IONIC PROCESSES IN URINE

A study of factors which may affect the renal excretion of inorganic phosphate.

A thesis submitted to the University of Cape Town for the degree of Doctor of Philosophy.

by

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P R E F A C E

This thesis is composed of two parts, each related to the problem of the mode of regulation of the renal excretion of inorganic phosphate.

Part One presents new data concerning the hypothesis of secretion of inorganic phosphate in the dog kidney, and as such is clearly relevant to the problem cited above.

Part Two arose from earlier observations suggestive of a passive transport process in the renal tubular reabsorption of inorganic phosphate, a hypothesis consistent with a physico-chemical mode of action of parathyroid hormone upon either the glomerular filtrate or the proximal renal tubular epithelium (19,20). At about the time of formulation of this hypothesis, investigations into the aetiology of renal stone formation were commenced in this laboratory (27), so creating an opportunity for the study of the physico-chemical structure of urine. As such a study was also a clearly desirable preliminary to the further investigation of possible physico-chemical renal effects of parathyroid hormone, it was embarked upon from this point of view.

The latter investigation has yielded results of general interest, quite apart from any relevance they may have to the problem of regulation of urinary phosphate excretion, and for this reason is presented here, with Part One, under the broad title of "Ionic Processes in Urine".

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Abbreviations- cont.

ni = non-ionic urinary particles

nu = non-ionic ,non-urea urinary particles

Osm.= osmolality (mOsm/kg water)

Osm_{ic}= milli-osmoles derived from ionic constituents.

Osm_{ni}= milli-osmoles derived from non-ionic particles.

Osm_{nu}= milli-osmoles derived from non-ionic, non-urea urinary particles.

P = inorganic phosphate

rt = room temperature

SO_4 = inorganic sulphate

Sp.K = specific conductivity. Superscripts denote degree of dilution,eg. $Sp.K^{u/10}$ is the specific conductivity of urine diluted ten fold. Subscripts denote temperature eg. $Sp.K_{20}$ is the specific conductivity as measured ,or corrected to, 20^{o} C.

E R R A T A

Errors of Commission:

Part 1: for 'arguement',read 'argument'.

Errors of Omission:

Part 1:Page 1 - "of inorganic phosphate, by administering substances known to enhance phosphaturia, or by" - 7th line from top.

Part 2:Legend to Fig.15:The 24-hour osmolar/ creatinine ratio is shown above the curve for each individual.

Appendix D: Sr^{85} concentrations were determined using a well-type scintillation counter. The concentrations given have been corrected for background radiation.

A B B R E V I A T I O N S

Part One:

C_{cr} = creatinine clearance

cr = creatinine

Cr_p = plasma creatinine concentration

Cr_u = urinary creatinine concentration

GFR = glomerular filtration rate

i.v. = intra-venous

K = potassium

Mg = magnesium

ml. = milli-litre

Na = sodium

P = Inorganic Phosphate

P_p = plasma inorganic phosphate concentration

P_u = urinary inorganic phosphate concentration

Sr^{85} = strontium isotope; a gamma emitter.

$U_{vol.}$ = urine volume

Part Two:

Ca = calcium

f = dilution factor

g = osmotic coefficient

i.c. = ionic constituent

I.S. = Ionic Strength

K = potassium

Mg = magnesium

mI = milli-Ions

mM = milli-Mole

Na = sodium

NH_4 = ammonium ion

C O N T E N T S

Contents- cont.

PART ONE

Demonstration of Secretion of Inorganic Phosphate in the Dog Kidney.

Chapter 1

INTRODUCTION.

Over the past twenty years, numerous investigators have sought evidence of inorganic phosphate secretion in the mammalian kidney, following the unequivocal demonstration of such secretion in the fish (15, 26, 41), alligator (18), and chicken (23). Stimulation of the hypothetical secretory mechanism was attempted by raising the plasma concentration of inorganic phosphate, or by adopting both these stratagems simultaneously. These manouevres led to conflicting results which on the whole did not favour the existence of such a mechanism in cat, dog or man (1, 2, 4, 14, 16, 19, 35, 43). The recent introduction of new techniques of physiological investigation - close-arterial injection (8, 9, 10), the administration of anatomically selective nephrotoxic agents (31, 32), and stop-flow localisation of intratubular function (24, 38, 39) - has however provided fresh evidence both for and against the hypothesis of secretion of inorganic phosphate.

An interesting variant to the theme of raised plasma phosphate concentration causing P secretion, was that adopted by Carrasquer and Brodsky (8, 9); close-arterial injection of P and Cr, in dogs loaded with acid phosphate, produced a far greater (20% - 400%) increment of excreted P than of Cr. They interpreted this as evidence of secretion. Others however have felt that these results are equally conistent merely with decreased P reabsorption (4, 16).

Nicholson selectively poisoned various

segments of the dog nephron before assaying the phosphaturic effect of Parathormone (3, 32). He found that lesions to the proximal tubule led to a marked increase in P excretion, whereas lesions to the distal tubule produced a fall in P excretion. He then showed that parathyroid extract could still cause an increase in P excretion in the presence of proximal tubular lesions, but was without effect in distal tubular lesions. He concluded that phosphate is normally reabsorbed in the proximal, and secreted in the distal, tubule, and suggested that the sole action of parathyroid extract might be to increase this secretion.

Even this work, suggestive as it is, is far from being conclusive proof of secretion. The fact of proximal tubular damage producing increased phosphaturia implies damage to a proximal tubular reabsorptive mechanism. Assuming parathyroid extract to normally inhibit such a mechanism, it does not seem surprising that the administration of Parathyroid extract to the damaged mechanism would lead to still greater phosphaturia.

Where distal tubular lesions were produced, the kidneys were so severely damaged as to lead to large falls in creatinine clearance, and the urinary phosphate content fell to low levels. Nicholson himself ascribed these findings to back diffusion of intratubular fluid. The lack of phosphaturic effect of parathyroid extract in such cases need not therefore necessarily be ascribed solely to injury of a distal tubular P secretory mechanism, but may equally well have been due to such massive back diffusion of P as to absorb all the additional P brought down from the proximal tubule. The damaged epithelium may simply have been incapable of sustaining a P concentration gradient.

In stop-flow experiments on dogs, the P content of 'intratubular' urines has never been found to exceed the amount filtered. (36, 38).

Samiy et al (38, 39) performed stop-flow experiments on parathyroidectomised dogs, before and after administering Parathormone. They found that injection of P^{32} into the renal artery one minute before release of stop-flow, caused only a small net flux of P^{32} into the tubular fluid. This was not appreciably altered

by Parathormone, despite an accompanying increase in phosphaturia. They concluded that a distal tubular P secretory mechanism did not exist, and that Parathormone acted solely by inhibiting proximal tubular reabsorption.

It is clear that the results of these recent investigations are mutually contradictory.

Chapter 2

ARGUEMENT

The experience and difficulties of previous workers, cited in Chapter 1, lead to two conclusions; viz., (1) inorganic phosphate secretion, if it occurs at all, will be found in the distal tubule (23, 32), and (2) will be quantitatively less than the simultaneous proximal tubular reabsorption.

These assumptions underlie the approach to the problem of demonstration of renal P secretion adopted here. The arguement which follows devolves entirely upon the stop-flow method of localisation of renal tubular function, details of which are given in appendix A.

Arguement: The definitive criterion of secretion of inorganic phosphate sought in the past has been the appearance of a greater urinary phosphate content than could be accounted for by the process of glomerular filtration alone. That is, the ratio of urinary phosphate content to that of the glomerular filtrate had to exceed unity.

During conventional stop-flow experiments in the dog, 'intra-tubular' urines never achieve this figure, even after the administration of Parathormone (Fig. 1); this has been cited as evidence against the hypothesis of P secretion (38, 39). The possibility remains however that some distal tubular secretion may occur but in amounts too small to raise

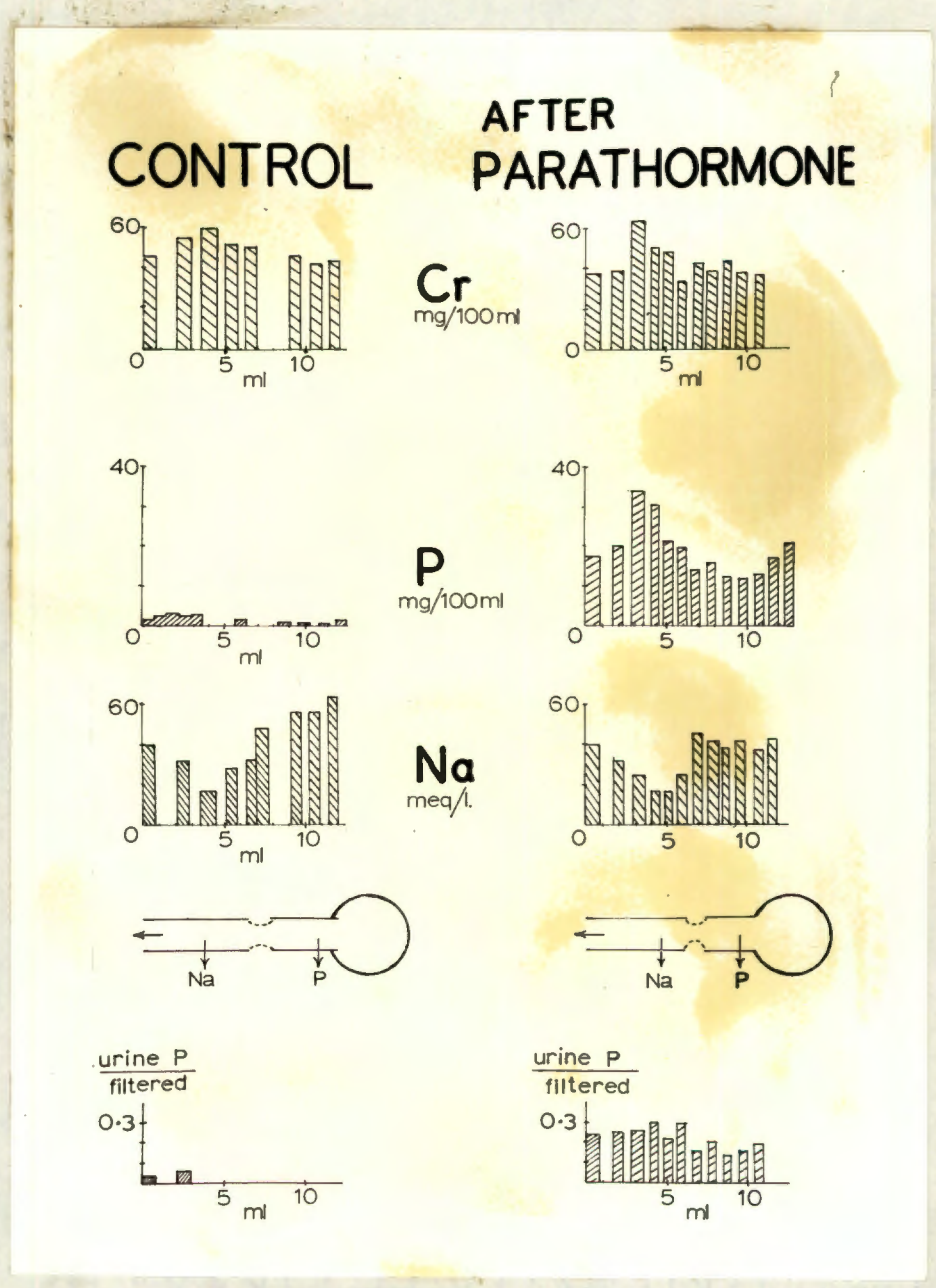

Fig. 1: Stop-flow concentrations of Cr, Na and P, before and after the administration of Parathormone (Expt. 1).

the above ratio to unity or beyond. The procedure outlined below permits the detection of just such small increments in ratio.

The anaesthetised dog is prepared as for a conventional stop-flow experiment (of Appendix A). Once the rate of urine flow has stabilised at between 3 - 10 ml. per minute, a number of control urine and blood specimens are taken. Parathormone is then given intravenously, and some twenty minutes later more urine and blood samples are collected. A stop-flow experiment is then performed in the usual way. As soon as this is completed, the ureter is again clamped off. A few minutes later the clamp is briefly released so that some 2 or 3 ml. of urine may be collected, before occluding the ureter for yet a third period. After a further few minutes of stopped-flow, the ureteric clamp is finally removed, and the ensueing urine collected as in a conventional stop-flow experiment. More control urine and blood samples are then taken.

The rationale is as follows. The control specimens reveal the degree of phosphaturia induced by the Parathormone. Analyses of urinary samples obtained immediately after the first period of stopped flow delineate the variations in ratio of urinary phosphate content (as compared to content of the glomerular filtrate) throughout the length of the tubule. This pattern is assumed to be reproduced during the second period of stopped flow. The subsequent escape of 2 ml. to 3 ml. of urine moves that urine opposite the proximal tubular site of P reabsorption, and thus of low ratio, downstream towards the site of presumed P secretion. The third stop-flow

period allows time for secretion to occur. Subsequent comparison of distal tubular ratios (as obtained after the third stop-flow period) with those found earlier at the more proximal tubular sites from which the selfsame urine was displaced, should now reveal the presence or absence of any additional phosphate.

This procedure has been called an 'interrupted' stop-flow (30), and has been used successfully to demonstrate the sodium dependency of distal tubular secretion of potassium (45).

It may be pertinent to note that, in the dog, the renal tubular reabsorption of inorganic phosphate expressed as a fraction of that filtered is influenced by neither variations in glomerular filtration rate, nor by generalised kidney damage (11, 37); this relative immunity to extraneous disturbance renders the phosphate ion one particularly suited for study by the interrupted stopflow technique.

Chapter 3

EXPERIMENTAL DESIGN AND CALCULATIONS

All the experiments were performed on anaesthetised dogs, prepared as described in Appendix A.

Experiment 1 is simply a reduplication of earlier work (38) and is included here solely to illustrate typical stop-flow data as obtained before and after the administration of Parathormone. The experiments on Dogs A to J all adhere more or less closely to the procedure described in Chapter 2. They are presented here not in the sequence in which they were performed, but rather in order of Parathormone-induced phosphaturia; this simplifies presentation and discussion of the results. Some idea of the actual order in which the experiments were performed can be gauged from the dose of Parathormone administered. Thus Dogs B and G each received 100 units, Dogs A, C, D, E and F each 200 units, and Dogs H, I and J each 400 units, of Parathormone.

In each experiment, the stop-flow urinary concentrations of Na (and Sr^{85} too, in Dog A) were determined in addition to those of P and Cr; these were needed for subsequent checks on the accuracy of the procedure - cf Discussion.

Details of individual experimental procedures and analytical results are given at the conclusion of this Thesis.

Calculations: Stop-flow urinary P concentrations are expressed as fractions of filtered phosphate. This is calculated as equal to:

$$U_{vol.} \times P_u / GFR \times P_p$$

which simplifies to:

$$P_u \times Cr_p / Cr_u \times P_p$$

on equating Ccr^{+} with $GFR.P_p$ is assumed^{+} to be completely filterable. The P concentration of each control urine collection is expressed as a percentage, rather than as a fraction, of that filtered.

The total volume of the multiple urine specimens obtained immediately after a period of stopped flow, up to and including that containing the lowest fraction of filtered P, is taken as the total intra-tubular volume. Any point along the length of the tubule is located by expressing the volume at this point as a percentage of the total intra-tubular volume.

For convenience in exposition, calculation and discussion, the first, second and third stop-flow periods are designated as periods A, B and C, respectively; the stop-flow urine samples obtained immediately after each of these periods are similarly designated.

The transient release of ureteric occlusion between stop-flow periods B and C displaces the intra-tubular urine downstream. The degree of displacement is calculated by expressing the total volume of urine ejected during this

brief period of free flow (B samples) as a percentage of the total intra-tubular volume (as measured in the C samples). This permits the comparison of P concentrations at distal tubular sites (during stop-flow period C) with those opposite the upstream sites from which they were displaced (stop-flow period A).

Comparison is thus effected by subtraction of P concentrations in the A samples from those in the C samples, at corresponding percentages of the total intratubular volume.

‡ Neither of these assumptions is correct. cf Discussion.

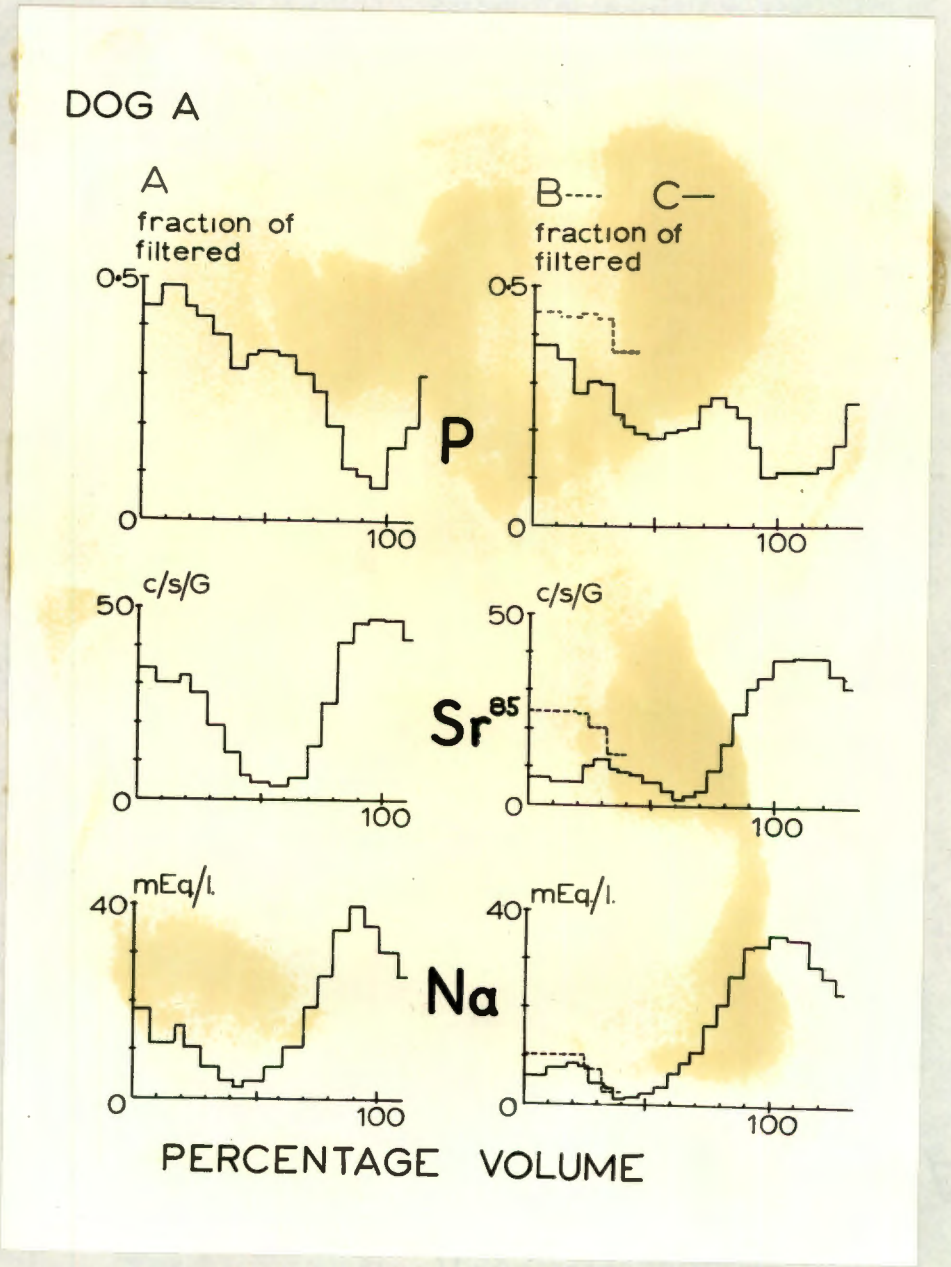
DOG A
A
fraction of filtered
0·5
0
100
B---- C—
fraction of filtered
0·5
0
100
P
c/s/G
50
0
100
c/s/G
50
0
100
Sr85
mEq/l.
40
0
100
mEq/l.
40
0
100
Na
PERCENTAGE VOLUME

Fig. 2

Chapter 4

SUMMARY OF RESULTS

Response to Parathormone:

Parathormone evoked a phosphaturic response in all but 3 dogs. The percentage excretion of filtered P fell in dogs A and B, and remained unaltered in dog C.

Stop-flow Urinary Concentration Patterns:

(1) Dog A: Urine concentrations of P, Na and Sr^{85} after stop-flows A, B and C are presented graphically in Figs.2 and 3.

Fig. 2: Concentrations in stop-flow A urines are depicted on the left hand side of the figure; those in stop-flow urines B and C are on the right.

The concentration minima of Na and Sr^{85} are each at almost identical fractions of the total intratubular volumes of stop-flows A and C.

The concentration curves differ in configuration in A and C. In A (and B) the concentration of each substance rises progressively from a proximal minimum to a distal maximum. This is in contrast to C, where the concentration of each substance, distal to its minimum rises then falls.

