazide (HD) alone.

(Fig. 2). No change of potassium excretion occurred, and decreases of plasma volume and pulse pressure were accompanied by significant increases of urinary aldosterone (Table II).

Prednisolone.—Seven patients received this steroid in daily doses of 40 mg. for a minimal period of 10 days. Sodium diuresis occurred in only one (Case 3) of the patients with cardiac failure, and in two patients with cirrhosis (Cases 6 and 7). In two of these patients

FIG. 2.—Relationship between spironolactone and sodium excretion in patients with cirrhosis and cardiac failure.

(Cases 3 and 6) a latent period of six or seven days preceded the onset of sodium diuresis, and during this interval a marked fall of urinary aldosterone was observed in both patients. Thus, in Case 3 (Fig. 3) urinary aldosterone fell from a mean value of 67 μ g./day to 20 μ g./day before the onset of a massive sodium diuresis. In Case 6 (Fig. 4) the urinary aldosterone fell from a mean value of 169 μ g./day to 50 μ g./day before the urinary sodium rose to equal the intake of 50 mEq daily. Sodium diuresis was enhanced when prednisolone was added to hydrochlorothiazide and spironolactone in Case 6 (Fig. 4), but not in Case 5, who proved resistant to prednisolone.

Sympatholytic Agents.—Phenoxybenzamine, in doses of 60 mg. daily for three or four days, and dibenamine, given as a single intravenous dose of 250 to 300 mg. over two hours, were ineffective in producing sodium diuresis in cardiac or cirrhotic patients (Table III).

FIG. 3.—Case 3. Effects of prednisolone on aldosterone and electrolyte balance.

FIG. 4.—Case 6. Effects of hydrochlorothiazide (HD) in combination with spironolactone (S) and prednisolone.

TABLE III.—Relationship Between Sympatholytic Drugs and Sodium Excretion

Case No.	Dibenamine Intravenously		Phenoxybenzamine Orally		
	Dose	Total Na Excretion (mEq)	Dose	Days	Total Na Excretion (mEq)
1	—	—	30 mg.	3	0
2	250 mg.	0	50 „	3	4
3	300 „	0	—	—	—
4	300 „	4	—	—	—
5	250 „	0	60 „	3	0

Discussion

A schema illustrating current concepts regarding renal sodium and potassium excretion in normal subjects and in patients with primary and secondary aldosteronism is shown in Fig. 5 (Bartter, 1956). About 85% of filtered sodium and all filtered potassium (Berliner *et al.*, 1951) are reabsorbed in the proximal tubules (Fig. 5, A). The majority of the remaining sodium is then actively

FIG. 5.—Renal sodium and potassium excretion in normal subjects (A) and in patients with primary (B) and secondary (C) aldosteronism. Numbers at top of each diagram represent the glomerular filtration rate in ml./min.

reabsorbed in the distal tubules, in exchange for potassium or hydrogen ions, under the influence of a physiological quantity of aldosterone. Active reabsorption of sodium in the loops of Henle (not shown) produces "free" water. Distal ion exchange is enhanced by an excess of aldosterone in primary aldosteronism (Fig. 5, B). The increased reabsorption of sodium produces an expansion of extracellular fluid volume and an increase of glomerular filtration, and these changes, in turn, further magnify exchange in the distal tubules, to produce potassium loss and hypokalaemic alkalosis. Oedema is rare (Goldsmith *et al.*, 1960), but severe renal damage may follow prolonged potassium depletion. In contrast, most of the filtered sodium is reabsorbed proximally in oedematous patients with secondary aldosteronism. Little sodium reaches the distal tubules and exchange for potassium is limited (Fig. 5, C). Thus, despite an increased secretion of aldosterone, potassium depletion does not occur in untreated patients. For the same reason, free water clearance is also limited, and this may lead to a state of hyponatraemia in patients with cirrhosis (Schedl and Bartter, 1960) and cardiac failure (Bell *et al.*, 1960).