Fig. 3: The P, Na and Sr^{85} concentrations of

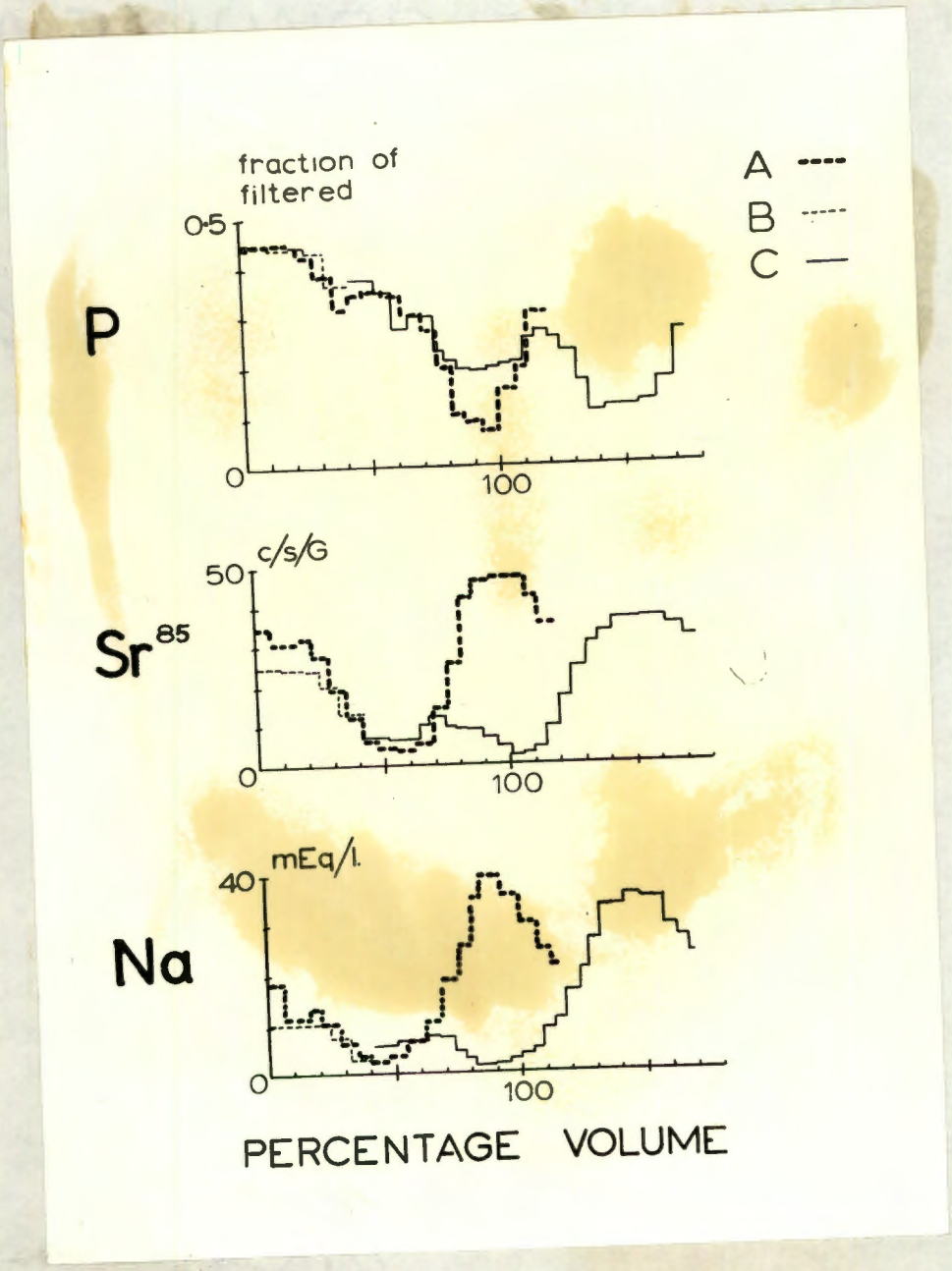
fraction of filtered
0·5
0
100
A
B
C
P
c/s/G
50
0
100
Sr85
mEq/l.
40
0
100
Na
PERCENTAGE VOLUME

Fig. 3

stop-flow urines A, B and C are compared at corresponding percentages of total intratubular volume, by superimposition of the data presented in Fig. 2.

The distal tubular concentrations of P in C are very similar to those at the upstream sites from which they were displaced.

The concentration troughs distal to the sites of the concentration minima, as seen in C (Fig. 2), correspond to the concentration minima in A. In each case the nadir of the trough is of higher concentration than the corresponding concentration minimum in A.

Distal troughs of P concentration, similar to that present in Dog A (stop-flow C), are present in the C stop-flow urines of Dogs E and H.

(2) Dogs A to J: Fig. 4 depicts the comparisons between P concentrations in stop-flow urines A, B and C in Dogs A to J. The patterns of P concentration in stop-flow A urines are roughly similar in all the dogs, rising from proximal tubular minima to distal tubular maxima. In all cases, small fluctuations in P concentration are superimposed upon this general pattern. The P concentrations of distal tubular urines range from 0.1 to over 0.5 of that filtered.

The P concentrations of stop-flow B urines fluctuate in similar fashion to those of the corresponding A urines, but may be at higher or lower levels. The concentrations in A and B urines vary in parallel to the

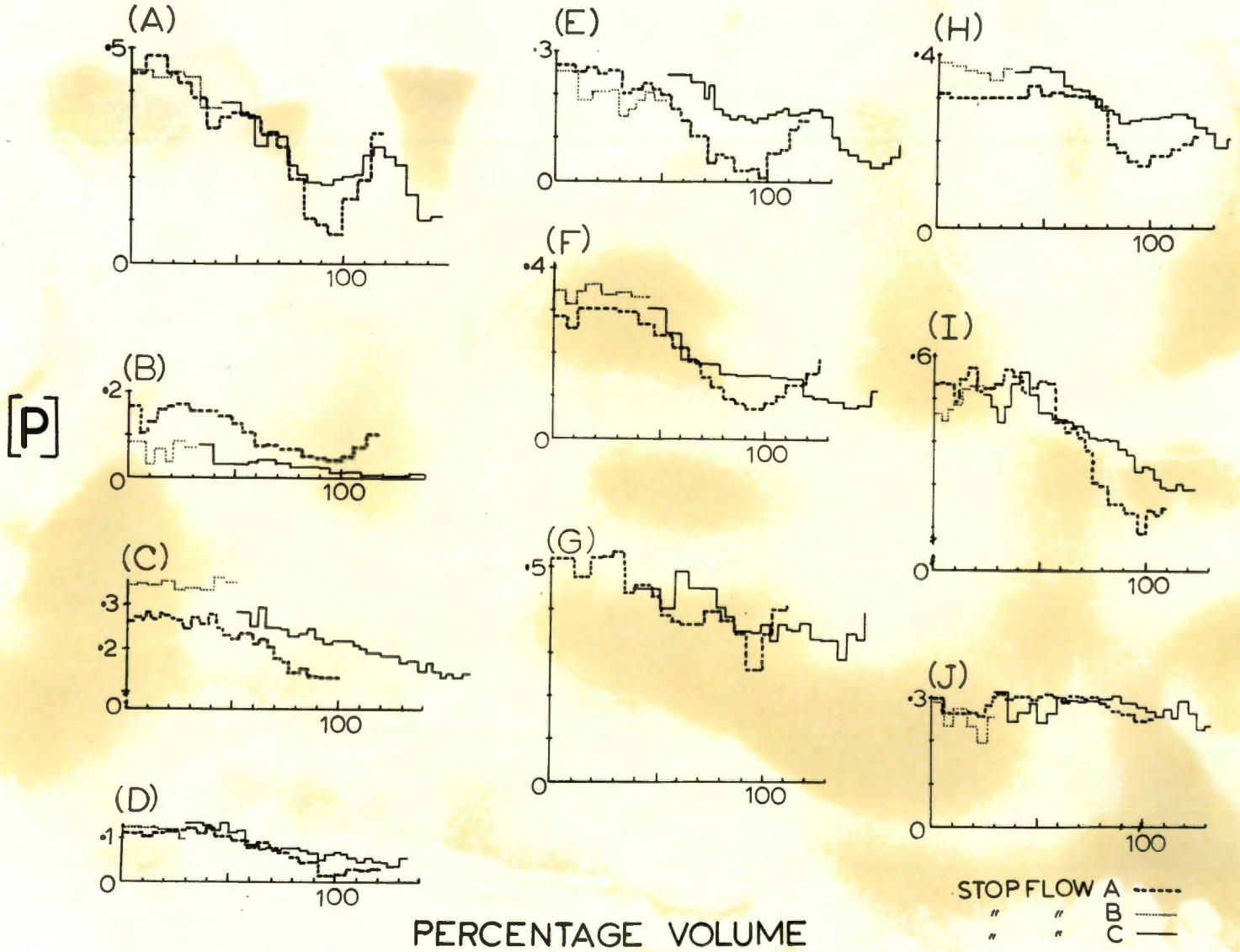

Fig. 4

changes in percentage P excretion in pre- and post- stop-flow control urines.

With three exceptions (Dogs G, I and J) the P concentrations in distal tubular C urines fluctuate roughly in parallel with the corresponding A urines.

Stop-flow Urinary Creatinine concentration Patterns:

Dog G shows marked distal tubular peaks in Cr concentration, in both stop-flows A and C. These peaks are at 28.7% and 31.2% of the intra-tubular volumes, respectively.

The stop-flow urines of the remaining dogs manifest relatively little change in Cr concentration along the length of the tubule.

The distal tubular peaks in Dog I lie at 23.4% and 25.5% of the intra-tubular volumes in stop-flows A and C, respectively.

Creatinine concentration of proximal tubular stop-flow urine (at 100% intratubular volume) is appreciably greater than that of the free flow control urine, in all the dogs other than A, C and G.

Volumes of B samples as percentages of the total Intratubular C Volumes:

Range: 23% to 53%. Mean: 39%.

Comparison of P excretion in Control and Extreme "Distal Tubular" Stop-flow Urines:

With 2 exceptions, the P concentrations in extreme distal tubular urines of stop-flows A and B, correspond to the percentage excretion in the control urines collected immediately before and after the stop-flow procedures. The former are higher than the latter in Dog A, and vice versa in Dog J.

D I S C U S S I O N

Appraisal of the Interrupted Stop-flow Technique:

The interrupted stop-flow technique, as used here, is not strictly comparable to that adopted by previous workers. Both Murdaugh and Robinson (30), and Walker et al (45) - in attempting to demonstrate distal tubular secretion of Mg and K, respectively - liberated only sufficient urine (B samples) to move that intratubular fluid of minimal Mg or Na concentration to a yet more distal part of the distal tubule. This represented release of probably less than 20% of the total intratubular volume. The fluid thus brought to the site of presumed secretion was of minimal concentration and little affected (presumably) by new glomerular filtrate.

This contrasts strongly with the procedure presented here, in as much as (a) a much greater percentage of intratubular fluid is released and (b) the fluid brought to the distal tubule is at best of intermediate rather than minimal P concentration, and might well be modified by the influx of fresh glomerular filtrate.

For these reasons the arguement presented in this work must meet a number of fundamental criticisms, viz:

(i) localisation of apparent P-secretory and Na-reabsorption sites in terms of percentage of total intratubular volumes implies a constant relative distensibility of various parts of the nephron; such constancy may be disturbed upon repeated, and particularly interrupted, stop-flows.

(ii) Calculation of the degree of distal displacement of

intratubular urine during the interrupted stop-flow procedure is based upon the assumption of identical total intratubular volumes during stop-flow periods B and C; such may not be the case.
(iii) Stop-flow urinary P concentrations, in repeated experiments in individual dogs, may not be similar even where such experiments are performed within a few minutes of each other; this is the more likely to be true when carried out soon after the administration of Parathormone.
(iv) The analytical techniques employed may be too inaccurate to impart any significance to the small differences actually observed.

The first criticism is perhaps the most easily answered. Loci of minimal Na concentration remain at relatively constant fractions of the total intratubular volume during each of these experiments (Table 1). Had the procedure caused disproportionate trapping of fluid in portions of either proximal or distal tubules, these loci would have been displaced.

The identity of total intratubular volumes during stop-flow periods B and C can be only indirectly corroborated.
In as much as stop-flow periods A, B and C follow rapidly each upon the other, the finding of equal total intratubular volumes in A and C strongly supports the assumption, in such cases, of identical intra-tubular volumes during stop-flow periods B and C (Dogs A, D, E, F, H; Table 2a).

Figures 2 and 3 contrast and compare the P concentrations

TABLE 1

DOG	a		b
	LOCI OF Na MINIMA:		
	A	C	A - C
A	46.9	42.1	4.8
B	53.8	44.0	9.8
C	42.1	48.7	-6.6
D	±35.2	±41.3	-6.1
E	35.3	40.6	-5.3
F	39.5	34.3	5.2
G	46.6	42.1	4.5
H	42.7	46.0	-3.3
I	36.9	28.9	8.0
J	43.5	?	?
Mean	42.3	39.7	6.0

(a) Loci of Na concentration minima, in preliminary (A) and subsequent interrupted (C) stop-flow urines. Loci are expressed as perdentages of the total intratubular urine volumes.

(b) Differences in loci of Na concentration minima between A and C.

in Dog A, in stop-flow urines A, B and C. It is apparent that the proximal tubular site of minimal P concentration in A, is represented by a distal dip in P concentration in C. Should the total intratubular volume during stop-flow period B have been equal to that during stop-flow period C, one might expect:

$$\frac{\left(\begin{array}{l}\text{Volume of urine}\\ \text{released after}\\ \text{stop-flow B}\end{array}\right) + \left(\begin{array}{l}\text{Volume of Stop-flow C}\\ \text{urine up to distal dip}\\ \text{in P concentration}\end{array}\right)}{\text{Total Intratubular Volume of C}} = 1$$

Only dogs A, E and H showed clear-cut dips in distal P concentrations in the C urines. In these dogs, the above calculation yielded figures of 0.96,0.96 and 0.90, respectively (table 2(b)). These figures are in keeping with the postulate (Fig. 5 cf below) of slight downstream displacement of the nadir of the distal trough in P concentration.

Yet a third approach to the problem of establishing identity of total intra-tubular volumes during stop-flow periods B and C, is comparison of the respective cumulative stop-flow urine volumes up to and including those containing the minimal Na concentrations. This was found helpful in only 2 cases (Dogs E, F - Table 2c) as in most of the remainder insufficient urine was released after stop-flow period B to ensure inclusion of that of minimal Na concentration. In two others (Dogs C and J) the Na concentrations varied too little or too irregularly to be of help.

Identity of intra-tubular volumes during stop-flow

TABLE 2

Dog	a		b			c	
	Total intratubular volume during stop-flow period:		(i) Vol. of B / Vol. of C	(ii) Vol. upto P concentration trough in C / Vol. of C	(i) + (ii)	Cumulative volume upto that containing the minimum Na concentration	
	A	C				B	C
A	8.8	8.6	.417	.539	.956	3.58 ●	3.61
B	10.2	12.2	-	-	-	3.91 ●	5.35
C	17.8	12.9	-	-	-	5.23 ?	6.28
D	13.5	13.5	-	-	-	4.02 ●	5.56 ?
E	13.5	13.6	.525	.439	.964	5.18	5.52
F	6.3	6.6	.443	.512 ?	.955 ?	2.44	2.27
G	8.7	12.0	-	-	-	-	-
H	11.4	11.9	.350	.551	.901	4.17 ●	5.47
I	15.0	16.3	-	-	-	3.73 ●	4.72
J	15.0	13.2	-	-	-	3.46	?

? = uncertain ; ● = last urine sample in B

periods B and C can therefore be said to have been fairly shown only in Dogs A, D, E, F and H, and must be assumed for the remainder. Inasmuch as only a fraction of the total intra-tubular volume is released between stop-flow periods B and C, and as the one follows immediately after the other, this does not seem unreasonable.

The absolute concentrations of substances found in stop-flow urine samples have little significance in themselves, the value of the stop-flow technique lying largely in depicting relative fluctuations in concentration along the length of the tubule (36). The arguement advanced in Chapter 2 however does not depend on strictly comparable urinary P concentrations in repetitive stop-flow experiments. It is the pattern, rather than the magnitude, of the differences between P concentrations in stop-flow urines A and C, which determines the presence or absence of P secretion. This will be elaborated upon below (fig. 5).

The calculation of urinary P concentrations, - as fractions of that filtered - assumes the plasma P to be completely filterable, and that Cr is neither secreted nor reabsorbed within the tubule. Both of these assumptions are incorrect. Error in the former (46) is of little significance as this can lead only to fractionally lower calculated urinary P concentrations than in fact exist.

Cr has recently been shown to be secreted in the proximal tubule of the (male) dog kidney, at a site coincidental with that of PAH secretion (33, 42). This

is in apparent conflict with previous experience (5, 40), an anomaly explicable by the weakness of the secretory process; hence its demonstration only during stopped flow. Operation of this factor - possible Cr secretion - renders suspect any calculation of stopflow urinary P concentration (expressed as a fraction of that filtered) where this is based on Cr concentration. The actual values of stop-flow urinary P concentrations must be higher than those calculated here, particularly those for the proximal tubule.

The work described in this thesis was well under way when this complication came to my attention. Fortunately, as pointed out above, the actual values of P concentration do not affect the arguement on which this study is based. Until such time as Cr is shown to be reabsorbed in the distal tubule - and there is no reason to suspect such a phenomenon - only P secretion can be said to bring about the phenomenon to be described below.

Glomerular filtration does not cease during stopped flow (34). It follows that the longer the period of ureteral obstruction, the greater the fraction of intratubular fluid derived from post-occlusive filtrate. Stop-flow urines A and B are obtained after 4 minute periods of ureteral occlusion; most of the C stop-flow urine is exposed to 8 minutes of ureteral occlusion (4 minutes during stop-flow period B, and a further 4 minutes during stop-flow period C). It is clear that the distal tubular C urine may contain a higher fraction of new filtrate than the corresponding A urine.

As new filtrate enters the proximal tubule during stopped flow, its P content is largely reabsorbed. Cr however is not reabsorbed (5, 42) and may even be secreted (cf above). Once past the site of P reabsorption the new filtrate therefore consists of P - poor fluid (relative to creatinine); this dilutes that fluid already present in the distal tubule to effectively lower its P concentration. The greater the fraction of new filtrate, and the more the proximal tubular secretion of Cr, the greater the apparent dilution effect.

It follows that the distal tubular C urines may be of somewhat lower P concentration than the corresponding A urines, even in the absence of factors operating to alter the renal handling of P. Inasmuch as this study was designed to seek evidence of a rise in distal tubular P concentration in the C urines, such an artefactual fall in P concentration is of no consequence.

The accuracy of the analytic techniques employed leaves much to be desired. Scrutiny of serial stop-flow urinary Cr or P concentrations, in any of the experiments presented here, reveals random fluctuations which can only be due to technical error. In other experiments, not reported here, these errors were sometimes so large and the actual concentration gradients so slight, as to make it impossible to exactly define the site of minimal P concentration. In such cases one had no alternative but to discard the experimental data in their entirety; this was found necessary in no fewer than 6 instances.

In view of this relative technical inadequacy - inadequate, that is, in terms of the precision shown necessary by this study - two safeguards must be adopted in assessing the data presented in Figs. 4 and 6; these are (i) small abrupt deviations from general trends must be ignored, and (ii) apparently convincing findings must be present in a number of experiments and at comparable points along the length of the tubule to be significant.

Detailed Postulate of Intratubular Events during the preliminary and interrupted stop-flow manouevres:(Fig. 5)

On initiation of ureteric occlusion, the pattern of P concentration along the length of the tubule is presumably that of Fig. 5 - 1; this assumes no renal handling of P anywhere within the tubule other than near the site of entry of the glomerular filtrate. With continued occlusion, this pattern rapidly changes to that of Fig.5 - 2, as proximal P reabsorption continues. Splay in distribution of individual nephron lengths, (24) - admixture of post-occlusive filtrate (34), and downstream diffusion of proximally secreted creatinine (33, 42) all contribute towards the gradual slope in intratubular P concentration. Release of the ureteric obstruction, with rapid escape of the total intratubular content, now yields the concentration distribution pattern normally seen after a stop-flow experiment.

If however, only a few ml. of urine are allowed to escape, before again obstructing the ureter, the pattern of intratubular P concentrations at the moment of cessation of urinary flow will be that of Fig.5 - 3. Here 25% of the

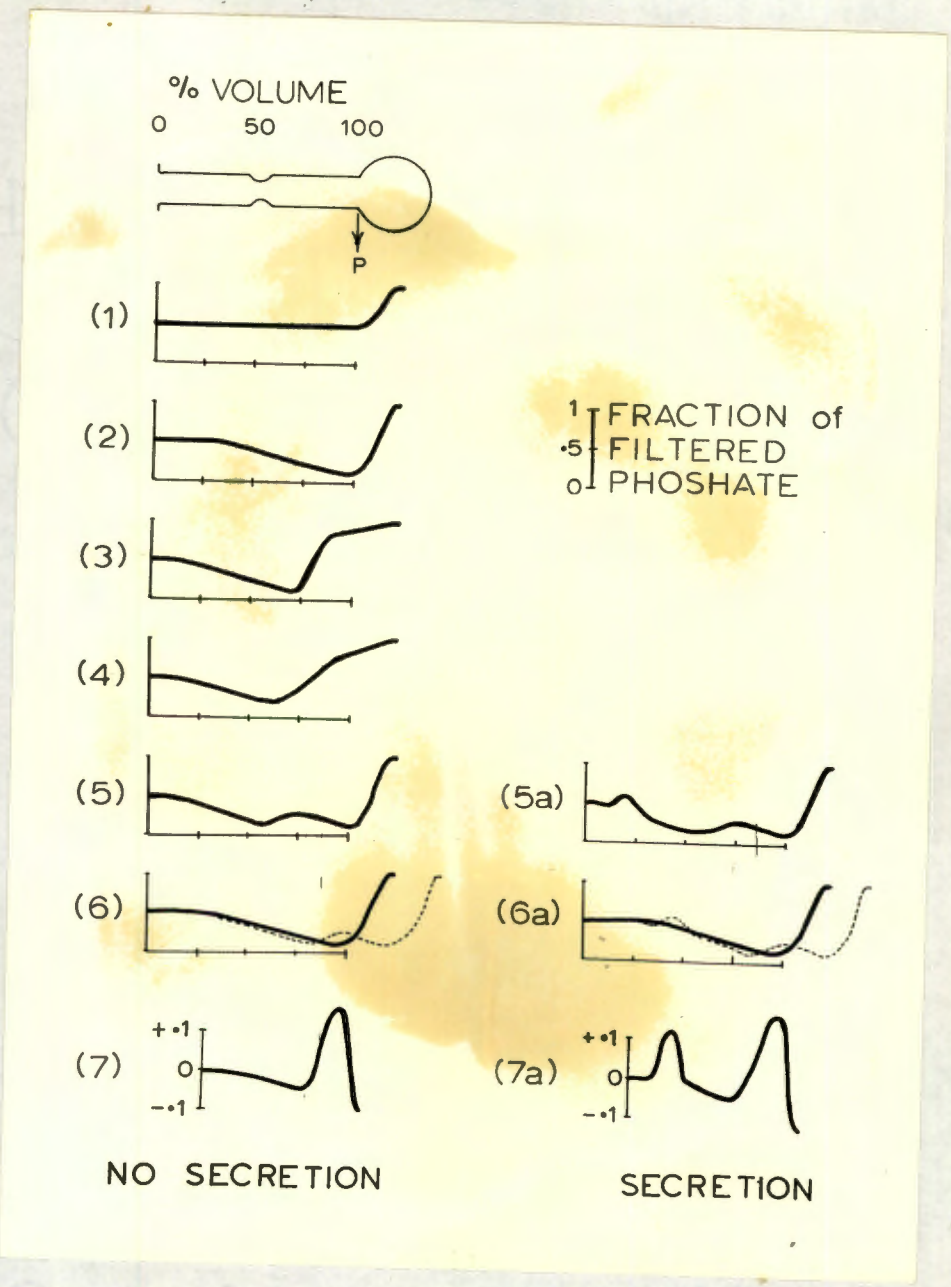
% VOLUME
0
50
100
P
(1)
(2)
(3)
(4)
(5)
(6)
(7)
1
.5
0
FRACTION of
FILTERED
PHOSHATE
(5a)
(6a)
(7a)
+.1
0
-.1
NO SECRETION
SECRETION

Fig. 5

intratubular volume is assumed to have escaped. The site of minimum P concentration has accordingly moved 25% downstream. Proximal to this, P concentrations rise sharply to higher levels than in Fig.5 - 1; this is consequent upon the more rapid passage of glomerular filtrate over the site of P reabsorption, immediately following a period of stopped flow, than pertains during free flow.

Several processes now occur. During stopped flow there is continuous slight downstream movement of intratubular fluid (34); this leads to diffusion and mixing, with blurring of the pattern of Fig.5 - 3, to that of Fig.5 - 4. In effect, the proximal high-P-concentration hillock falls forward to partially, or completely, fill the more distal P-concentration trough. If filling is not complete, the nadir of the partially filled P-concentration trough may be displaced distally.

As occlusion continues, the advent of post-occlusive filtrate, and downstream diffusion of newly secreted Cr, (as in Fig.5 - 2) effectively lower the midtubular P concentration. At the same time, proximal tubular reabsorption of P proceeds uninterruptedly, so that the pattern of intratubular P concentration becomes that of Fig.5 - 5. There are now two P concentration troughs, (if filling of the distal trough was incomplete) the lowest and most proximal of which marks the site of P reabsorption.

This then is the pattern which whould be present in the urine samples obtained immediately after restoration of free flow, assuming no distal tubular secretion of P.P concentrations

at distal tubular sites may be a little less than the P concentrations opposite those upstream sites from which they were displaced (Fig.5 - 6). Subtraction of P concentrations of Fig.5 - 2 from the corresponding concentrations of Fig.5 - 5 yields a curve of configuration as in Fig. 5 - 7. (For clarity, the scale of the ordinate of Fig. 5 - 7 has been exaggerated.)

The same sequence of events should occur in the presence of distal tubular secretion of P, but now urinary P concentrations at distal tubular sites will be higher than those which pertained at the more proximal sites from which they were displaced (Figs.5 - 5a and -6a. Arithmetical subtraction of P concentrations in Fig. 5 - 2 from the corresponding concentrations in Fig. 5 - 5a, yields a double peaked curve (Fig. 5 - 7a).

Evaluation of Results in terms of Postulated Intratubular Events:

The arithmetical comparisons of P concentrations in stop-flows A, and C for Dogs A to J, are presented in Fig.6. The P concentrations of the A urines have been subtracted from those in the C urines, at corresponding percentages of intra-tubular volume. The sites of minimal Na concentration are also shown, as well as the mean values of percentage excretion of P in control urine collections before and after the administration of Parathormone.

Dogs A, B and F present no evidence of a distal peak in P concentration.

Dogs C, D, E and H show small distal tubular irregularities in P concentration, but these are based upon equally irregular

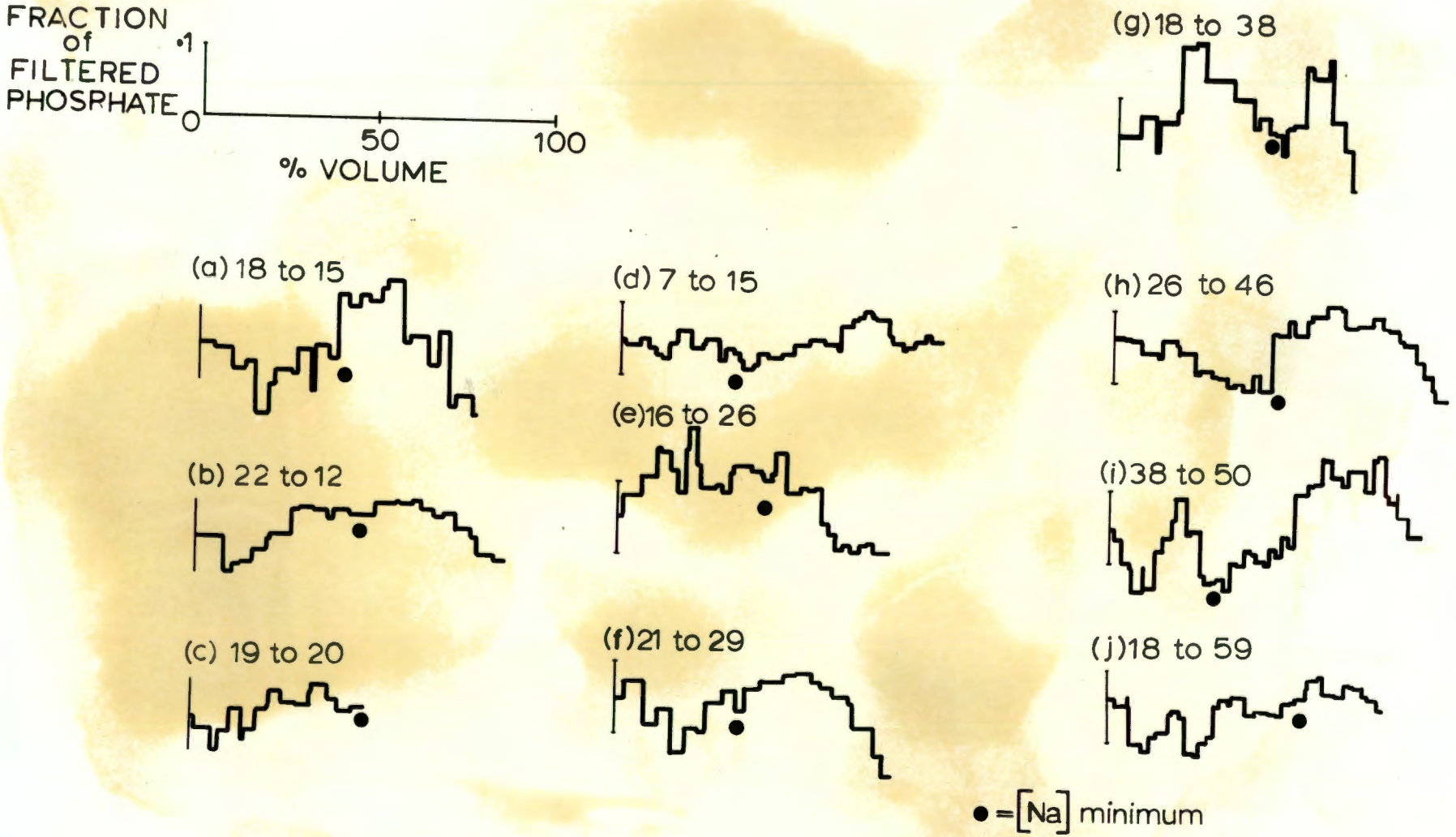
FRACTION of FILTERED PHOSPHATE
1
0
50
100
% VOLUME
(a) 18 to 15
(b) 22 to 12
(c) 19 to 20
(d) 7 to 15
(e)16 to 26
(f)21 to 29
(g)18 to 38
(h) 26 to 46
(i)38 to 50
(j)18 to 59
● =[Na] minimum

Fig.6

fluctuations of P concentration in those stop-flow urines from which the graphs of Fig.6 are derived(Fig.4)

Dogs G and I have distal tubular peaks in P concentration similar to those postulated to occur in P secretion (Fig.5-7a). These peaks lie distal to the sites of minimal Na concentration, are maximal at 24.5% and 21.7% of the total intratubular volume respectively, and represent apparent changes in P concentration of just over 0.1 of that filtered.

Dog J also has a distal tubular peak in P concentration, at 20.0% of the intratubular volume. This peak is smaller and less clearly defined than those of Dogs G and I, but is larger than the irregular fluctuations of P concentration in the stop-flow urines A and C. (Fig.4-j).

The Cr concentration of proximal tubular stop-flow urine in Dog G is approximately equal to that of its free-flow control urines. That is, Dog G presents no evidence for proximal tubular secretion of creatinine. This may be a factor accounting for the difference in configuration of Figs.6 -g, 6 -i, and 6 -j. In the latter two, distal P concentration peaks arise from negative troughs in P concentration (as postulated; Fig.5), whereas this is not a feature of Fig. 6 -g.

Dogs G, I and J are amongst those dogs in which the identity of total intratubular volumes during stop-flow periods B and C was assumed, and not demonstrated. Reference to Fig. 4 reveals that, in these dogs, considerable error in this assumption still yields a double peaked curve

upon comparison of the data of stop-flow periods A and C.

Dogs G, I and J are amongst the 4 dogs showing the greatest phosphaturic response to Parathormone (that of Dog G may be even higher than indicated - post stop-flow controls were not collected). Dogs G and I have the highest concentrations of 'intratubular' P; Dog J has the highest percentage excretion* of filtered P. All three show the pattern postulated for distal tubular P secretion, and the apparent sites of such secretion are at comparable points along the length of the tubule.

In short, P secretion is demonstrated in those dogs in which it was most likely to have occurred.

P Secretion:

It may be pertinent to stress that the clearest evidence for secretion is found in the dogs with the highest 'intratubular' P concentrations; this provides some assurance that the process is not simply one of diffusion from medullary interstitium to tubular fluid.

Na reabsorption against a concentration gradient occurs in the distal tubule (25,36). This site is at

---

* The extreme 'distal tubular' urines (A 1 and C 1) lie within the ureteric catheter during the stop-flow periods; their P and Cr concentrations should therefore approximate to those in the free-flow control urines. This is not the case in Dogs A and J, and presumably reflects technical error.

approximately 40% of the total intratubular volume (Table 1). Yet the site of P secretion is at only 20% -25% of the intratubular volume (Dogs G, I and J), and therefore presumably lies within the collecting ducts, an area known to participate in ionic transport (6, 44).

Where present, the Cr concentration peak in distal tubular stop-flow urines coincides with that of inulin (32), and marks the site of free -water reabsorpiton. This peak can just be discerned* in Dog I, and is very clearly evident in Dog G. In each of these dogs, comparison of the locus of the P secretory site with that of free-water reabsorption (in C stop-flow urines) reveals that the former lies just distal to the latter.

The possibility of Cr secretion, and the unknown degree of dilution of distal tubular urine with post-occlusive filtrate, make it impossible to draw exact quantitative conclusions from the data available. Nevertheless, as the distal tubular peaks in P concentration (Dogs G, I and J) represent only small fractions of their respective free-flow urinary P concentrations - even after 4 minutes of stopped flow - and as there is no evidence of P secretion despite fair phosphaturia in the remaining dogs, it seems reasonable to infer that secretion normally contributes little to the

---

* Evidence of a distal tubular peak in Cr concentration in Dog J is even less impressive than in Dog I; the presumptive site of water reabsorption (stopflowC) lies at 43% of the total intratubular volume; the distal tubular site of Na reabsorption cannot be discerned.

urinary P content.

The results similarly indicate that the phosphaturic effect of Parathormone is very largely mediated by inhibition of proximal tubular reabsorption; distal tubular secretion, where it occurs at all, occurs only after profound stimulation.

The regulation of urinary P excretion thus appears to be analogous to that of weak organic acids and bases, failure of absorption rather than secretion being the major determinant of urinary content (29).

Comparison of Results with Previous Findings:

Although the findings of Carrasquer and Brodsky (8, 9) and Samiy et al (38, 39) lead to opposing conclusions concerning the existence of P secretion, the results presented here seem consistent with the data obtained by both groups; evidence of secretion is so slight that it may well have been missed in the latter. Nicholsons' (32) conclusions however are irreconcilable with any of the above; this has been discussed in Chapter 1.

The strenuous efforts by other workers to demonstrate P secretion by the administration of a variety of phosphaturic agents may well have failed simply because their criterion of secretion - a greater free-flow urinary P content than could be accounted for by filtration alone - was too demanding. A close analogy exists in the recent demonstration of Cr secretion.

In both cat and fish, urinary P may be derived from organic precursors (27, 43). In the cat, net secretion of P can be demonstrated only on loading with organic phosphate esters. Possibly application of the interrupted stopflow technique to dogs similarly treated, may result in the demonstration of greater P secretion than occurred here. There is reason to believe that acidosis may similarly enhance P secretion (7, 9, 17).

APPENDIX A

Stop-Flow Technique

Introduced in 1958 by Malvin, Wilde and Sullivan (24) the stop-flow technique of localisation of intra-tubular function - "the poor man's micropuncture technique" - has proved of considerable value to renal physiologists.

The best description of rationale and technique remains that of the original paper, extracts from which follow.

"Localisation of transtubular transport of substances along the nephrons of a pentobarbitalized dog is characterised by allowing concentration patterns to develop during stopped tubular flow (ureteral occlusion with stopped filtration). Previous administration of an osmotic diuretic, mannitol, provides a watery menstruum against which characteristic concentration patterns are developed point to point along the nephron.....After ample time has been allowed for the concentration patterns to develop during stopped flow the ureteral occlusion is released. Rapid serial urine samples are taken from the new flow. The concentration pattern is caught in these samples collected rapid fire from the polyethylene ureteral catheter after the brief occlusion is released. Thirty to thirty five samples are collected within about 2.5 minutes, each sample averaging about 0.5 ml. The pattern of concentration is oriented along the column of fluid moving out of each nephron. Serial urine samples segment this into an ordered array which is best caught on

a graph if plotted as concentration against the accumulated volume of fluid which has appeared between re-instatement of flow and the appearance of the sample.

...The filtration indicator inulin is injected late after occlusion to reach filter surfaces and to signal new entry of filtrate into the urine samples after the occlusion is released. The rising concentration pattern of this inulin delineates the randomising effect of variable lengths among nephrons.

...Postocclusively injected K^{42} and Na^{24} reach all stop-flow samples. Evidently peritubular blood continues to reach all points along the nephron.

...Technique: The dog is anaesthetised with sodium pentobarbital, 30 mg/kg intraperitoneally. The left ureter is exposed by a flank incision and catheterised with polyethylene tubing. The catheter is pushed as close to the renal pelvis as possible and held securely in place with ligatures. The wound is then closed leaving only the free end of the catheter protruding. This was then fixed to a support in such a way that the urine flowed quickly into successive close-spaced cylindrical wells cut into a Lucite bar. By sliding the bar with its sample wells at a suitable rate past the catheter tip, about 0.5 ml. of urine was collected in each sample."

With minor modifications, the technique used in this study followed that of Malvin et al very closely. Dextrose rather than mannitol was used to produce osmotic diuresis,

as stop-flow concentration patterns are more marked with the former (25).

It was found convenient to collect 'rapid fire' postocclusive urine samples in series of small preweighed test-tubes (Fig.7). These were bound together with Scotch Tape, in banks of ten. At the conclusion of the experiment the tubes were numbered, separated one from the other, and weighed. The increase in weight (in G.) of each tube was assumed to equal the volume of urine (in ml.) contained within.

Since publication of the original stop-flow technique, it has been shown that glomerular filtration does not cease when the ureter is clamped; fluid continues to shift down the tubule (34). Thus, where inulin is injected intra-arterially 2 minutes after the beginning of an 8 minute period of ureteric occlusion, subsequent analysis reveals its presence in distal tubular stop-flow samples. For this reason, a 'filtration-indicator' was not used - its appearance in the urine would be as much a measure of time of injection as of 'beginning of filtration' - and ureteric occlusion periods were kept down to 4 minutes, so as to minimise admixture of new filtrate with that already within the tubule.

Blood samples were drawn from an indwelling catheter in the right femoral artery; this was kept patent by flushing with 'normal' saline containing 100 u. heparin per litre.

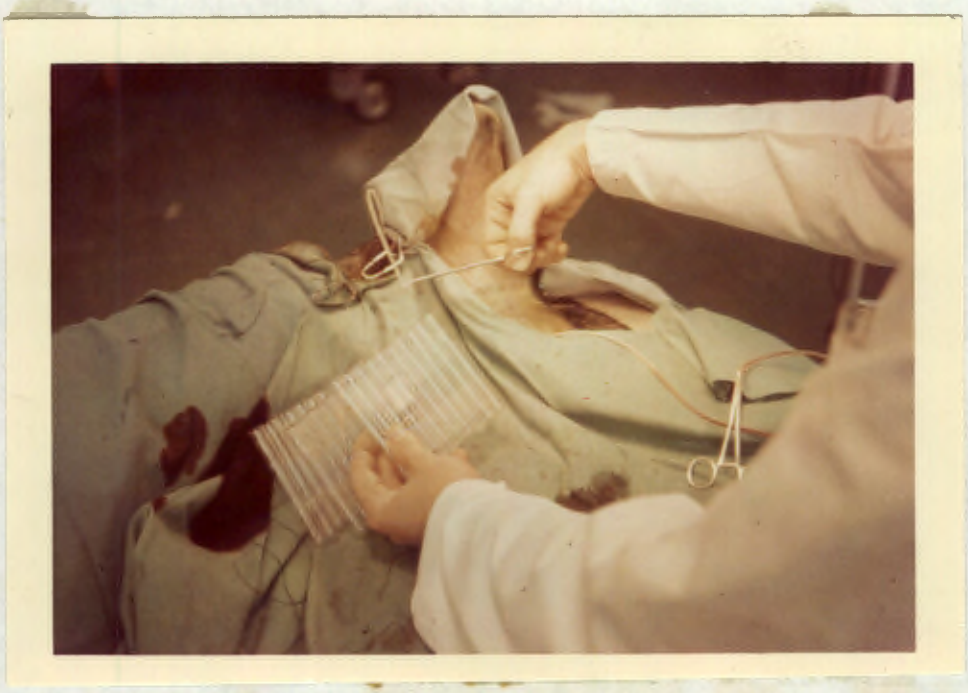

Fig. 7: Urine is about to be collected 'rapid-fire' after a period of stopped flow. The anaesthetised dog lies concealed beneath the green drape; only its left flank and thigh are visible. The polyethylene ureteral catheter is seen superiorly, emerging from the wound in the left flank; it is clamped off at its tip by a mosquito forceps. The femoral artery catheter lies inferiorly and to the right. The small test-tubes in which urine will be collected lie ready to hand; these are bound together in banks of ten.

Each dog received two intravenous infusions. One consisted of 'normal' saline, or 5% dextrose water, containing 1.0 G creatinine per litre; this was infused at an arbitrary rate of about 20 drops/minute. The other consisted of 5% or 10% dextrose water; this was run in rapidly enough to cause a diuresis of between 3ml. and 10 ml. per minute. As tubular reabsorption of inorganic phosphate-expressed as a fraction of that filtered - is largely independent of glomerular filtration rate (11, 37), and as the critical periods of interrupted stop-flow experiments occupy but a few minutes, constant-infusion machines were not used; drip rates were regulated by a simple screw clamps.

All the dogs weighed between 15 Kg to 20 Kg.

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PART 2

THE IONIC STRUCTURE OF URINE.

"The various physiological fluids can be quoted as another example where a theory of mixed electrolyte solutions would lead to progress".

Robinson and Stokes.

Chapter 1

Introduction

Urine differs markedly from glomerular filtrate in volume, pH, and osmotic concentration. These alterations are brought about, directly or indirectly, by renal ionic transport. Facultative control of urinary electrolyte content is mediated by ionic exchange (1). It is apparent that an appreciation of ionic processes in urine is a pre-requisite to an understanding of renal tubular transport mechanisms.

Little is known of the ionic structure of urine. Clinical teaching - based largely upon speculation concerning the aetiology of renal stone formation - suggests that it might, in some indefinable way, be very different to that of simple salt solutions. Thus,although possibly supersaturated with respect to these ions,urine may be 'good' or 'bad' ,according to its ability to inhibit or promote -withhold or donate Ca and inorganic phosphate - calcification in rachitic rat cartilage (17,25,40). Physiologists,on the other hand, for want of clear-cut evidence to the contrary, frequently assume ionic processes of individual electrolytes to be identical to those pertaining to simple aqueous solutions.This contrast in outlook is understandable when one recalls that the ionic processes of even mixed electrolyte solutions -unbedevilled by the pesence of large amounts of extraneous material - have so far escaped full analysis (35).

The approach adopted here is straightforward, and

consists essentially of comparison of the colligative● properties of the urinary ionic constituents with those of an equivalent solution of inorganic salts.

The results are presented in Chapter 2, each section of which represents a separate experiment. The work reported here arose initially from the need for a means of rapid estimation of urinary ionic strength; considerable attention has therefore been devoted to establishing correlations between ionic strength, specific conductivity and osmolality. The remaining experiments are given more or less in the order in which they were conceived, and so represent the sequence of ideas developed during the course of this investigation.

● Specific conductivity is included in this term, in as much as the conductivity of electrolyte solutions is dependent, at least in part, upon the number of ions present.

CHAPTER 2

Section 1

Analyses of Normal 24-Hour Urines

Aliquots of 24-hour urine collections were obtained from 60 normal Bantu and 54 normal 'White' South Africans. The Bantu were a selected rural group, partaking of a self-selected basically maize diet; this was in contrast to the 'Whites' who were all city dwellers and consumed a more sophisticated diet (26). All urines were collected under toluene.

Each urine was analysed for pH, Na, K, Ca, Mg, inorganic phosphate and sulphate, ammonium and osmolar content, and specific conductivity (of Appendices B and D). The urines were diluted twenty five times with distilled water prior to estimation of their specific conductivity; conductivity measurements were carried out at room temperature (17° - 27° C).

The ionic strength of each urine was then calculated as follows. The divalent fraction of the total inorganic phosphate content was derived from the Henderson-Hasselbalch equation (38) :

$$pH = pK + \log \frac{(HPO_4)}{(H_2PO_4)}$$

The pK was taken as 6.8 (37). This divalent fraction of the total inorganic phosphate, and the inorganic sulphate content, were assumed to be the only divalent anions present in significant amounts. The sum of their concentrations, deducted from the sum of the cation concentrations (in mEq/l.), yielded the total univalent anion concentration. Converting

mEq/l. to mI/l., ionic strength was then calculated as;

$$I.S. = \frac{1}{2} (C V^2) n$$

where I.S. is ionic strength, and C and V are the concentration and valency, respectively, of each of the n ionic constituents.‡

The combined concentration of the divalent ionic constituents (sulphate, basic phosphate, calcium and magnesium) was then calculated as a percentage of the total ionic constituent concentration, in each urine.

The results are summarised in Table 1.

---

‡ Each radical of a salt, eg. Na in NaCl, is an Ionic Constituent.

One Gram-Molecular weight of NaCl contains one Gram-Mole of NaCl, one Gram-Ion of Na, and one Gram-Ion of Cl. Milli-Ions are therefore analogous to milli-Moles, but refer to ionic constituents rather than molecules. Conversion of mEq/l. to mI/l. (milli-Ions per litre) is effected simply by dividing by the valency of the ionic constituent concerned.

TABLE 1

IONIC CONCENTRATIONS NORMAL 24-HOUR URINES

	Whites			Bantu			Both	
	No.	Mean	S.D.	No.	Mean	S.D.	Mean	S.D.
Na (mEq/l.)	54	199.3	35.8	60	163.6	32.7	180.5	38.7
K "	54	66.5	18.9	60	32.2	11.3	48.5	23.1
NH_4 "	54	92.6	27.5	60	47.3	23.0	68.8	33.9
Ca "	54	5.8	2.8	60	2.3	1.4	3.9	2.8
Mg "	53	9.8	4.2	60	5.8	3.2	7.7	4.2
SO_4 "	54	33.8	18.8	56	47.9	13.3	40.9	17.7
P (mM/l.)	54	26.6	9.2	60	11.1	6.5	18.4	11.1
Vol.(ml/24 hrs.)	54	1178	434	60	2073	691	1649	735
Osm(mOsm/kg H_2O)	53	980	223	56	747	150	860	222
pH	54	6.30	0.32	60	6.19	0.80	6.24	0.62
Sp.$K^{u/25}_{rt}$	53	1.035	.258	56	0.754	.166	0.891	.257
Ionic Strength	53	0.404	0.076	56	0.281	0.050	0.341	0.089
% Divalent mI/l.	53	4.5	1.6	56	6.9	1.6	5.7	2.0
mI/mOsm.,per litre		74.1	7.3		63.6	7.8	68.7	9.2

All distributions Gaussian, except that of Ca; this was positively skewed.