By the technique of "stop flow" analysis in dogs, Vander *et al.* (1959) found that electrolyte exchange in the distal tubules was unimpaired with chlorothiazide, and concluded that chlorothiazide acted maximally on the proximal tubules to inhibit reabsorption of sodium and chloride. Thus chlorothiazide and its derivatives may allow large quantities of sodium to reach the distal tubules in oedematous patients, but active exchange of sodium for potassium at this site, induced by an excess of aldosterone, may curtail sodium excretion and produce substantial loss of potassium. This result was observed, to a varying degree, in both types of patients studied here, and produced some interesting changes in urinary aldosterone and plasma volume. An inhibitory effect of potassium depletion on aldosterone excretion was demonstrated by Laragh and Stoerk (1955) in dogs and by Bartter (1956) in normal subjects. In the present studies, despite contraction of the plasma volume in three patients, hypokalaemia and potassium loss was associated with a marked decrease of urinary aldosterone. However, this decrease of aldosterone, even to normal values, was not accompanied by any increase of sodium excretion. Conservation of sodium during potassium depletion has been documented (Black and Milne, 1952; Womersley and Darragh, 1955) but never adequately explained. The expansion of plasma volume which occurred in two patients, one of whom had lost over 500 mEq of sodium, is difficult to explain, and suggests a transfer of sodium from cells or from bone.

The spironolactone compounds, synthesized by Cella and Kagawa (1957), have been shown to block the tubular action of aldosterone (Liddle, 1958; Gantt, 1960). In the present studies, spironolactone apparently inhibited electrolyte exchange in the distal tubules, and, in combination with hydrochlorothiazide, produced sodium diuresis without appreciable loss of potassium. Contraction of plasma volume now induced further secretion of aldosterone (Table I), but hypokalaemia or potassium depletion inhibited this response. There was a 24- to 48-hour delay in the action of spironolactone, which probably accounts for the initial potassium loss when chlorothiazide and spironolactone are given together (Shaldon *et al.*, 1960). Potassium loss with hydrochlorothiazide alone, however, was maximal on

the first two days and was not accentuated by increments of dosage (Fig. 1). Further, spironolactone, given for two days preceding and during treatment with hydrochlorothiazide, did not entirely prevent this early loss of potassium.

Spironolactone alone, in doses of 100 to 400 mg. a day, produced little sodium loss in these patients, but this drug or its analogue, SC 8109, produced considerable sodium diuresis in patients with cirrhosis, in doses of 1 g. daily over periods of four to eight days (Fig. 6). In contrast to the results with hydrochlorothiazide, no significant change of potassium excretion occurred with these diuretic agents, so that it was possible to observe the relative changes of plasma volume and aldosterone excretion after diuresis of sodium alone. In each patient a decrease of plasma volume was associated with a rise in urinary aldosterone.

Studies by Eisenberg (1956) showed that expansion of plasma volume in patients with cirrhosis was dependent upon the presence of a dilated collateral circulation, and preceded the appearance of ascites. Thus accumulation of ascites at a later date may occur at the expense of circulating plasma to produce a relative contraction of plasma volume.

An increase of aldosterone secretion in dogs follows a reduction of arterial pulse pressure (Gann *et al.*, 1960). A similar mechanism may explain the rise of aldosterone secretion which follows decrease in plasma volume. This mechanism may be activated as ascites first develops, and accentuated by sodium loss induced by diuretics or on rapid accumulation of ascites after paracentesis (Wolff *et al.*, 1958). The evidence therefore suggests that aldosterone plays an important part in sodium reabsorption by the proximal and distal tubules, and may determine continued conservation of sodium in patients with cirrhosis and established ascites.

The patients with cardiac failure showed a marked difference from those with cirrhosis in their response to spironolactone. Thus large doses of spironolactone (1.6

FIG. 6.—Case 6. Effects of spironolactone (S) and SC 8109 on fluid and electrolyte balance and aldosterone.

to 2 g. daily) produced little sodium loss in three patients with cardiac failure (Fig. 2). Urinary aldosterone values were comparable with those of normal subjects on similar dietary sodium intake in Cases 1 and 2, whereas Case 3 showed a markedly elevated aldosterone excretion. This suggests that sodium reabsorption may be essentially independent of aldosterone in congestive heart failure. However, the fact that one patient with cardiac failure (Case 4, Table II) obtained significant sodium diuresis with smaller doses of spironolactone (800 to 1,600 mg.) indicates that the mechanism of sodium retention in this patient differed from that of the other cardiac patients.