Section 2

Inter-relationships between urinary Ionic Strength, $Sp.K_{rt}^{u/25}$, and Osmolality, in Normal 24-Hour Urines.

These interrelationships were derived from the urines analysed in Section 1.

Correlations:

	Whites	Bantu	Both
Between Osmolality and Ionic Strength:	+.927	+.897	+.926
" $Sp.K_{rt}^{u/25}$ and Ionic Strength:	+.838	+.940	+.924
" Osmolality and $Sp.K_{rt}^{u/25}$:	+.861	+.777	+.881

Standard Errors of Estimate of Ionic Strength:

as derived from (1) Osmolality: 0.034

(2) $Sp.K_{rt}^{u/25}$: 0.034

Regression Equations interrelating Ionic Strength: Osmolality and $Sp.K_{rt}^{u/25}$:

$$I.S. = .000371 (Osm.) + .022 \quad (1)$$

$$Osm. = 2317 (I.S.) + 71 \quad (2)$$

$$Sp.K_{rt}^{u/25} = 2.617 (I.S.) - .001 \quad (3)$$

$$I.S. = 0.312 (Sp.K_{rt}^{u/25}) + .063 \quad (4)$$

$$Osm. = 761 (Sp.K_{rt}^{u/25}) + 183 \quad (5)$$

$$Sp.K_{rt}^{u/25} = .00102 (Osm.) + .0114 \quad (6)$$

Partial Regression Equation interrelating Ionic Strength, Osmolality and $Sp.K_{rt}^{u/25}$:

$$I.S. = .000255 (Osm.) + .135\ Sp.K_{rt}^{u/25} + .002 \quad (7)$$

Multiple Correlation Coefficient: + .941

Standard Error of the Estimate of Ionic Strength, as derived from equation (7): 0.030

Section 3

Analyses of random urine samples obtained from patients with renal or electrolyte disorders.

Random urine samples were obtained from hospitalised patients, all of whom were acutely ill, and all of whom were suffering from renal and/or electrolyte abnormalities. Urines were collected under toluene.

Each urine was then analysed for pH, Na, K, Ca, Mg, inorganic phosphate and sulphate, ammonium and osmolar content, and specific conductivity ($Sp.K_{rt}^{u/25}$) , as in Section 1.

Patient Diagnoses (number of patients in parentheses):

(A) Renal Lesions: Bilateral nephrocalcinosis, with renal stone (1); nephrotic syndrome of unknown cause (4); idiopathic hypercalciuria, on Prednisone therapy (1); Subacute glomerular nephritis (1); proteinuria ? cause (2).

(B) Extra-renal Lesions: Diabetes Insipidus - urines analysed before and after Pitressin therapy (1); 6 cases of diabetes mellitus, 4 of whom were in severe ketosis; hypertensive congestive cardiac failure, on diuretic therapy (5); malignant hypertension (1); rheumatic valvular heart disease, in congestive cardiac failure, on digitalis and diuretic therapy (2); parenchymatous hepatitus with jaundice (6); systemic lupus erythematosus, on Prednisone therapy (1); cerebro-vascular accident, in coma and dehydrated (1); tuberculous ascites (3); congestive cardiac failure secondary to severe anaemia, respiratory failure or myocardial infarction (4); subacute bacterial endocarditis (2), one of whom had a cerebral embolus; dehydration and collapse of unknown aetiology (1); carcinomatous ascites (1); amoebic liver abscess (2); carcinoma of the breast, with bilateral adrenalectomy, in Addisonian crisis (1);

bronchopneumonia (1); congestive cardiac failure, ? cause, on digitalis and diuretic therapy (4).

Summary of Results of Analyses:

(A) Concentrations:

		No.	Mean.	S.D.
Na	(mEq/l.)	52	91.1	65.2
K	"	52	78.7	55.5
NH_4	"	52	58.5	36.6
Ca	"	46	3.3	3.9
Mg	"	52	6.9	4.1
SO_4	"	52	55.5	37.3
P	(mM/l.)	52	14.81	11.18
Osm.	(mOsm/kg. water)	52	695	207
Sp.$K_{rt}^{u/25}$	(mMhos/cm.)	52	0.653	0.231
pH		52	6.15	0.88
Ionic Strength		52	0.274	0.087
% Divalent ionic constituents	(mI/l.)	52	10.1	7.0
(mI/l.)/Osm. X100		52	64.4	19.6

(B) Correlations:

between Osmolality and Ionic Strength: +.653

" Sp.$K_{rt}^{u/25}$ and Ionic Strength: +.818

" Osmolality and Sp.$K_{rt}^{u/25}$: +.677

(C) Standard Error of Estimate of Ionic Strength, as derived from:

(i) Osmolality: 0.066

(ii) Sp.$K_{rt}^{u/25}$: 0.050

Section 4

Comparison of concentrations of Ionic Constituents in Normal and Abnormal Urines

The mean ionic concentrations, and ionic strengths, of 114 normal (24-hour) and 52 abnormal (random sample) urines have been given in Sections 1 and 3. Correction for differences in ionic strength permits direct comparison of ionic consituent concentrations in these two groups.

This has been accomplished here by converting all data to an ionic strength of 0.100. Each standard deviation is expressed as a percentage of the mean, that is, as the Coefficient of Variation.

Results:

	Normals		Abnormals		
	Mean	Coeff. of Variation	Mean	Coeff. of Variation	P
Na (mEq/l.)	53.0	21.4	33.3	71.5	<.001
K "	14.2	47.4	28.7	70.6	<.001
NH_4 "	20.2	49.3	21.4	62.6	
Ca "	1.14	71.8	1.21	118.1	
Mg "	2.26	54.6	2.52	59.4	
SO_4 "	12.0	42.0	20.2	67.2	<.001
P (mM/l.)	5.4	44.6	5.4	75.7	

Summary: (1) For a given ionic strength, abnormal urines have, on the average, lower Na but higher K and SO_4 concentrations than do normals. (2) Individual ionic constituent concentrations show greater variability, relative to each other, in abnormal than in normal, urines.

Section 5

Relationship between Osmolality and $Sp.K_{rt}$ in normal undiluted urines.

(A) Random urine samples were obtained from normal subjects. The osmolality and $Sp.K_{rt}$ of each were then determined. Note: A few urines were diluted with distilled water, so as to vall into the very low $Sp.K_{rt}$ - Osmolar range (cf Fig. 8).

Results:

	No.	Mean	S.D.
Osmolality(mOsm/kg water)	136	446	319
$Sp.K_{rt}$ (mMhos/cm.)	136	13.7	9.1

Correlation between $Sp.K_{rt}$ and Osmolality: + .955

Regression Equations:

$$Sp.K_{rt} = .0273 \text{ (Osm.)} + 1.57 \qquad (8)$$

$$Osm. = 33.5 \ (Sp.K_{rt}) - 13.8 \qquad (9)$$

Standard Error of Estimate of (1) Osm. from $Sp.K_{rt}$=95 mOsm/kg water

(2) $Sp.K_{rt}$ from Osm.=2.7 mMhos/cm.

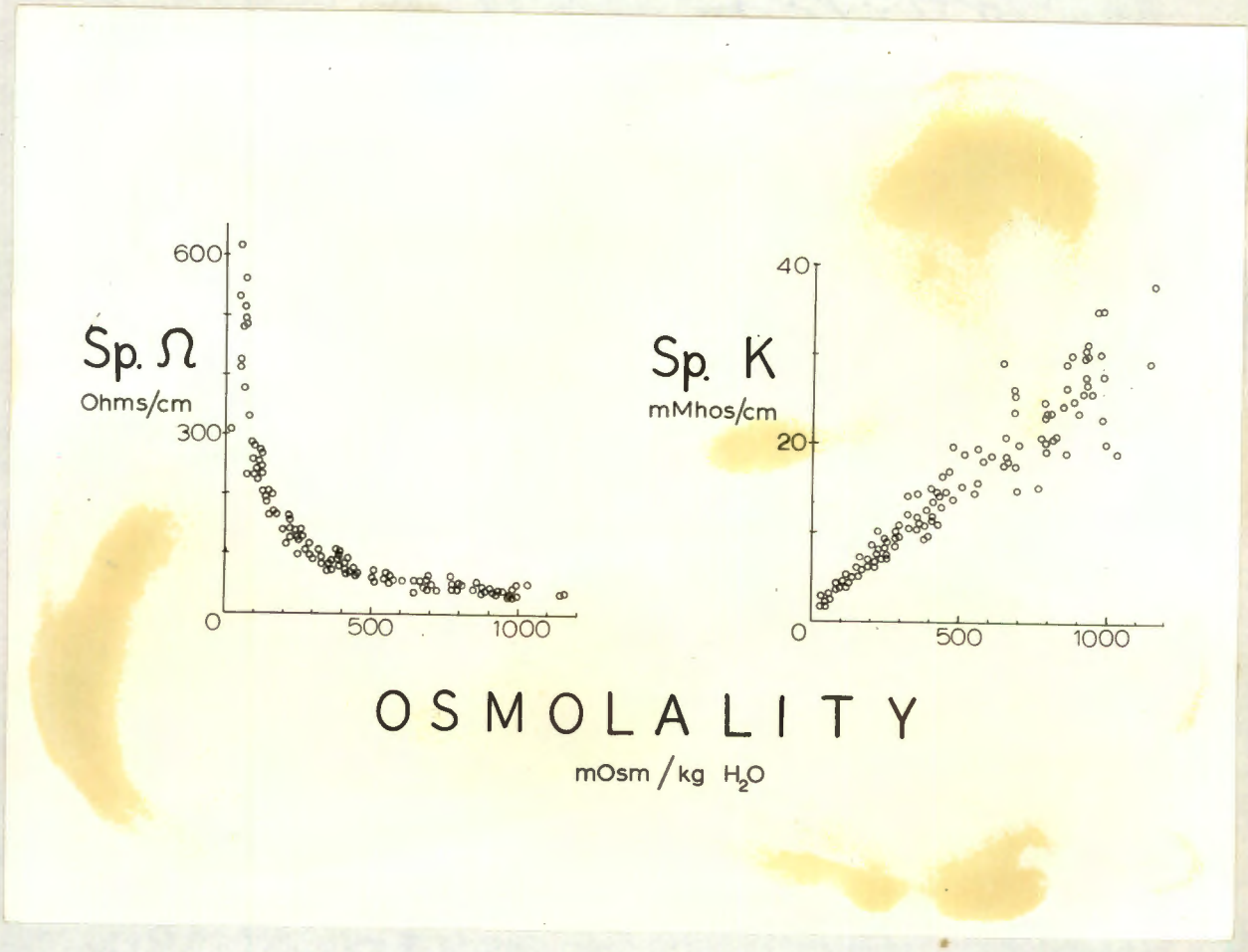

Fig. 8: Relationship between Osmolality and $Sp.K_{rt}$ in normal undiluted urines.

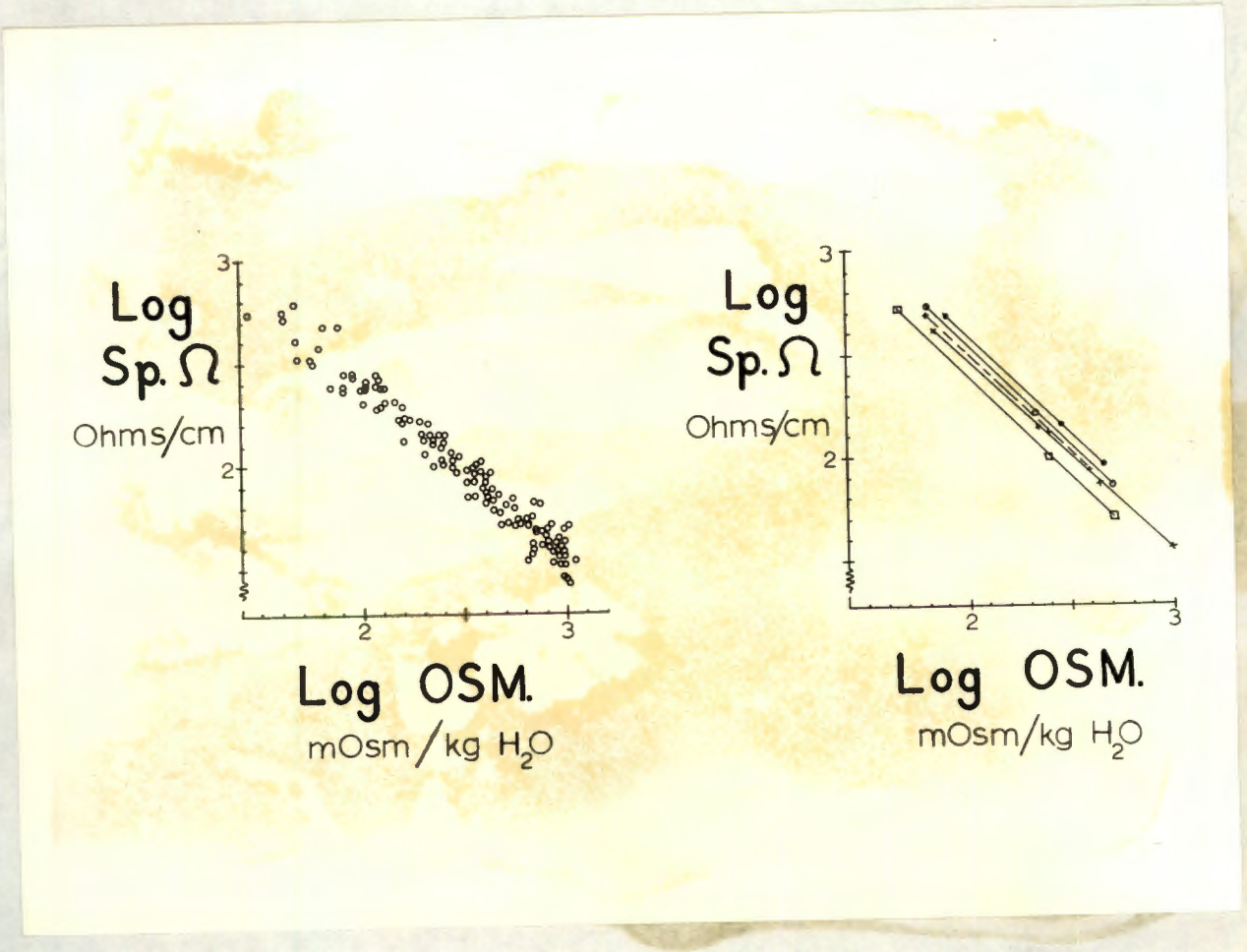

Fig. 9: Linear relationship between Log.Specific Resistance and Log.Osmolality.

(B) Osmolar - Specific Resistance relationships:

Specific conductivity is derived from measurement of specific resistance (of Appendix B). Variation of specific resistance with osmolality is shown in Fig. 8 (data from same urines as above). It was found possible to effect a linear transformation of this relationship by transposition of the resistance and osmolar data into their logarithms (Fig.9).

Results:

	No.	Mean	S.D.
Log Osmolality	136	2.4923	0.4182
Log Sp. Resistance	136	1.9807	0.3474

Correlation between Log. Osm. and Log. Sp. Resistance = -.969

Regression Equations:

$$\text{Log. Sp.Resistance} = 3.988 - 0.8055\ (\text{Log. Osm}) \qquad (10)$$

$$\text{Log. Osm.} = 4.807 - 1.1685\ (\text{Log. Sp. Resistance}) \qquad (11)$$

Progressive dilutions of individual urines similarly yielded linear Log.Osm. - Log. Sp. Resistance interrelationships (Fig.9) (Table 2).

(C) Linear Transformation of Osmolality-Sp.K_{rt} interrelationship:

The regression equations (8) and (9), were derived on the assumption of a linear relationship between osmolality and Sp.K_{rt}. The same data however give a slightly better correlation between Log. Osmolality and Log. Sp. Resistance than between Osmolality and Sp.K_{rt}. Furthermore, progressive dilutions of individual urines do not show a

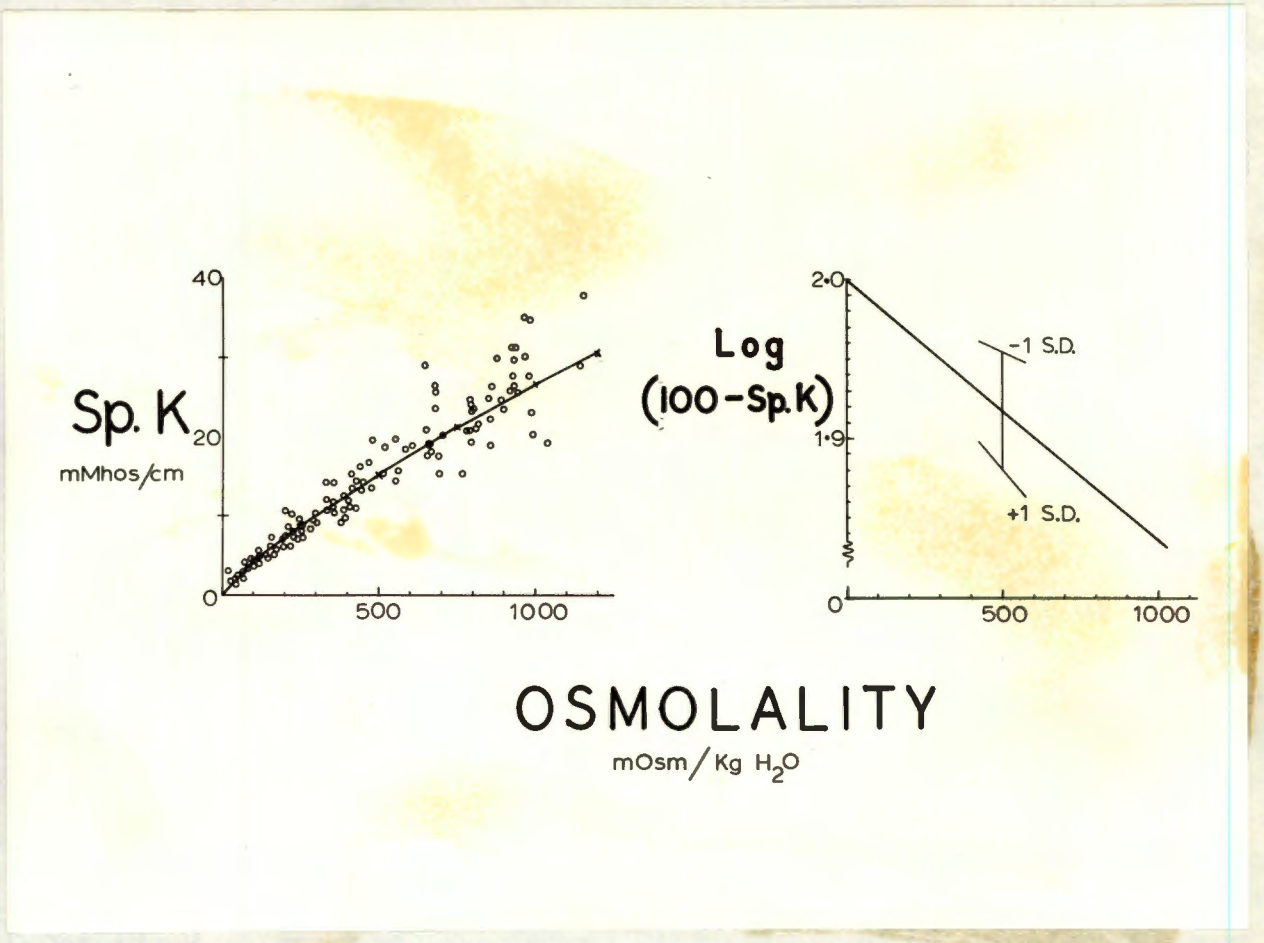

Fig. 10: Linear transformation of observed curvilinear relationship between urinary osmolality and $Sp.K_{rt}$

linear fall in Sp.K with osmolality (Table 2). Superimposition of the regression line of equation (10) - with conversion of Log. Sp. Resistance to Sp.K, and of Log. Osmolality to Osmolality - onto the graph relating $Sp.K_{rt}$ and Osmolality, reveals the relationship to be curvilinear (Fig.10).

Linear transformation of this relationship was effected (34) empirically, by assuming an exponential approach of $Sp.K_{rt}$ to an asymptote of 100 mMhos/cm., with increasing urinary osmolality. Thus:

$$100 - Sp.K^X = (100 - Sp.K^O)\, e^{-s\,x} \qquad (12)$$

where $Sp.K^X$ and $Sp.K^O$ are specific conductivities at x and zero mOsm/kg water, respectively, and s is an experimentally derived constant. Or, as $Sp.K^O$ is zero,

$$Sp.K^X = 100\,(1 - e^{-s\,x}) \qquad (13)$$

In practice, it was found convenient to work with logarithms to the base 10. The experimentally derived constant, s, then becomes‡ s' , where

$$s' = \frac{2 - \log\,(100 - Sp.K^X)}{x} \qquad (14)$$

In the 136 urines analysed here, the mean value of s' was found to be 0.1634×10^{-3}, with S.D. of 0.0741×10^{-3}

---

‡ Since $100 - Sp.K^X = (100 - K^O)\, e^{-sx}$

Therefore $\text{Log}\,(100 - Sp.K^X = \text{Log}\,(100 - Sp.K^O) - s'x$

But $Sp.K^O = 0$

Therefore $\text{Log}\,(100 - Sp.K^X) = 2 - s'x$

or $S' = \frac{2 - \text{Log}\,(100 - Sp.K^X)}{x}$

Section 6

Preparation of a salt mixture of composition similar to that of 'average' urine.

A mixture of inorganic salts, of composition and concentration identical* to that of 'average' normal urine, was prepared as a basis for comparative measurements of osmolality, Sp.K and dielectric constant.

Composition of 'average' normal urine: The 'average' normal urine ionic constituent composition given in Section 1 includes five urines in which ionic strengths were not calculated (as one or other of the ionic consituent concantrations were not determined). Excluding these, mean concentrations in the remaining 109 normal urines were:

Na	(mEq/l.)	180.7
K	"	48.4
NH_4	"	68.6
Ca	"	4.0
Mg	"	7.9
SO_4	"	40.4
P	(mM/l.)	18.7
pH		6.22
Ionic strength		0.341

At this pH, the divalent inorganic phosphate concentration is 3.9 mM/l., or 7.8 mEq/l (Henderson-Hasselbalch equation).

---

* This assumes all the undetermined univalent anions, other than $H_2PO_4^-$, were Cl^-; HCO_3^- was not measured, and is taken here as zero. This assumption probably introduces little error, as the average pH is below 7.0 (15).

Calculation of ionic strength now yields a figure of 0.340. Per 0.100 ionic strength, 'average' urine therefore contains:

Na	53.1	mEq/l.,
K	14.2	"
NH_4	20.2	"
CA	1.18	"
Mg	2.32	"
SO_4	11.9	"
HPO_4	2.29	"
H_2PO_4	4.35	"

The Composition of the salt mixture was determined by the above.

Salt	mEq. desired	Weight Required(G./l.)	ml/l.
$Na_2HPO_4.12H_2O$	2.29	0.4099	3.435
Na_2SO_4	9.58	0.6802	14.370
$CaCl_2$	1.18	0.0655	1.770
NH_4Cl	20.20	1.0807	40.400
KCl	14.20	1.0579	28.400
$NaH_2PO_4.2H_2O$	4.35	0.6786	8.700
NaCl	36.88	2.1575	73.760
$MgSO_4.7H_2O$	2.32	0.2859	2.32

This mixture, when dissolved to one litre with distilled water, gives a solution of 0.100 ionic strength. In practice, five times these concentrations were used to give a solution of ionic strength of 0.500. This is referred to subsequently as 'the salt mixture'.

Section 7

Variation of Sp.K with temperature.

The Sp.K of various concentrations of the salt mixture was determined at 20°, 30° and 40°C. The salt mixture was brought to the requisite temperature by immersion of the conductivity cell in a water bath.

Results:

	Sp.K (mMhos/cm.)		
Temp. (°C)	I.S. 0.56	I.S. 0.112	I.S. 0.056
40	60.2	13.5	7.13
30	50.0	11.2	5.89
20	40.5	9.14	4.77

That is, the Sp.K increases with temperature, and the degree of increase is a function of the initial conductivity.

It was found possible to simplify this relationship by assuming it to be exponential:

$$Sp.K_t = Sp.K_{20} \cdot e^{k(t - 20)} \qquad (15)$$

where $Sp.K_t$ and $Sp.K_{20}$ are the specific conductivities at temperatures t° and 20° Centigrade, respectively, and k is an experimentally derived constant. Substituting the above data into this equation, to obtain K:

	k			
Temp. (^{o}C)	I.S. 0.56	I.S. 0.112	I.S. 0.056	
30^{o} - 40^{o}	.01856	.01868	.01911	Mean = .0188
20^{o} - 30^{o}	.02107	.02034	.02110	Mean = .0208

As most determinations would be carried out at room temperature, (17^{o} - 27^{o}), k was taken as .0208. The Sp.K of any solution, determined at room temperature, t^{o}, can now be corrected to the value pertaining at 20^{o} C., by substitution into the equation:

$$Sp.K_t = Sp.K_{20}\, e^{.0208\,(t-20)} \qquad (16)$$

In practice, as some determinations were performed above and some below 20^{o}C., and as the determination of Sp.K of diluted solutions necessarily incorporates dilution errors, this equation was 'rounded off' to:

$$Sp.K_t = Sp.K_{20}\, e^{.02\,(t\,-\,20)} \qquad (17)$$

Section 8

Correlation between Urinary Osmolality and $Sp.K_{20}$

Random urine samples were obtained from 63 normal subjects. These were analysed for osmolality and Sp.K as before. The temperature of the urine, at the time of determination of Sp.K was measured with a mercury thermometer. Sp.K values were then 'corrected' to 20° C., by equation 17.

Results:

	No.	Mean	S.D.
Osmolality(mOsm/kg water)	63	787.9	255.4
$Sp.K_{20}$ (mMhos/cm.)	63	19.86	6.35

The correlation between Osmolality and $Sp.K_{20}$ was + .917 (assuming a linear relationship).

Section 9

(1) Ionic composition of random normal urine samples, and

(2) Correlation between urinary Ionic Strength, and $Sp.K_{20}$ in (A) normal and (B) abnormal urines.

Random urine samples were obtained from 42 normal subjects, and 11 acutely ill hospitalised patients. Urine was diluted ten times with distilled water prior to estimation of $Sp.K_{20}$. Ionic strength and osmolality were determined as in Section 1.

Patient Diagnoses (number of patients in parentheses): Hypertension, (3) one with uraemia; nephrotic syndrome of uncertain aetiology (2); congestive cardiac failure of unknown cause (1); Infective Hepatitis with jaundice (1); acute renal failure (2); rheumatoid arthritis, on Prednisone therapy (1); primary carcinoma of the liver (1); and malignant hypertension (1).

Results:

(A) Normals:

Concentrations:

	Mean	S.D.	Coefficient of Variation
Na (mEq/l.)	131.6	69.9	53.1
K "	56.4	30.3	53.7
NH_4 "	51.4	23.2	45.2
Ca "	4.62	3.09	66.8
Mg "	7.10	3.16	44.5
SO_4 "	29.1	13.0	44.6
P (mM/l.)	15.24	9.42	61.8
Osm.(mOsm/kg water)	718	276	-
$Sp.K_{20}^{u/10}$ (mMhos/cm)	2.459	1.000	-
pH	5.96	0.63	-
Ionic Strength	0.272	0.110	-

Correlations between $Sp.K_{20}^{u/10}$ and I.S. = + .970

Osm. and I.S. = + .954

$Sp.K_{20}^{u/10}$ and Osm. = + .943

Standard Error of Estimate of Ionic Strength

from $Sp.K_{20}^{u/10}$ = .027

" Osmolality = .033

Regression Equations relating $Sp.K_{20}^{u/10}$ and I.S.:

$$Sp.K_{20}^{u/10} = 8.798\ I.S. + .063 \quad (18)$$

$$I.S. = 0.1069\ Sp.K_{20}^{u/10} + .009 \quad (19)$$

Partial Regression Equation relating $Sp.K_{20}^{u/10}$, Osmolality and Ionic Strength:

$$I.S. = 0.0001232\ Osm. + 0.07443\ Sp.K_{20}^{u/10} + .0005 \quad (20)$$

Multiple Correlation Coefficient: + .975

Standard Error of Estimate of Ionic Strength, using Equation 20: .025

Comparison of Ionic concentrations with those of 24-hour Normal urines and Random Abnormal urines:

Per 100 ionic strength, these random normal urines have a mean Na concentration of 48.4 mEq/l., and a mean SO_4 concentration of 10.7 mEq/l. These concentrations are not significantly different to those of the normal 24-hour urines, but differ significantly ($P<.001$) from those of the abnormal urines (Section 4).

The mean K concentration (20.7 mEq/l, per 100 ionic strength) differs significantly from those of both the normal 24 hour urines ($P<.01$) and the abnormal urines ($P<.02$).

(B) Abnormals:

	No.	Mean	σ
Sp.$K_{20}^{u/10}$	11	1.3076	0.6572
Osm.(mOsm/kg water)	11	410.6	205
I.S.	11	0.1553	.0753

Correlation between Sp.$K_{20}^{u/10}$ and I.S. = +.870

" Osmolality and I.S. = +.729

Section 10

Some Physico-chemical properties of the salt mixture:

(a) The salt mixture as composed in section 6 is a molar solution. The same weights of salts were mixed with one kilogram of water (20°C.) to obtain a molal solution, and the osmolality of this then determined.

(b) Osmolality and Sp.K_{20} were determined on serial dilutions of molar salt mixture.

Results: (a) Osmolality of 0.500 ionic strength molal salt mixture was 753 mOsm/kg water.

(b) Osmolar salt mixture:

Osm. (mOsm/kg) water	I.S.	Sp.K_{20} (mMhos/cm.)	ml/l.	g	Log (200-Sp.K_{20})	s' .10-3
759	.500	38.01	855.3	.887	2.2092	.1223
381	.250	20.64	427.65	.891	2.2539	.1236
195	.125	10.88	213.83	.912	2.2767	.1246
100	.0625	5.70	106.92	.935	2.2885	.1259
					Mean:	.1239

where g = osmotic coefficent.

Relationship between Osmolality and Sp.K_{20}:

Using the same arguement as in section 5 (c),

$$K^x = 200(1 - e^{-sx}) \qquad (21)$$

where x is the osmolality of the mixture, and K is Sp.K_{20}.

$s = 2.303 \times (s' 10^{-3}) = .2853 \times 10^{-3}$

The Osmotic Coefficient (g)

was calculated as:

$$g = \frac{\text{mOsm/kg water}}{\text{mI / l.}}$$

This assumes mI/l. identical to mI/kg water. The close similarity of osmolality of molal and molar salt mixture solutions was taken as sufficient justification for this assumption.

Regression Equations:

$$\text{Osm.} = 0.88\ \text{mI/l.} + 7 \qquad (22)$$

$$\text{mI/l.} = 1.134\ \text{Osm.} - 7 \qquad (23)$$

Section 11

Comparison of the Sp.K / Osmolar relationship of the Salt mixture, with those of solutions of individual Electrolytes:

Solutions of various electrolytes were made at arbitrary concentrations (cf below). The Sp.K and osmolality of these were then determined. All specific conductivities, including that of the salt mixture, were measured at room temperature (26° C.)

Results: (Fig. 11)

	Osmolality (mOsm/kg water)	$Sp.K_{26}$ (mMhos/cm.)
Salt mixture	297	16.1
$MgCl_2$	257	17.0
$CaCl_2$	262	18.2
Na_2SO_4	272	17.3
NaH_2PO_4	279	9.0
KCl	196	12.7
NaCl	300	16.5
NH_4Cl	318	20.6

Salt solutions have curvilinear Sp.K/Osmolar relationships. At concentrations below about 500 mOsm/kg water, linear transformation of these relationships can be effected by use of the same equation (Equation 12) as was applied to urine. To facilitate comparison with the latter, solutions of individual electrolytes and of the salt mixture were therefore kept below this concentration. cf Fig. 11.

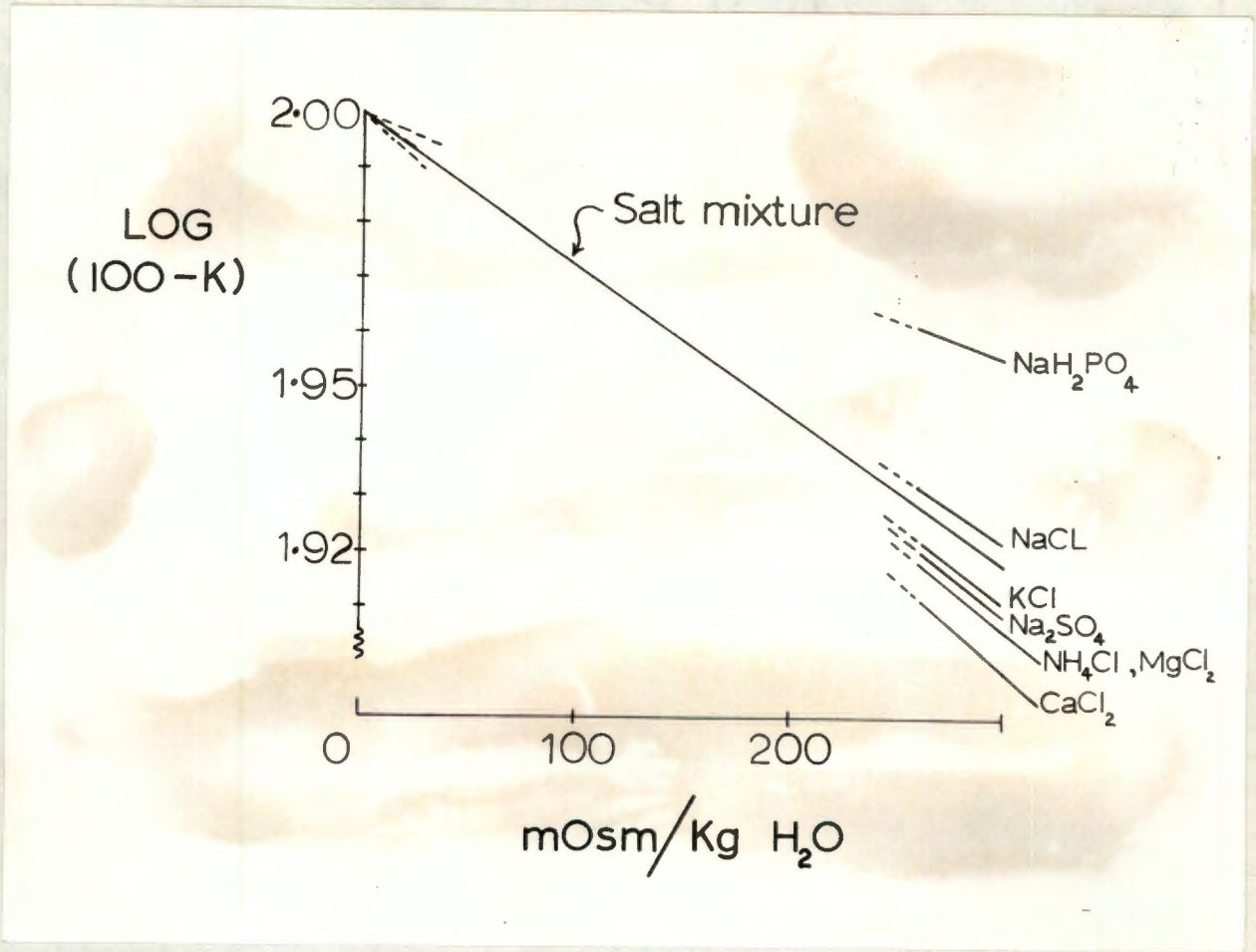

Fig. 11 : Comparison of the Sp.K / Osmolar relationship of the salt mixture, with those of solutions of individual electrolytes. Linear transformations of the curvilinear relationships have been effected by use of equation 12. Compare with Fig. 10 (b).

Section 12

Some Physico-chemical properties of the salt mixture, with urea added.

Urea was added to the molar salt mixture (2 Grams per 100 ml.) and osmolality and $Sp.K_{20}$ then measured as before. The osmolality of 2 Grams urea per 100 ml. distilled water was also noted.

Results: (a) 2 G. urea / 100 ml. water yielded 322 mOsm/kg water
4 G. urea/100 ml. water yielded 640 mOsm/kg water.

(b) 2 G. urea / 100 ml. salt mixture:

Osm. (mOsm/kg water)	$Sp.K_{20}$ mMhos/cm.	I.S.	mI/l.	mM_u	g_{mI}	$g_{(mI + mMu)}$
1082	38.02	.500	855.3	322	.889	.919
541	20.42	.250	427.65	161	.889	.919
275	10.81	.125	213.83	80.5	.910	.934
141	5.71	.0625	106.92	40.25	.942	.958
72.6	2.99	.0313	53.46	20.13	.982	.987

where mM_u = milli-moles urea; this is derived from (a) above and assumes the osmotic coefficient of urea to be unity.

g_{mI} = osmotic coefficient of the ionic constituents. Derived by subtracting mM_u from the observed osmolality, and then calculating g, as before (section 10).

$g_{(mI + mM_u)}$ = osmotic coefficient of the entire solute; derived by dividing the observed osmolality by the total concentration of milli-ions and milli-moles urea.

Conclusions: (1) The $Sp.K_{20}$ of the salt mixture, in varying dilutions, is unaffected by the presence of urea (compare section 10)

(2) The overall osmotic coefficient of the mixture of ionic constituents is unaffectéd by the presence of urea (compare section 10).

Section 13

The overall Osmotic Coefficient of Urinary Electrolytes.

Two approaches were made to this problem.

(a) The overall osmotic coefficient (g) of the urinary electrolytes was assumed equal to that of the salt mixture of identical ionic constituent concentration. That is,

$$mM_u/l. + mI/l.(g) = Osm \qquad (24)$$

(b) The osmolality of greatly diluted urine was assumed equal to the concentration of non-electrolyte (in mM/l.) plus ionic constituents (in mI/l.). It follows that

$$g = Osm. - f(Osm.^f - mI/l.^f) \,/\, mI/l. \qquad (25)$$

where f = dilution factor, and Osm^f and $mI/l.^f$ are the osmolality and concentration of milli-ionic constituents per litre, respectively, in the diluted urine.

(The derivations of these equations are considered further in the Discussion.)

These assumptions were tested on 13 of the normal, and 10 of the abnormal, urines described in section 9.

Note on Methodology: In method (a), the number of mOsm/kg water derived from ionic consituents was calculated by equation 22.

In method (b), the osmolalities of the diluted urines were estimated in either one of two ways. (i) The Fiske osmometer - which estimates osmolality by measurement of depression of freezing point - was recalibrated using urea standards; this avoided difficulties with ionic dissociation as encountered in very dilute NaCl standards. The osmolalities of the dilutions of urines 34, 40, 43, 46, 47, and 48 were measured in this way.

(ii) The osmolality and $Sp.K_{20}$ of the undiluted urine were obtained as before; s' (equation 14) was then calculated. The osmolality of the diluted urine was then obtained simply by measurement of the $Sp.K_{20}$ and application of equation 13. This method was applied to urines 30, 35, 36, 37, 38, 42, and 45, as well as to all the abnormal urines.

Results: (1) Normals:

Urine	Method (a)			Method (b)			
	ml/l.	$Osm_{ob.}$	Osm_{calc}	f	mM_{nu}	$\frac{mM_{nu} \times 100}{Osm.}$	g
24	520	636	644	50	29	4.6	.822
28	837	1128	1093	84.2	160	14.2	.738
29	139	286	266	25	54	18.9	.681
30	101	177	174	25	13	7.4	.847
31	205	331	299	25	72	21.7	.717
32	344	544	502	25	92	16.9	.753
34	696	928	921	32	132	14.2	.724
36	587	829	773	100	74	8.9	.860
37	598	876	813	64	146	16.7	.753
39	87	141	171	20	0	0	.757
40	556	1023	936	72.7	168	16.4	.747
41	340	509	514	32	0	0	.897
42	510	894	827	32	110	12.3	.808

Mean : 11.7

Osm_{ob} and Osm_{calc} = observed and calculated osmolality, respectively

f = dilution factor

mM_{nu} = calculated concentration of non-electrolyte, non-urea substance, in milliMoles per litre of undiluted urine. See Discussion.

Where $mM_{ni} < mM_{u}$, mM_{nu} taken as zero; see Discussion.

(ii) Abnormals:

		Method (a)			Method (b)			
Urine No.	Protein--uria.	ml/l	Osm_{ob}	Osm_{calc}	f	mM_{nu}	$\frac{mM_{nu} \times 100}{Osm.}$	g
1	+	190	287	274	20	43	15.0	.758
2	++++	180	370	299	25	166	44.8	.394
3	++	282	625	605	50	160	25.6	.408
4	-	443	701	668	50	137	19.6	.664
5	-	77	106	128	10	0	0	.688
6	-	368	695	664	50	201	28.9	.438
7	-	156	387	314	33.3	187	48.4	.194
8	+++	368	490	494	50	90	18.4	.645
9	+	169	251	249	25	31	12.4	.751
10	-	473	446	523	50	118	26.5	.482

Mean: 24.0

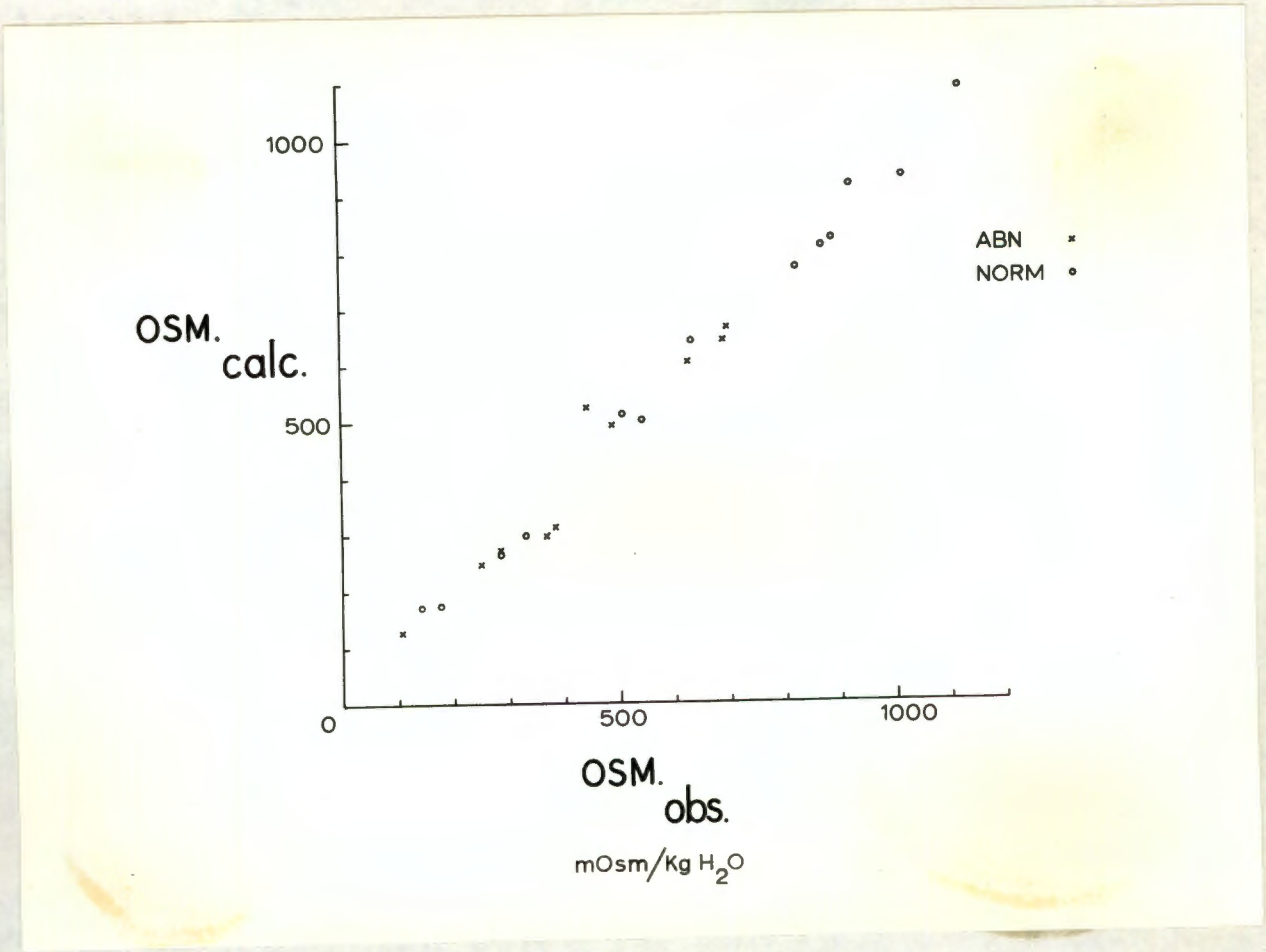

Fig.12: Comparison of calculated and observed urinary osmolalities.

Section 14

Overall Osmotic Coefficient of Urinary Electrolytes on Progressive Dilution:

Six urines (no.s 28, 34, 37, 40, 41 and 42 of Section 9) were diluted progressively; the osmolality of each dilution was measured on the Fiske osmometer, calibrated with urea standards as above.

The results are given below.