To determine whether the difference was at the renal level we performed tests of renal function in Cases 1, 2, and 4. Normal values for serum creatinine and blood urea nitrogen indicated that renal function was adequate in all patients. Clearances of inulin (Walser *et al.*, 1955) and of para-aminohippurate (Bratton and Marshall, 1939) were performed, and mean values for glomerular filtration rate (G.F.R.) and renal plasma flow (R.P.F.) obtained for five consecutive periods after adequate equilibration (Table IV). The filtration

TABLE IV.—Renal Function in Three Patients with Congestive Heart Failure

Case No.	G.F.R. (ml./min.)	R.P.F. (ml./min.)	Filtration Fraction	Blood Urea Nitrogen (mg./100 ml.)	Serum Creatinine (mg./100 ml.)
1	92	241	38.2	7	0.9
2	85	246	35.0	8	0.8
4	68	288	23.6	9	0.8

fraction (F.F.), derived from these latter values, was found to be within normal limits in Case 4, but markedly elevated in the other two patients.

Merrill (1946) and Mokotoff *et al.* (1948) demonstrated a marked decrease of G.F.R. and R.P.F. in congestive heart failure, and postulated that sodium retention was due primarily to a reduction of glomerular filtration. Since the quantity of sodium presented to the tubules is reduced, an impairment of G.F.R. must participate in sodium retention, but the inconstant relationship between the filtered sodium load and sodium excretion in congestive heart failure has indicated that other factors may also be involved in sodium reabsorption. In fact, the studies of Seymour *et al.* (1942) and those of Heller and Jacobson (1950) in patients with heart failure strongly suggested that the essential defect, in congestive failure, as regards renal function, was a reduction of R.P.F. with an increase of the filtration fraction; values for G.F.R. obtained during congestive failure did not differ significantly from those obtained after recovery.

The precise relationship between the observed increase of filtration fraction and sodium reabsorption by the proximal tubules has not been evaluated, but this relationship, which is probably independent of aldosterone, could account for sodium retention in the three patients with congestive failure who proved to be resistant to spironolactone.

If, despite gross decrease of G.F.R. and R.P.F., the filtration fraction is still within normal limits, proximal sodium reabsorption may be controlled to a greater extent by aldosterone. Sodium retention could be explained on this basis in Case 4, and also in patients with cirrhosis in whom estimations of renal function are reported to be normal (Patek *et al.*, 1948; Goodyer *et al.*, 1950), and response to aldosterone antagonists generally good.

Limitation of free water clearance in patients with cirrhosis and ascites was found to be related to the restricted quantity of sodium and water reaching the distal tubules (Schedl and Bartter, 1960). Inhibition of proximal sodium reabsorption should correct this defect, and free water excretion was increased (without change in intake or metabolic regimen) in Case 6 during the administration of spironolactone and SC 8109.

Maintenance of G.F.R. in the presence of marked reduction of R.P.F. suggests vasoconstriction of the efferent glomerular vessels. If this occurs it may reflect an autoregulation of renal haemodynamics in response to a decrease of cardiac output, or represent a local manifestation of the generalized vasoconstriction observed in congestive heart failure (Relman and Epstein, 1949).

To evaluate the latter concept, Barger *et al.* (1959) infused phenoxybenzamine into one renal artery of dogs with experimental cardiac failure. A unilateral sodium diuresis ensued, and this suggested that vasoconstriction was initially induced by an excess of circulating catechol amines. Interpretation of this result must be guarded, however, since normal values of urinary catechol amines have been shown in patients with heart failure. It is conceivable that local infusion of phenoxybenzamine may have induced other renal haemodynamic changes.

After intravenous infusion of dibenamine, Fejfar (1958) noted an increase of cardiac output and R.P.F. in patients with congestive heart failure, and ascribed the change to a decrease of peripheral vascular resistance. He stated that these changes were associated with a diuresis of chloride. We were unable to demonstrate any sodium loss (Table III) in three such patients given similar quantities of dibenamine intravenously, and no diuretic response was observed with a related compound, phenoxybenzamine, given by mouth.

Medication with prednisolone was continued for one week before it was decided that a patient was unresponsive to the drug. During this interval four patients showed insignificant changes of urinary aldosterone or sodium excretion, but in Cases 3 and 6 prednisolone produced a decrease of aldosterone excretion before the occurrence of sodium diuresis (Figs. 3 and 4). On this basis it also contributed to the sodium diuresis produced by hydrochlorothiazide and spironolactone. A maintenance dose of prednisolone, 15 mg a day, was continued in Case 6. The ascites disappeared, and, on withdrawal of the drug after six months, normal sodium balance was restored. This result confirms similar reports by Cattani and Vesin (1957), who noted this response in a large group of patients with cirrhosis.