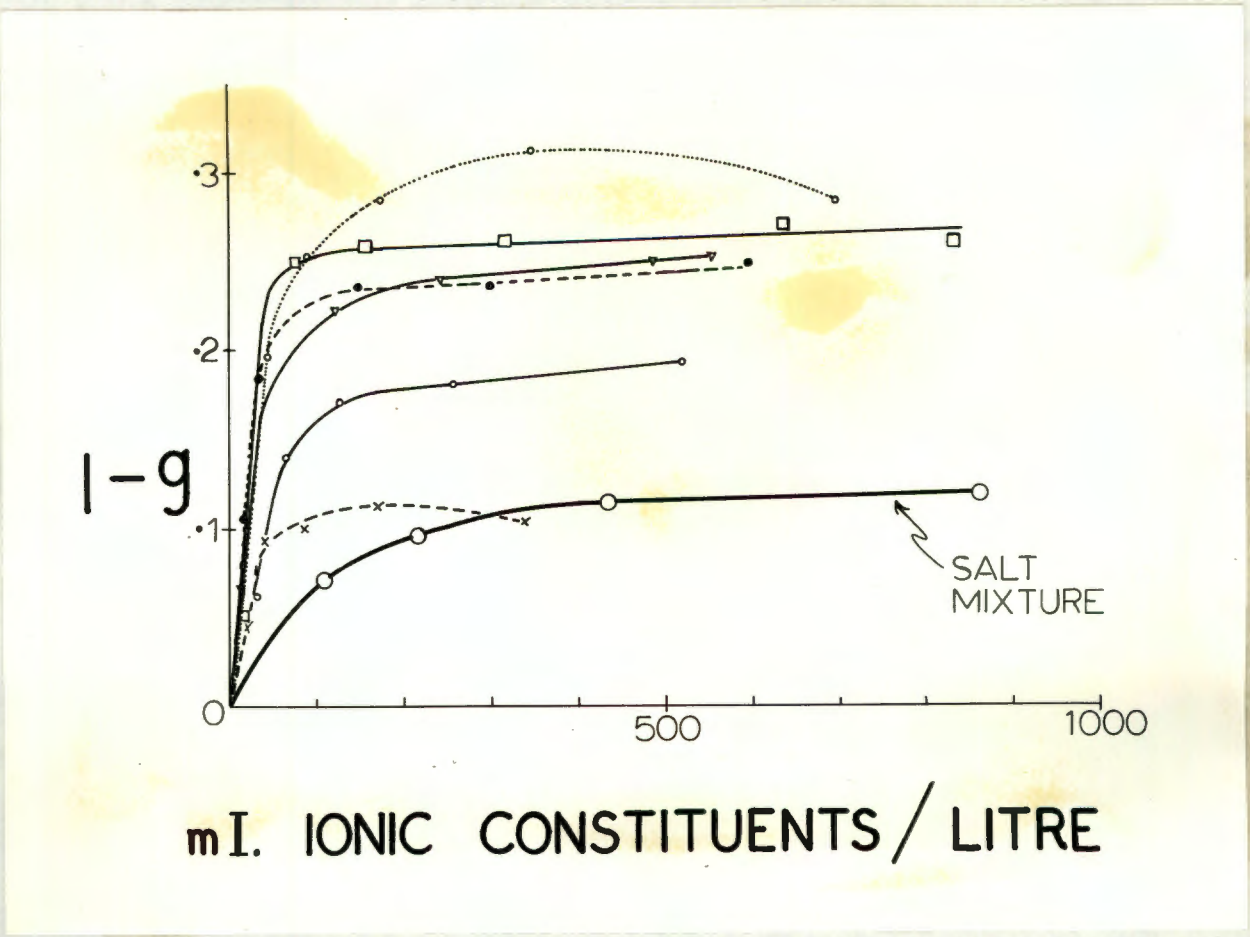

Fig.13: Relative depression of the apparent osmotic coefficients (g) of a number of normal urines, in comparison to that of the 'salt mixture'.

Osmotic coefficients are plotted as 1-g, for graphic convenience only.

Apparent Osmotic Coefficients of Urinary Electrolytes as obtained on progressive dilution. - Section 14

Urine No.	Dilution factor (f)	Osm.	g
28	0.76	ǂ 1128	.738
	1	857	.737
	2	428	.736
	4	214	.736
	8	108	.748
	16	56	.799
	32	31	.950
	64	16	
34	1	928	.724
	2	455	.698
	4	232	.724
	8	119	.759
	16	62	.816
	32	35	
37	1	876	.753
	2	442	.766
	4	221	.766
	8	110	.759
	16	57	.813
	32	30	.893
	64	16	

Urine No.	Dilution factor(f)	Osm.	g
40	0.88	ǂ 1023	.747
	1	901	.748
	2	454	.763
	4	228	.771
	8	114	.771
	16	59	.836
	32	31	.934
	64	16	
41	1	509	.897
	2	253	.888
	4	128	.906
	8	64	.906
	16	33	.953
	32	17	
42	1	894	.808
	2	450	.820
	4	226	.827
	8	115	.859
	16	60	.937
	32	31	

Osm. = mOsm/kg water
g = osmotic coefficient

Urines are those of section 9.

ǂ Urine diluted initially by addition of an arbitrary volume of water, to bring osmolality to below 1000 mOsm/kg water. Osmolalities above this figure are read inaccurately on our apparatus.

Section 15

Estimation of concentration of ionic constituents from Specific Conductivity:

The concentrations of ionic constituents and the urinary specific conductivity have been measured in a large number of urines (sections 1, 3 and 9). These estimations were also made on the salt mixture (section 10). The data are used here to find the correlations and relationships between mI/l. and Sp.K.

Results: (A) Normal Urines (i) $Sp.K_{rt}^{u/25}$:

	No.	Mean mI/l.	S.D.
Whites	53	715.1	130.6
Bantu	56	471.0	83.8
Both	109	589.7	163.7

Correlation between mI/l. and $Sp.K_{rt}^{u/25}$: Whites : +.923
Bantu : +.909
Both : +.920

(ii) $Sp.K_{20}^{u/10}$:

No.	Mean mI/l.	S.D.
42	489.1	203.8

Correlation between mI/l. and $Sp.K_{20}^{u/10}$ is +.968

Regression equations:

$$mI/l. = 199.3\ Sp.K_{20}^{u/10} - 1 \qquad (26)$$

$$Sp.K_{20}^{u/10} = 0.00475\ mI/l. + .134 \qquad (27)$$

(B) Abnormal Urines: $Sp.K_{rt}^{u/25}$:

No.	Mean ml/l.	S.D.
52	440.3	163.3

Correlation between ml/l.

and $Sp.K_{rt}^{u/25}$ = +.819

(C) Salt Mixture: $Sp.K_{20}$:

When diluted ten fold, the $Sp.K_{20}$ equals 4.28 mMhos/cm.

This figure is calculated by substitution in equation 21.

That is, 855ml/l. yield 4.28 mMhos.

or, $ml/l. = 200\ Sp.K_{20}^{u/10}$ (28)

Section 16

Estimation of urinary urea concentration from measurement of osmolality and specific conductivity.

(a) Fig. 12 reveals the relationship between $Osm_{calc.}$ and $Osm_{ob.}$ to be slightly curvilinear. This can be corrected, empirically, by:

$$Osm._{calc} = 10{,}000 \left(1 - e^{-.0001\ Osm_{ob}} \right) \qquad (29)$$

(b) It was shown (section 13) that:

$$mM_u/l. + mI/l.\ (g) = Osm. \qquad (24)$$

Therefore, $Osm. - mI/l.\ (g) = mM_u/l.$

But $$mI/l. = 200\ Sp.K_{20}^{u/10} \qquad (26,28)$$

and $$Osm. = 0.88\ mI/l. + 7 \qquad (22)$$

Therefore $$Osm. - 176\ Sp.K_{20}^{u/10} + 7 = mM_u/l. \qquad (30)$$

Measurement of urinary osmolality and specific conductivity, and application of equations (29) and (30) should therefore yield a fair estimate of urinary urea concentration. This has been tested in a number of the normal and abnormal urines of section 9.

Results: The results are presented graphically in Fig. 14.

Normals:

Urine No.	Urea concentration	
	Actual	Estimated
22	300	285
23	237	198
24	180	157
26	262	225
28	350	292
29	137	103
30	78	73
31	112	108
32	193	183
34	302	268
35	308	314
36	250	244
37	280	238
38	352	360
39	87	65
40	440	440
41	208	162
42	372	364

Abnormals:

Urine No.	Urea concentration	
	Actual	Estimated
1	100	105
2	133	187
3	350	365
4	270	237
5	53	36
6	333	353
7	170	227
8	163	177
9	93	85
10	100	99

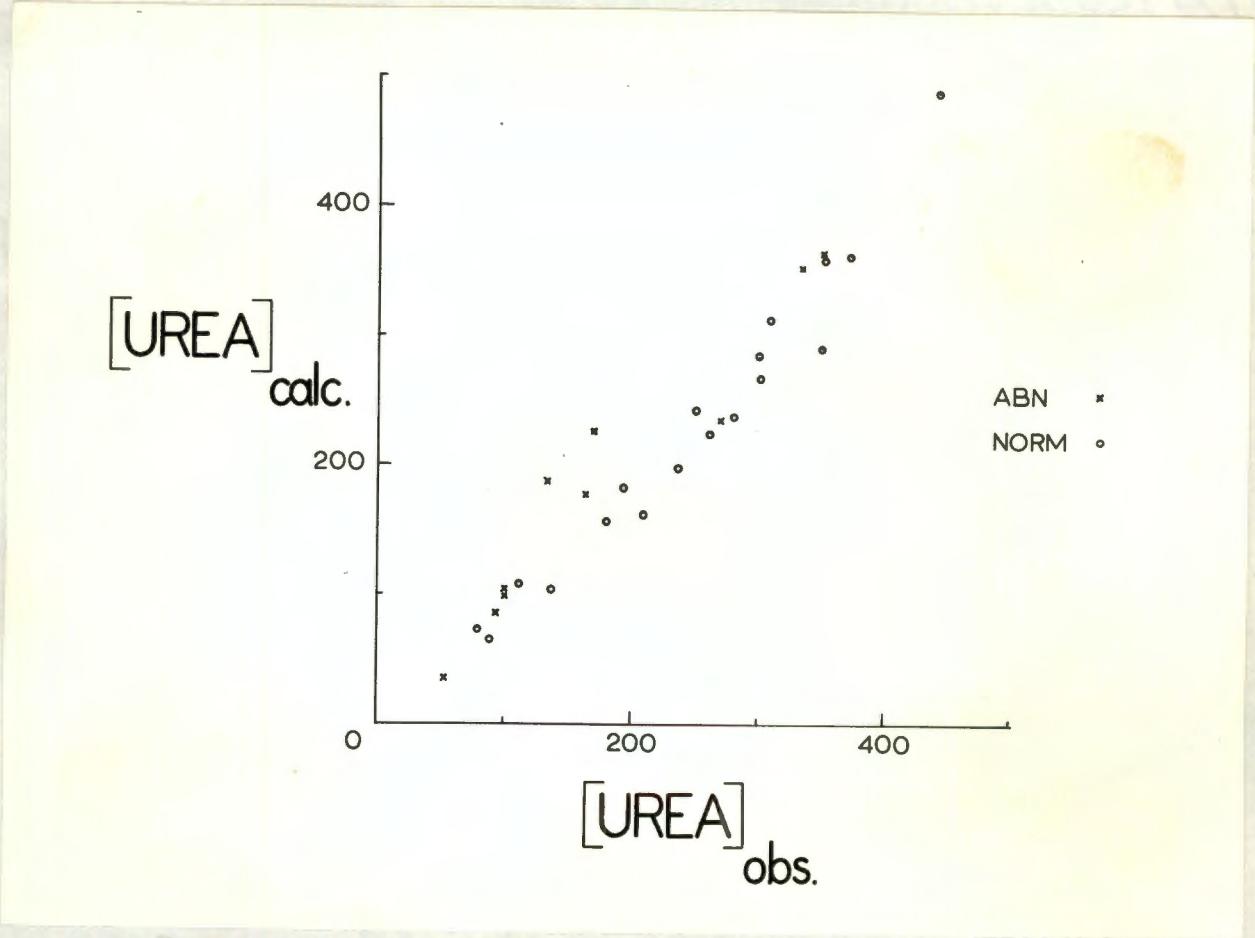

Fig.14: Comparison of calculated urea concentration with that actually observed.

Section 17

Measurement of the Bulk Dielectric Constant of Random normal urines.

The dielectric constant was measured - as described in Appendix C - on random urine samples obtained from 13 normal subjects. Recoveries of glycine (1 M/l.) were attempted on 9 of these, as a check on the accuracy of the procedure.

Results:

Urine No.	Osmolality (mOsm/kg water)	Sp.K_{rt} (mMhos/cm.)	Dielectric Constant		G_I
			urine	urine + glycine	
1	518	11.21	70.2	93.1	22.9
2	910	23.6	45.8	65.5	19.7
3	940	26.8	61.2	84.8	23.6
4	1080	34.0	46.4	70.1	23.7
5	860	23.7	63.0	-	-
6	659	17.5	68.8	94.3	25.5
7	530	-	67.2	84.6	17.4
8	811	20.3	62.6	80.7	18.1
9	312	-	76.9	-	-
10	999	24.0	53.9	-	-
11	901	23.0	56.6	-	-
12	-	-	67.7	89.1	21.4
13	-	-	70.8	87.8	17.0

Mean : 21.0

G_I = Dielectric Increment of Glycine (1 Mole/Litre).

Section 18

The 24-hour Osmolar-creatinine Ratio

24-hour urine collections were obtained from 4 ‡ infants, and 24 normal adults. Multiple collections were obtained from the infants and from 2 of the adults. Fifteen adults collected each urine as passed during the 24 hours, in separate containers; the times of micturition were noted.

24-hour collections were also obtained from 7 grossly obese adults. These subjects were all encountered in the Groote Schuur Hospital Out-patient Department and were considered to be in good health (apart from their obesity).

Further 24-hour collections were obtained from 2 men - one very stout - engaged in heavy manual labour, and from a dietary faddist who "only ate fruit".

Similar collections were got from 7 ill persons who either attended the Groote Schuur Hospital Outpatient Department, or who were already hospitalised. They suffered from (numbers of patients in parentheses): thyrotoxicosis (2); grossly delayed physical development (2) marasmus (1); ascending paralysis (1); and infected bronchiectasis with anorexia (1).

---

‡ The infants' 24-hour urines were collected by the Dept. of Paediatrics, University of Cape Town, as part of their research into the electrolyte disorders encountered in Tetanus. I am indebted to Drs. d.v. Heese and A. Malan for permission to scrutinise their data and quote the figures relevant to this thesis.

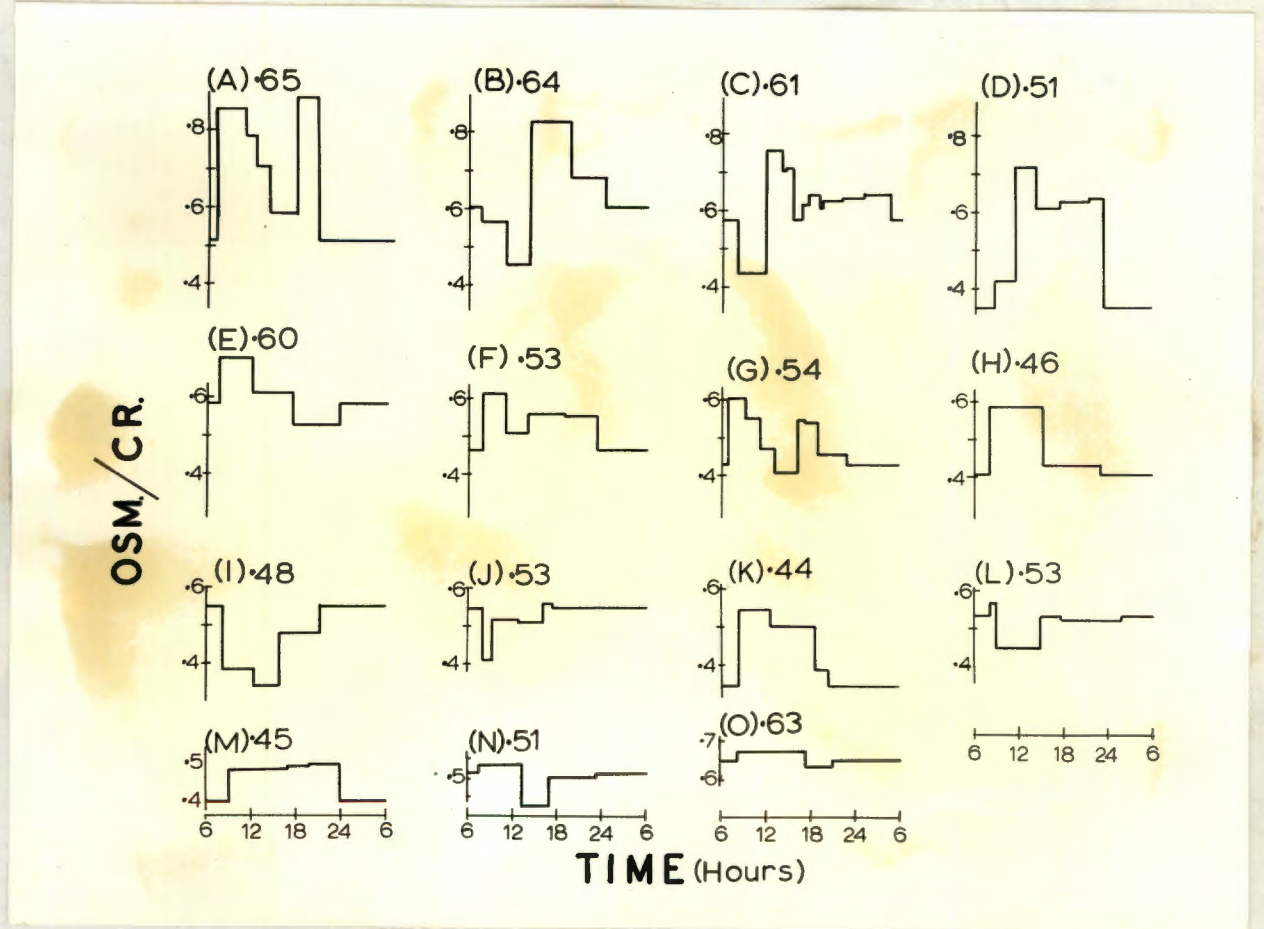

Fig. 15: Variation in urinary osmolar-creatinine ratio throughout the 24 hours, as observed in fifteen normal adults. Urines were passed at subjects' convenience.

The time of micturition is given in hours; thus 12 hours indicates midday, 24 hours midnight.

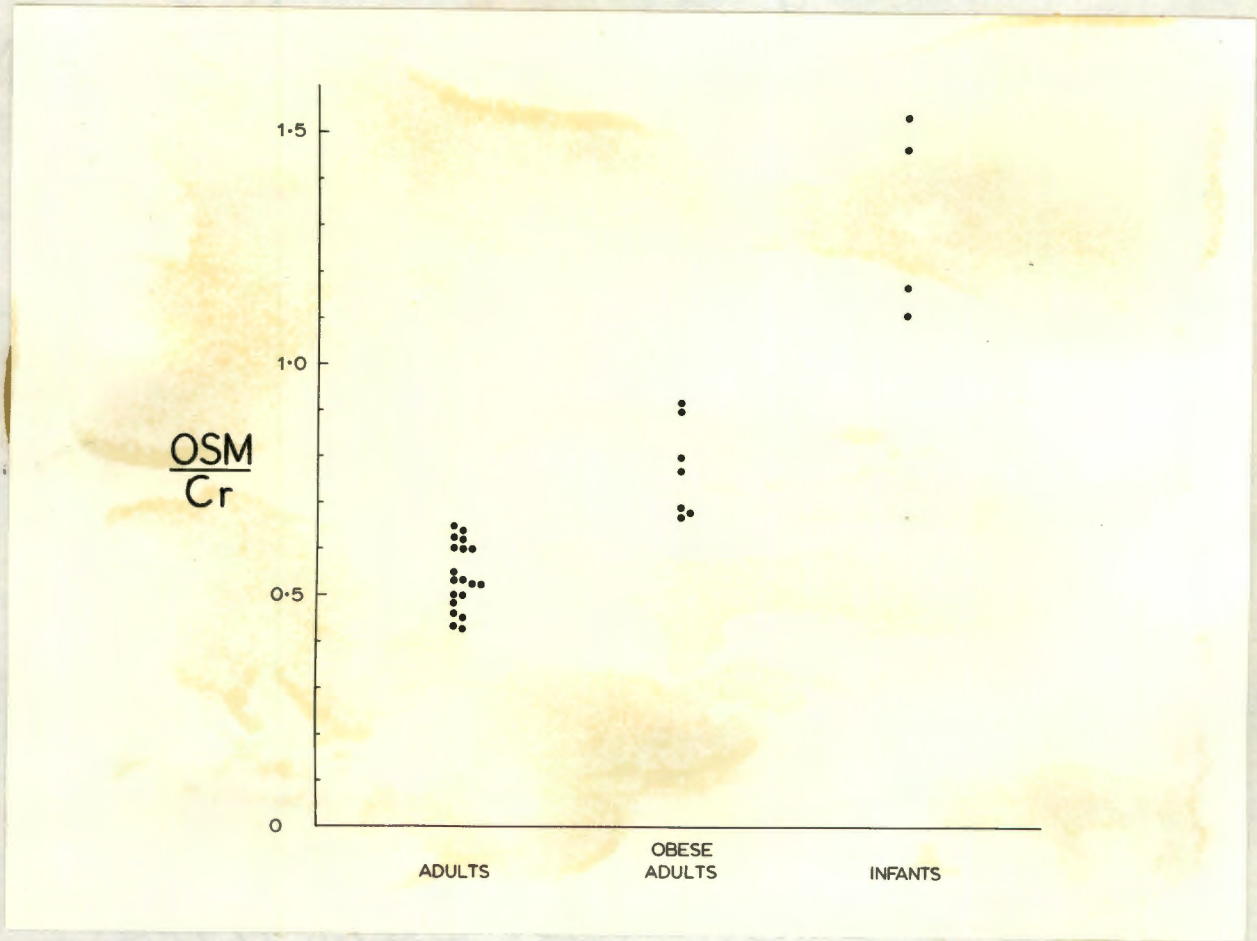

Fig. 16: 24-hour urinary osmolar-creatinine ratios as observed in normal and obese adults, and normal infants.

No restrictions of diet or exercise were placed upon any of these subjects. All urines were collected under toluene and stored at 4^{o} while awaiting analysis. This consisted of measurement of volume, and of creatinine and osmolar concentrations. The volumes of the urines from 3 of the obese and from 2 of the ill patients were not recorded.

Osmolar-creatinine ratios were then calculated, by dividing the osmolar (mOsm/Kg water) by the creatinine (mg/l.) concentration, for each urine.

Results: These are given in detail in Appendix F; they are summarised in Figs. 15 and 16.

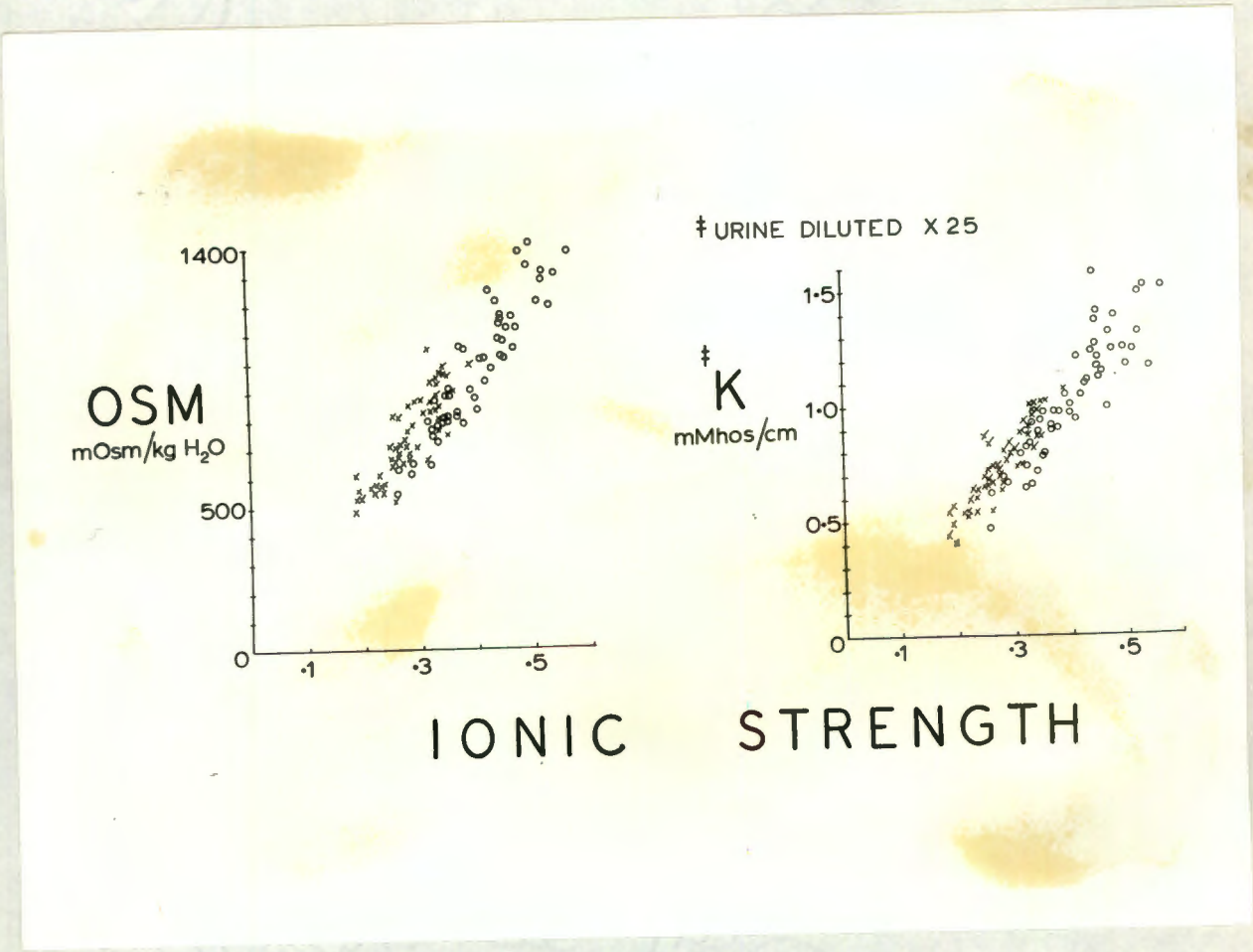

Fig. 17: Osmolar, Sp.$K_{rt}^{u/25}$ and Ionic Strength inter-relationships as observed in 60 normal Bantu and 54 normal 'White' adult South Africans.
Bantu: X; Whites: O

D I S C U S S I O N

(A) Inter-relationships between urinary Ionic Strength, Specific Conductivity and Osmolality.

Both osmolality, and particularly specific conductivity, might a priori be expected to vary in proportion to ionic strength. That this is indeed so is seen in Fig. 17 (based on the data of section 1). The relationships depicted are presumably of general validity as they were derived from two distinct populations, subsisting on very different diets.

The high correlations ($>.9$ - cf section 2) between ionic strength, specific conductivity and osmolality, make the determination of approximate ionic strength, in normal subjects, a simple procedure. Thus the equation

$$I.S. = .000255(Osm.) + .135Sp.K_{rt}^{u/25} + .002 \qquad (7)$$

permits the calculation of ionic strength from observed osmolality and specific conductivity to within a standard error of 0.030.

In patients suffering from renal or electrolyte disorders however, (section 3), $Sp.K_{rt}^{u/25}$ and particularly osmolality, were found to be less accurate indices of ionic strength. The reasons for this are not far to seek. Divalent ions were more variable in proportion, and formed a greater fraction of the total ionic constituents in abnormal (mean 10.7% ; S.D. 7.0 %) than in normal urines (mean 5.7%; S.D. 2.0%). Furthermore the proportion of the non-ionic to the ionic components of the total urinary osmolality was far more variable in the abnormal urines; this will be discussed later.

It might be argued that the discrepancies found between the abnormal and normal urines lay not in their origin, but in their mode of collection; the abnormal urines were random samples, while the normals were 24 hour collections. Diurnal variation in patterns of urinary excretion undoubtedly exist. The analyses of the randomly collected normal urines of section 9 disprove this arguement however. Standard errors of the estimate of ionic strength as derived from measurement of osmolality and Sp.K are identical, or even lower in these than in the 24 hour collections.

On initiating this study, the effect of temperature on Sp.K was deliberately ignored. The Sp.K's of electrolyte solutions have been said to increase by approximately 2% per degree Centigrade rise in temperature (13); as different urines may vary in both individual and total ionic concentrations by several orders of magnitude, it seemed apparent that temperature control during measurement of Sp.K would be of little value. Further study revealed that this conclusion was not entirely warranted. Correction for temperature by (section 7):

$$Sp.K_t = Sp.K_{20}\, e^{+.02\left[t-20\right]} \qquad (17)$$

brought about a worthwhile increase in accuracy of the estimate of ionic strength. Thus estimate of ionic strength from

$$I.S. = .0001232\ (Osm.) + .07443\ Sp.K_{20}^{u/10} + .0005 \qquad (20)$$

lowered the standard error of the estimate, in normal urines,

to 0.025. The most accurate estimate of ionic strength in abnormal urines is probably best got from:

$$I.S. = 0.1069\ Sp.K_{20}^{u/10} + 0.009 \qquad (19)$$

(B) Comparison of Sp.K, Ionic Strength and Osmolality relationships in 'average' normal urine, salt mixture, and salt mixture plus urea.

The inter-relationships between specific conductivity, ionic strength and osmolality, as found in a large number of normal urines, are described by (sections 2,5c):

$$I.S. = 0.000371\ (Osm.) + 0.022 \qquad (1)$$

and $$Sp.K^{x} = 100\ (1 - e^{-s.x}) \qquad (13)$$

These equations therefore typify the characteristics of an 'average' urine.

The Sp.K of any electrolyte solution is based upon the number, charge and mobility of its ions. The ionic composition of the salt mixture (section 6) is identical (ignoring the small fraction of organic anions) to that of the 'average' urine. Comparison of the specific conductivities of these two solutions - 'average' urine and salt mixture - might then be expected to yield information as to the similarity or otherwise of their overall electrolyte activity coefficents and ionic mobilities.

---

‡ The correlation between $Sp.K_{20}^{u/10}$ and I.S. (section 9) was appreciably higher than that between $Sp.K_{rt}^{u/25}$ and I.S.(section 3). The correlations between I.S. and osmolality rose almost in parallel however, and make it uncertain that the few abnormal urines of section 9 were quite as 'abnormal' as those of section 3.

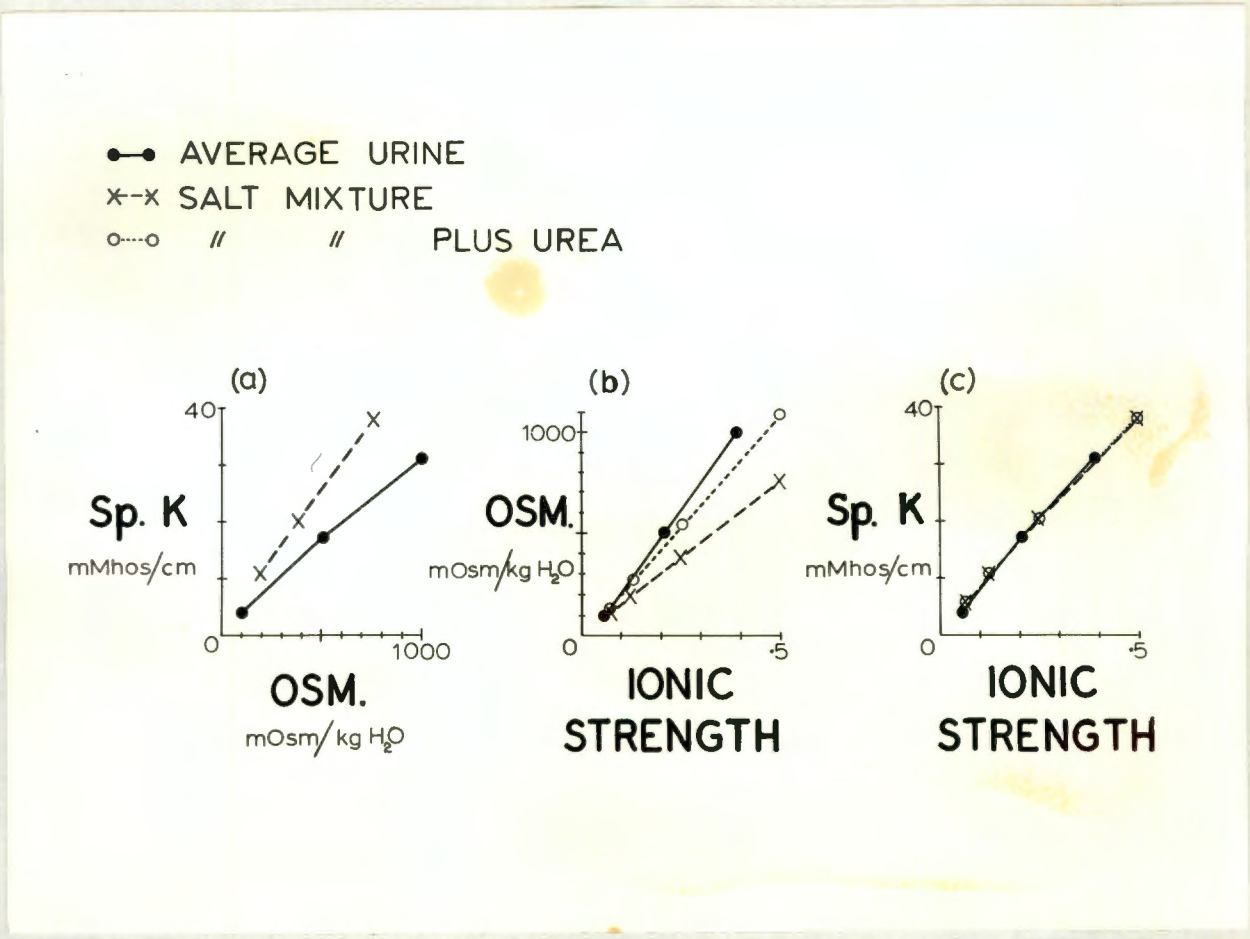

Fig.18: Comparison of Sp.K, ionic strength, and osmolality of 'average' urine, salt mixture and salt mixture plus urea.

The comparison is presented graphically in Fig. 18. The Sp.K of 'average' urine is seen to be about 2/3 that of an equi-osmolar salt mixture (Fig. 18a). Urine contains many non-ionic molecules; these are composed largely of urea, and comprise an appreciable proportion of the osmotically active particles present in 'average' urine (Fig. 18b). Comparison of the Sp.K of 'average' urine with that of salt mixture must therefore be based not upon equi-osmolar solutions, but upon solutions of equal ionic strength; on this basis the Sp.K's of 'average' urine and salt mixture (with or without urea) are seen to be identical (Fig. 18c).

Ionic mobility decreases with increasing viscosity of the solvent. Urinary viscosity rises, slightly, with increasing urinary concentration (7). The identity of Sp.K's therefore implies that the overall electrolyte activity coefficient of 'average' urine is at least equal to, or greater than, that of the salt mixture. As there is no reason to suspect the latter possibility, the overall activity coefficient and the ionic mobilities of urinary electrolytes must, as a first approximation, be regarded as those of an equivalent inorganic salt solution.

Striking confirmation of this hypothesis is found in the near-identity of the inter-relationships observed, in both urine and salt mixture, between ionic constituent concentrations and $Sp.K_{20}$ (equations 26 and 28, respectively.).

Recent studies, utilising the sodium permeable glass electrode, have shown that the activity coefficient of Na in urine is identical to that of a simple NaCl solution of comparable ionic strength (27). This observation strengthens the conclusions come to above.

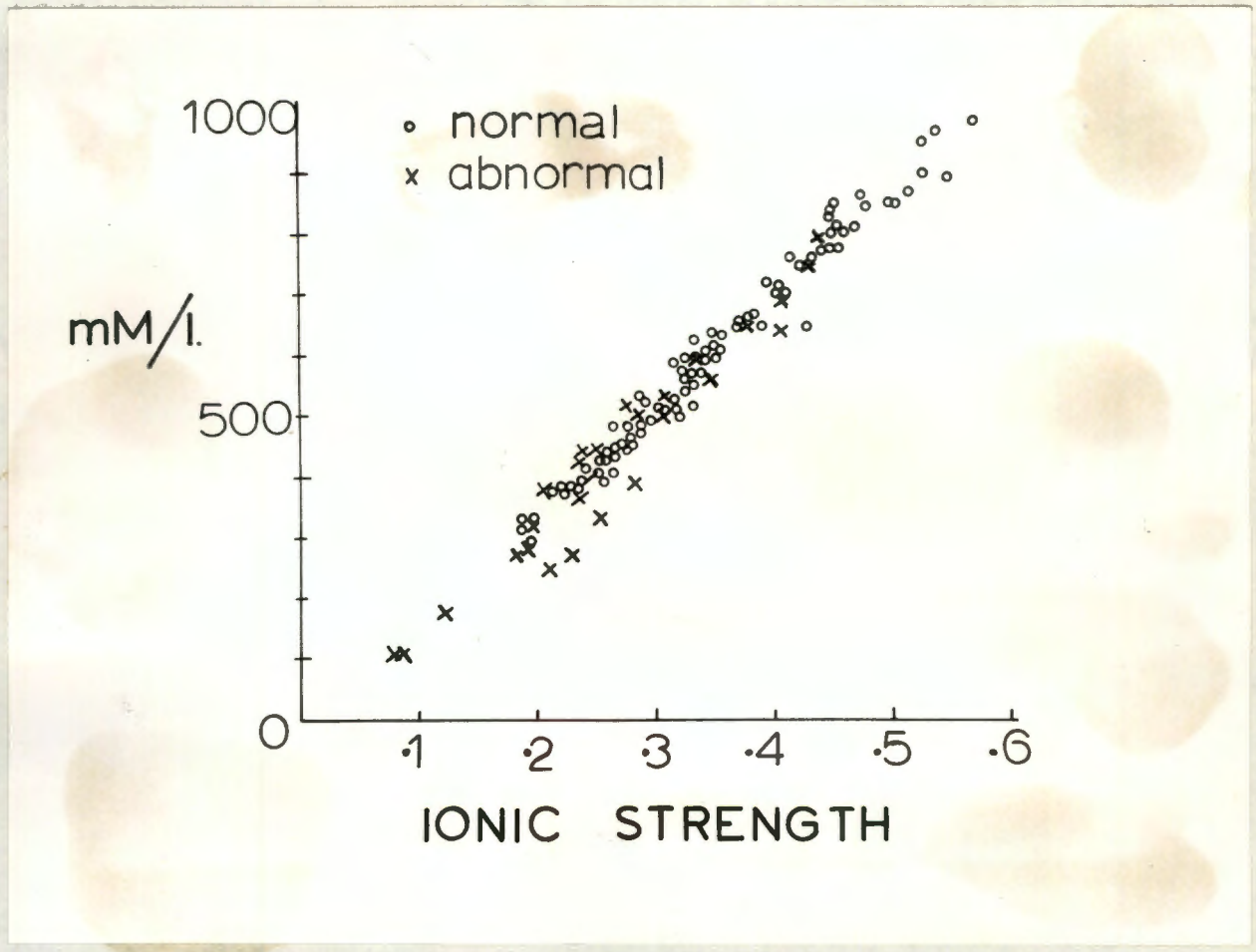

Fig. 19 : Concentration of ionic constituents as a function of ionic strength, in both normal (o) and abnormal (x) urines. (for mM read mI).

(C) Fractionation of the Osmolar content of individual urines into Ionic and Non-ionic components.

The overwhelming majority of urinary ionic constituents were found to be monovalent (Sections 1, 3). A close correlation therefore exists between urinary ionic strength and the urinary concentration of ionic constituents (Fig. 19). Couple this observation with that of the linear relationship between osmolality and ionic strength (Fig. 17) and it follows that the proportion of ionic to non-ionic components of the total urinary osmolality - in normal urines, at least - must necessarily vary within relatively narrow limits.

This corollary can be tested by assuming the osmotic coefficients of all urinary ionic constituents to be unity, and then calculating the proportion they constitute of the observed urinary osmolality. (Osmolarity is here equated with osmolality; this introduces altogether negligible error - cf section 10). The results are in accord with expectation; the ionic component of normal urines, represents 68.7 % of the total osmolality, with a S.D. of only 9.2 % (Section 1).

This mean percentage is of course too high, by an amount equal to the actual depression of the overall osmatic coefficient of the urinary electrolytes. This will be considered further below.

In abnormal urines, the ionic component of the total osmolality was found to vary considerably more than in the normals (mean 64.4 %, S.D. 19.6 % - section 3). This was a major cause for the poor correlation observed between osmolality and ionic strength in these urines.

(D) The Overall Osmotic Coefficient of Urinary Electrolytes:

The overall osmotic coefficient of urinary electrolytes

may be expressed as

$$g = Osm_{ic} / mI/l. \qquad (31)$$

where g is the osmotic coefficient, Osm_{ic} the concentration of milli-osmoles derived from the ionic constituents, and mI/l. the concentration of ionic constituents (in milli-ions per litre). Furthermore, the urinary osmolar content is composed of both ionic and non-ionic components:

$$Osm_{ob} = Osm_{ic} + Osm_{ni} \qquad (32)$$

where Osm_{ob} is the observed osmolality, and Osm_{ni} the non-ionic osmolal concentration.

Given Osm_{ob} and Osm_{ni} it is therefore possible to calculate Osm_{ic} , and, given mI/l., g. Osm_{ob} and mI/l. are estimated by direct determination; Osm_{ni} may be obtained in either of two ways, as follows. Both methods assume all non-ionic substances to have osmotic coefficients of unity.

(a) The overwhelming mass of non-ionic substance might be assumed to be urea. Should this be true, then

$$Osm_{ob} = Osm_{ic} + mM_u/l. \qquad (33)$$

$$= mI/l.(g) + mM_u/l$$

$$\text{or,} \quad g = \frac{Osm_{ob} - mM_u/l.}{mI/l.} \qquad (34)$$

where $mM_u/l.$ is the concentration of urea, in milliMoles per litre. Application of equation 34 to the data pertaining to urines 22 to 42 (section 9) yields values of g fluctuating about a mean of 0.965. This is a greater value than exists in even simple salt solutions of comparable concentrations (section 10)(35).

The initial assumption must therefore be false; substances other than urea must contribute to the non-ionic fraction of the urinary osmolar content.

A more realistic approach to the problem of determination of g is simply to assume it equal to that of the salt mixture, of identical ionic constituent concentration. That is,

$$Osm_{ic} = 0.88 \text{ mI/l.} + 7 \qquad (22)$$

Addition of Osm_{ic}, calculated in this way, to the observed urea concentrations (in mM/l.) in a number of urines should now yield calculated osmolalities rather similar to those actually observed. That is,

$$Osm_{ic} + mM_u/l. = Osm_{calc} \simeq Osm_{ob} \qquad (35)$$

where Osm_{calc} is the calculated osmolality. Disparities should conform to previous estimates of the non-urea non-electrolyte component of the total urinary osmolality.

Both Price et al (31) and Yardley (41) have estimated that this fraction of the 24-hour urinary solute output is composed of about 10 - 20 G. of dialysable, low molecular weight (mean molecular weight about 156) (41), organic matter; that is, about 15/156 X 1000, or 96 mOsm. The data in section 1 reveal that the average normal 'White' South African excretes 1178 X 980, or 1154 mOsm. per day. Therefore, per 1000 mOsm. excreted, about 1000 X 96 / 1154, or 83 mOsm., should be non-urea non-electrolyte substances.

Applying equation 35 to the data of urines 22 - 42 (section 9) gives the results depicted in Fig. 12. Close inspection reveals that at Osm_{ob} = 1000, the calculated osmolality falls short of this figure by approximately 50 mOsm. This is in fair agreement with that postulated, and so apparently confirms the initial assumption of an identical

overall osmotic coefficient for urinary and salt mixture electrolytes.

(b) At great dilution, complete dissociation of ionic constituents can be assumed. Therefore

$$Osm^{f}_{ob} = mI/l.^{f} + Osm^{f}_{ni}$$

$$\text{or,} \quad Osm^{f}_{ni} = Osm^{f}_{ob} - mI/l. \tag{36}$$

where f is the dilution factor, and Osm^{f}_{ni} , Osm^{f}_{ob} and $mI/l.^{f}$ are the non-ionic, total osmolal and ionic constituent concentrations of the diluted urine, respectively.

$mI/l.^{f}$ is obtained simply by dividing mI/l. by the dilution factor. Estimation of Osm^{f}_{ob} is more difficult. The Fiske osmometer - which measures osmolality by observation of depression of freezing point - is inaccurate at low osmolalities. Accuracy in this range may be enhanced by recalibrating with urea standards; as these do not dissociate on dilution (unlike the usual NaCl standards) several dilutions of a given urea standard may be made to obtain accurate readings in the low osmolar range. A better alternative is to make use of the Sp.K - osmolality relationship developed in section 5c, viz:

$$Sp.K^{x} = 100 \left(1 - e^{-sx} \right) \tag{13}$$

Measurement of osmolality (by freezing point depression) and Sp.K of the undiluted urine permits calculation of s; subsequent estimation of the Sp.K of the diluted urine then yields its osmolality with considerable accuracy.

Osm_{ni} is now got simply by multiplication of Osm^{f}_{ni} by the dilution factor, f. Substituting in equations 32 and 31 above, then yields g. In short,

$$g = Osm_{ob} - f \left(Osm^{f}_{ob} - mI/l.^{f} \right) / mI/l. \tag{25}$$

Application of this arguement to a number of normal urines (section 13 - Method B) revealed the overall osmotic coefficient of urinary electrolytes to be somewhat lower than that of an inorganic salt mixture of similar electrolyte composition (mean g = 0.78, as compared to that of about 0.89 for salt mixture).