Case 5 lost his ascites on a combination of hydrochlorothiazide and spironolactone, but experienced severe postural hypotension with continued therapy. Since spironolactone blocks the action of aldosterone on the renal tubules, severe salt depletion may follow sodium diuresis. Intermittent dosage is therefore necessary for maintenance therapy with this drug.

Summary

Hydrochlorothiazide produced a marked loss of potassium in oedematous patients, particularly during the first two days of therapy. Despite the decrease of aldosterone secretion so produced, sodium excretion was limited, presumably as a result of potassium depletion.

The addition of small doses of spironolactone permitted sodium diuresis with limited potassium loss, presumably by blocking electrolyte exchange in the distal tubules.

Corresponding doses of spironolactone, given alone, produced minimal sodium loss.

Large doses of spironolactone were ineffective in three patients with cardiac failure, but produced marked sodium loss in one patient with cardiac failure and in two patients with cirrhosis and ascites.

Aldosterone alone may account primarily for the sodium retention in patients with cirrhosis and established ascites, and may be the dominant factor also in some cases of congestive heart failure.

In most patients with congestive failure, changes of renal haemodynamics may be responsible for sodium retention. Our results suggest that these haemodynamic changes were not induced by an excess of circulating catechol amines.

Patients who responded to prednisolone showed a decrease of urinary aldosterone followed by a sodium diuresis.

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PORTABLE ANAESTHETIC APPARATUS FOR USE IN THE ANTARCTIC

BY

J. F. NUNN, Ph.D., M.B., Ch.B., F.F.A.R.C.S.

Leverhulme Research Fellow, Research Department of Anaesthetics, Royal College of Surgeons of England; Lecturer, Postgraduate Medical School, University of London; Honorary Consultant, Hammersmith Hospital, London

Expeditions are notoriously ill-equipped for the administration of a general anaesthetic. Current practice (to which the author has made no exception) is to rely upon local anaesthetics, thiopentone, and open ether. Since even experienced anaesthetists may find difficulty in the transition from thiopentone to open ether, it is perhaps fortunate that expeditions seldom offer an opportunity for the medical officer to exercise his skill.

This paper reviews the problem of anaesthesia in Antarctica and describes a technique which has been developed in conjunction with the Falkland Islands Dependencies Survey, the Medical Research Council (Division of Human Physiology), and British Oxygen Gases Ltd. The apparatus for this technique is now standard equipment with British and South African parties in Antarctica. It may also fulfil the requirements for general anaesthesia in other remote parts of the world.

It is not intended to discuss the merits of the alternatives to general anaesthesia. Clearly, local analgesia must be the method of choice when practicable, and, in Graham Land, Black (personal communication) has recently relieved and repaired a strangulated hernia under procaine field-block. Spinal analgesia is attractive to the single-handed medical officer, but carries dangers which cannot be overlooked. In addition, it is not applicable to the whole body and it is quite likely that an operation may outlast the effect of the drug.

Requirements of General Anaesthesia in Antarctica

It must be possible to provide anaesthesia for operations on any part of the body. Apart from trauma, the most likely operations are for appendicitis, strangulated hernia, and perforated peptic ulcer. Specialization in anaesthesia has hampered the training of undergraduates, and it can no longer be assumed that a newly qualified medical officer has acquired much skill or experience in anaesthesia. Thus it is essential to offer a simple technique. Furthermore, it is rare for an expedition to carry two medical officers, and it must therefore be possible for the maintenance of the anaesthetic to be delegated to a lay assistant. Inhalational anaesthetics should be non-inflammable, as open heating is used in the huts.

Size and weight of apparatus are now of less importance than formerly. A compact apparatus weighing a few kilograms is acceptable provided that large stocks of cylinders are not required. It may be assumed that an operation will be performed in a hut, caboose, or possibly a tent, where the temperature can be raised to at least 18° C., although during storage a fall to -70° C. is possible. Severe condensation follows the passage of warm fronts. Apparatus must also be