'Step-wise' dilution of individual normal urines, with calculation of g at each dilution, gave the results summarised in Fig. 13. The osmotic coefficients remained at constant levels until the urine ionic constituent concentrations fell to less than approximately 100 mI/l.; this is in contrast to the salt mixture, where g began to rise once the concentration fell below 200 mI/l.

Urea is a major component of the total non-ionic fraction of urinary solidsl That is,

$$mM_{ni}\ /l. = mM_{u} + mM_{nu}\ /l. \qquad (37)$$

where $mM_{nu}/l.$ is the concentration of non-ionic non-urea substances. Knowing $mM_{u}/l.$ and $mM_{ni}/l.$, mM_{nu} is therefore readily obtained. The average concentration of this non-ionic non-urea group of substances, for the 13 normal urines analysed in section 13, was 11.7 % (the concentration is expressed here as a percentage of the total osmolality). Translating this into G/24 hours - assuming a mean molecular weight of 156, as above (41) - yields a figure of 21 G/day. Price et al, and Yardley, found levels of 10 - 20 G/day. (It must be borne in mind that the urines analysed here were random specimens, not 24-hour collections).

It is apparent that the 2 methods of estimating g have yielded very different results. Neither seems unreasonable, and both give apparent concentrations of non-ionic non-urea substances more or less equally in agreement with the levels previously found by other workers.

The alternate hypotheses - of 'normal' or depressed overall osmotic coefficients for the urinary electrolytes -

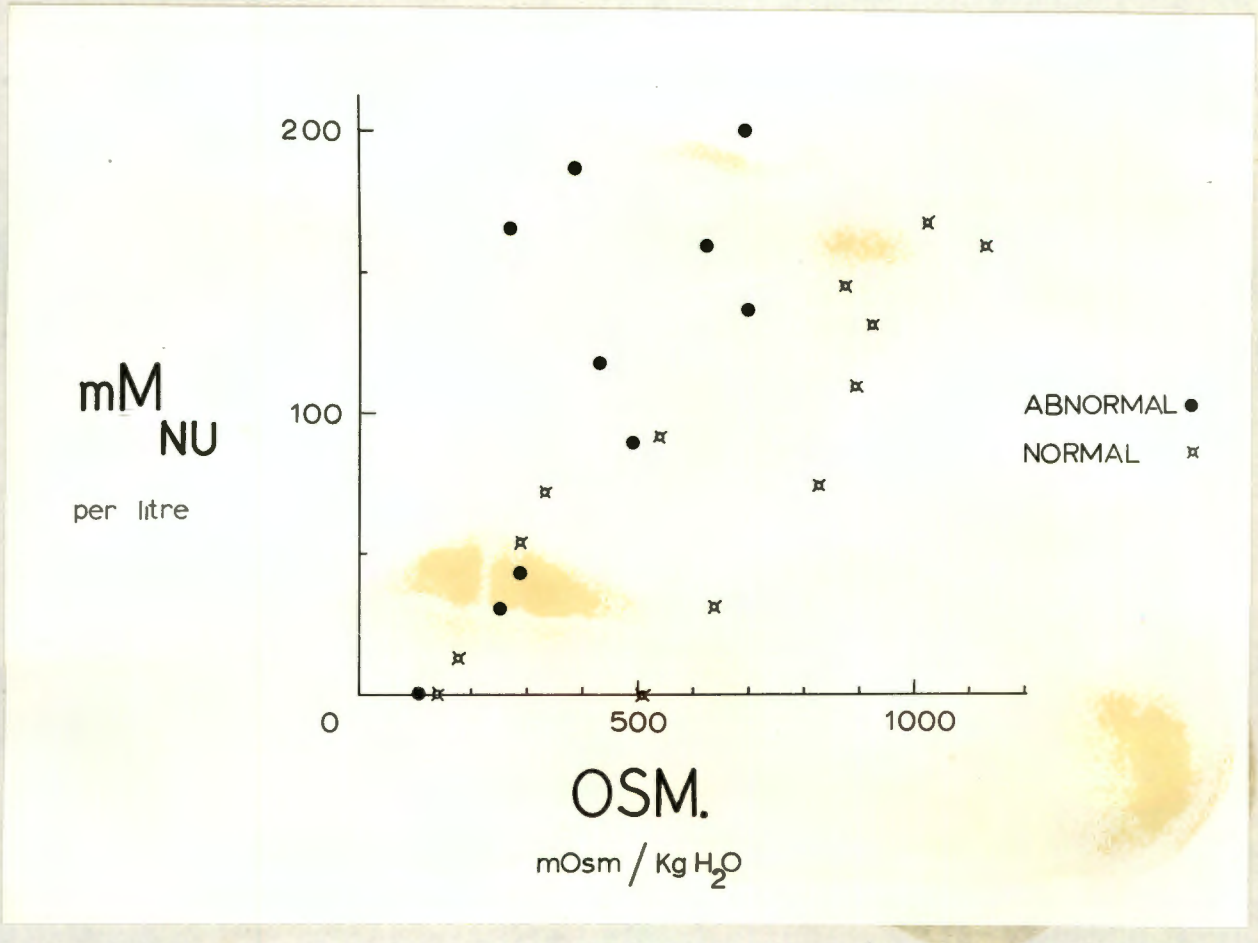

Fig. 20: More non-urea non-electrolyte (mM_{nu}) appears in abnormal than in normal urines.

may be further tested by applying both methods of estimation to abnormal urines. The results are given in detail in section 13. Estimation by method A reveals much the same relationship of Osm_{calc} to Osm_{ob} as pertained in the normals (fig. 12). Method B however appears to reveal the presence of large amounts of non-urea non-electrolyte, of mean concentration almost twice that of the normals (Fig. 20); the osmotic coefficient is considerably depressed in most of the abnormal urines.

These findings do not resolve the dilemma. However, urines derived from patients suffering from a variety of illnesses are known to contain much increased amounts of high molecular weight substances (22); this collateral evidence of increased urinary content of non-urea non-electrolyte substances in the ill, suggests that the findings of method B, above, might well be correct.

(E) Urinary Dielectric Constant:

In any discussion of urinary dielectric constant, it is important to differentiate clearly between the dielectric constant of water - the solvent - and that of urine - the solution. The dielectric constant of the former is a physical fundamental and a measure of its ability to store energy, or to separate charged particles. It is in this sense that the dielectric constant features in the Debye-Huckel equation (relating activity coefficients of dissolved electrolyte to the ionic strength and dielectric constant).

The dielectric constant of a solution, on the other hand, is a composite figure dependent upon the physico-chemical structure of the solute, the dielectric constant of the solvent, and the interplay of physico-chemical forces between solvent

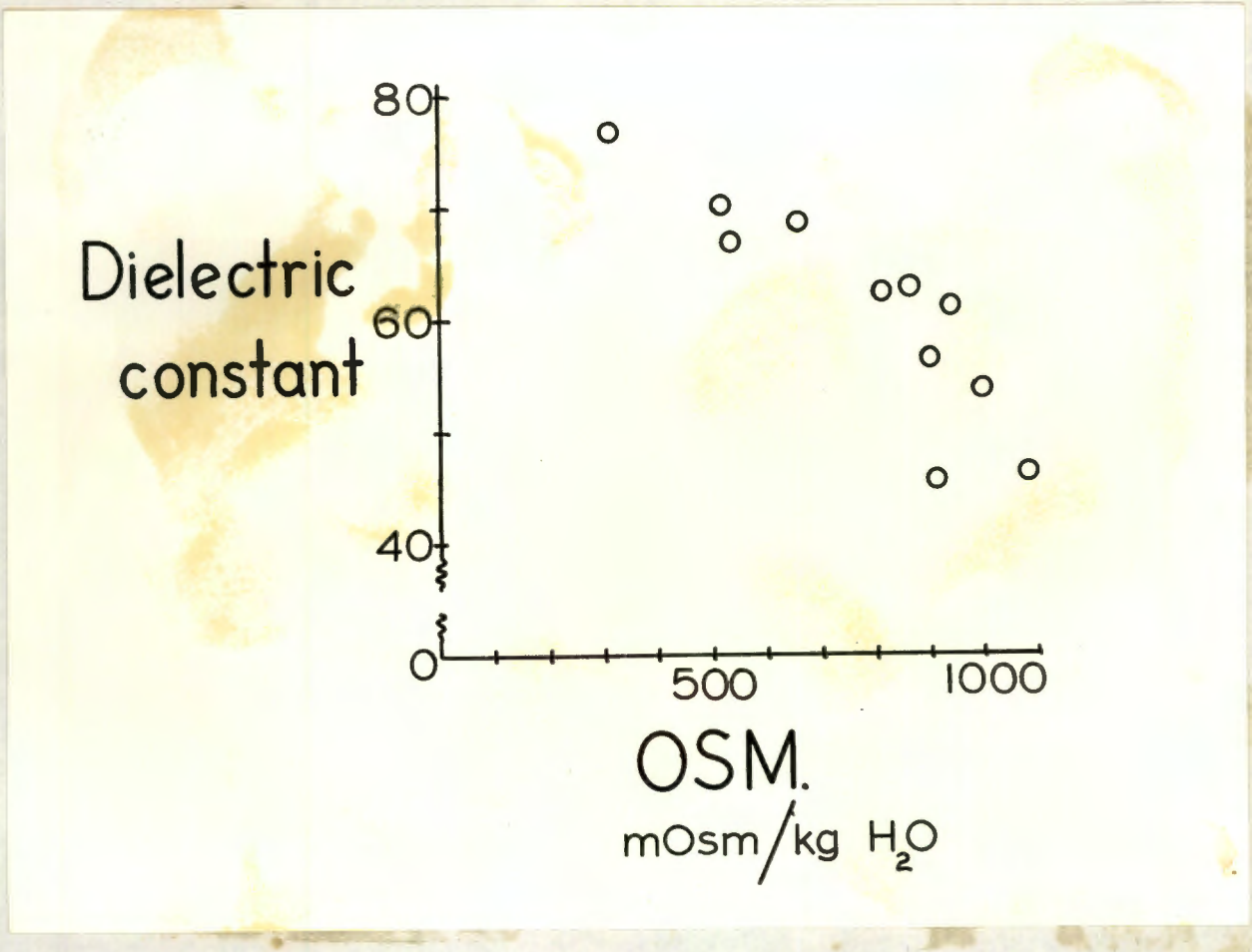

Fig. 21 : Variation of 'bulk' dielectric constant with urinary osmolality.

and solute. This is referred to as the 'bulk' dielectric constant, and it is in this sense that the term is employed here.

In any solution the significant quantity determining the bulk dielectric constant is the number of dipoles per unit volume. By far the most abundant dipoles to be found in urine are water molecules. Others, eg. amino acids, peptides or proteins are normally present in very small concentrations. Only urea may be present in sufficient quantity, in concentrated urines, to raise the dielectric constant fractionally above that of pure water. Non-dipolar molecules, and ions, reduce the number of water molecules per unit volume, and so may be expected to reduce the bulk dielectric constant of urine. Depending on the relative abundance of urea, or non-dipolar molecules or ions, urine may be expected to have a bulk dielectric constant somewhat above or below that of water. This effect might be the greater the more concentrated the urine.

The results (Fig. 21; section 17) of measurement of dielectric constant in a small number of normal urines in no way approached expectation. With increasing urinary osmolality, the bulk dielectric constant fell to almost half that of pure water.

(F) Attempted Synthesis Of Osmotic Coefficient and Dielectric Constant data:

The markedly low figures derived for urinary electrolyte osmotic coefficients (method B) - particularly in the ill - were no less surprising than the gross lowering of dielectric constant observed in concentrated urines. These effects seem too gross to be ascribed solely to technical error. What follows is pure speculation.

As pointed out above, the bulk dielectric constant of

a solution may be regarded as determined largely by the number of dipoles per unit volume. Thus, "many non-electrolytes and most ions have such small dielectric constants compared to that of water, that in aqueous solutions they may be treated as holes of zero dielectric constant, and the dielectric constant of such solutions may be assumed proportional to the concentration of water" (36). In effect, the mixture of solvent and solute is here treated as a suspension. Numerical quantitation has been given to this concept, (39), by:

$$\frac{D - D_1}{3D} = \frac{D_o - D_1}{D_o + 2D} \times F$$

where D is the bulk dielectric constant of the suspension D_1 and D_o the dielectric constants of the medium and suspensoid respectively, and F the fraction of the total volume of the suspension occupied by the suspensoid.

Inspection of Fig. 21 reveals that urines concentrated to 500 mOsm/kg water and 1000 mOsm/kg water, may have bulk dielectric constants of about 70 and 55, respectively. Assuming the dielectric constant of the suspensoid to be zero and taking that of the water as 80, substitution into the above equation yields fractions of total volume occupied by the suspensoid as 8% and 21%, respectively.

Besides urea and electrolytes, urine normally contains any number of diverse substances (organic acids, mucopolysaccharides, steroids, amino acids, proteins, colloids, red white and epithelial cells, hyaline casts and many others besides). While quantitatively insufficient to account on a strict volume-for-weight basis, for the suspensoid volume fractions calculated above, it seems conceivable that these

substances might lead to the formation of electrostatically-bound aggregates of ions, non-ions and water molecules - much as occurs in bile (28). The existence of such aggregates, or micellae, might explain both the depression of overall electrolyte osmotic coefficient and the presence of relatively large volume fractions of 'bound' water. This postulate is also in keeping with the observed correlation between depression of osmotic coefficient and raised concentration of non-ionic non-urea substances (section 13). On the other hand, the evidence for identity of electrolyte activity coefficients and ionic mobilities in 'average' urine and the salt mixture (cf B above) suggests that if such aggregates do indeed exist, their ionic binding must be relatively weak.

(G) <u>A method for the rapid estimation of approximate urinary urea concentration</u>:

Whatever its true value, equating the overall osmotic coefficient of the urinary electrolytes with that of the equivalent salt mixture permits use of the equation

$$mM_u/l. + mI/l. = Osm_{calc} \simeq Osm_{ob} \qquad (35)$$

where the relationship between Osm_{calc} and Osm_{ob} is as depicted in Fig. 12. As pointed out, Osm_{calc} falls short of Osm_{ob} at high levels of the latter. This curvilinear relationship can, quite arbitrarily, be described by

$$Osm_{calc} = 10{,}000\ (1 - e^{-.0001\ Osm_{ob}}) \qquad (29)$$

Equation 29 can therefore be used to reduce Osm_{ob} to Osm_{calc} . mI/l. can be estimated by measurement of $Sp.K_{20}$ (-cf Section 15). Given Osm_{calc} , an estimate of mI/l., and g equal to that of the salt mixture of comparable

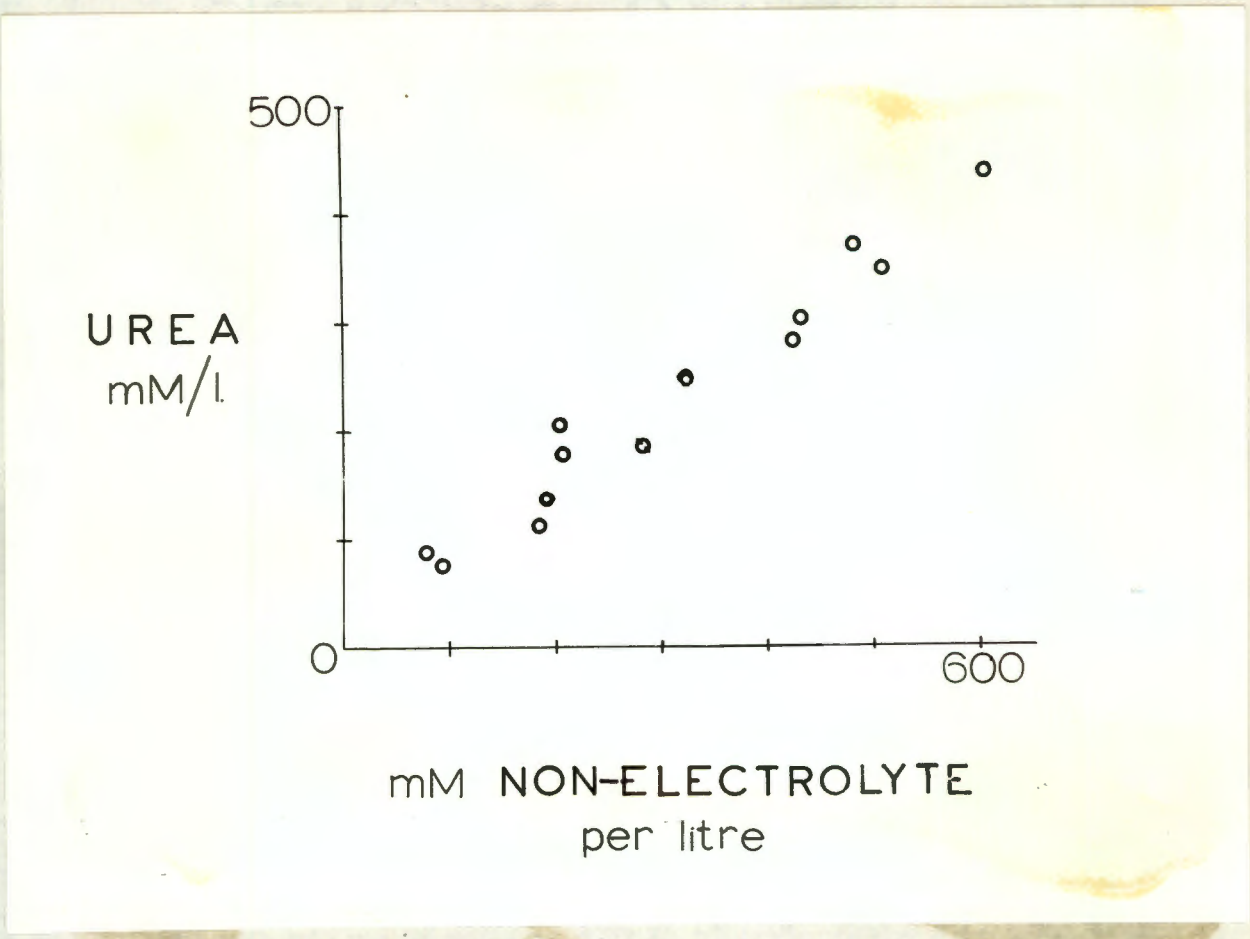

Fig.22: Linear correlation between urea and total non-electrolyte concentrations.

concentration, $mM_u/l.$ can be calculated by equation 35. The arguement is set out in detail in Section 16.

The results of such estimates of urinary urea concentration, in both normal and abnormal urines, are depicted in Fig. 14. It is apparent that a very fair approximation to the actual value can be achieved. The standard error of the estimate is 26 $mM_u/l.$

Similar results can be obtained without recourse to assumptions concerning the value of g. ml/l. is first estimated by measurement of $Sp.K_{20}$ as above (equation 28). The urine is diluted and its osmolality determined. Substitution into equation 36 now gives Osm^f_{ni}, and therefore $mM_{ni}/l.$ Normal urines exhibit a linear relationship between $mM_u/l.$ and mM_{ni}/l (Fig. 22; section 9); this may be arbitrarily described by

$$mM_u/l. = 0.66\ mM_{ni}/l. + 30 \qquad (38)$$

Estimates of $mM_u/l.$ derived in this way, have a standard error almost identical to that given above.

(H) <u>The 24-Hour urinary Osmolar-creatinine ratio; an index of relative caloric intake.</u>

Even assuming relative depression of the osmotic coefficient of urinary electrolytes, the data of section 13-b reveal that 90 % of the osmolar content of normal urine is quantitatively derived from electrolytes and urea. It follows that the urinary osmolar output, in normal subjects in the steady state, must be a function of the dietary intake of these substances (or their metabolic precursors).

Urea is derived from protein; electrolytes are present in all major foodstuffs, whether plant or animal in origin. The urinary osmolar output may therefore be said to be a function of the quantity of food eaten, or, even more broadly, of the total caloric intake.

In any one individual, the 24-hour urinary excretion of creatinine is a constant, and is related to lean body

mass (9, 11, 14, 24). These facts are frequently used to facilitate comparison of the urinary excretion of given substances in various individuals; expressing the excretion as a proportion of the simultaneous excretion of creatinine, 'corrects' for differences in lean body mass.

The statement relating urinary osmolar output to caloric intake, can readily be tested by examination of the urine of individuals on different dietary regimes. As small differences of caloric intake would be difficult to estimate, the test is best performed on groups of subjects of widely differing caloric intake. Differences in size, or lean body mass, can be corrected by expressing the osmolar output as a function of that of creatinine.

Three groups of subjects were chosen. The first was simply a number of normal adults, all engaged in either sedentary or light work. Grossly obese adults were obvious examples of over-eating. Young infants formed the third group; their daily caloric intake, of about 45-50 cal./lb. body weight (12) is some two and a half times greater than that of the average adult (assuming 3000 calories per day for a 150 lb. adult)

The results are depicted in Fig. 16. It is apparent that the osmolar/creatinine ratios do indeed differ in accord with expectation. The osmolar/creatinine ratio in the infants averages about 1.3; that of the adults about 0.52; these figures are in proportion to the relative caloric intakes of the two groups.

Further confirmation of the parallelism in osmolar/ creatinine ratio and relative caloric intake may be found in some of the other subjects studied in section 18. Thus high ratios were present in two males engaged in heavy manual labour; a female vegetarian consuming an estimated 1000 cals./day

presented a low ratio.

When first studied, the urinary osmolar creatinine ratio offered promise of a rapid means of establishing adequacy of dietary intake, by simple analysis of random urine samples. However, unpredictable diurnal fluctuations in this ratio demand 24-hour urine collections (Fig. 15). The latter, as judged by serial collections in six subjects, seems quite consistent for any given individual.

It is obvious that the concept is applicable only to steady-state conditions. Disease or muscle wasting, by lowering creatinine excretion, or diuretics or high salt diets by increasing electrolyte excretion, will all give high osmolar/creatinine ratios. Even rigorous fasting may, paradoxically, be expected to give normal or high ratios; loss of weight will be accompanied by cellular breakdown, so leading to excretion of formerly intracellular electrolyte. Section 18 contains some example of easily rationalised (non-steady-state) anomalies.

The concept advanced here is helpful in an altogether different context. The urinary calcium/creatinine ratio has been proposed as a means of comparison of calcium excretion in different individuals (30); this calculation however gives false results when applied to normal children; their urinary calcium excretion then appears to be pathologically high. The empirical substitution of the calcium/creatinine ratio by the calcium/osmolar ratio has been shown to correct this anomaly(19). The mechanism of the correction is laid bare by the fore-going: urinary calcium excretion in the young must be a function of dietary intake, not of lean body mass.

APPENDIX B

Determination of Specific Conductivity

Specific conductivity was determined in the conventional manner, viz. passage of an audio frequency signal through a Wheatstone bridge and conductivity cell (13). While in actuality this technique measures resistance rather than conductance - the one is of course the reciprocal of the other - the latter term is employed throughout this work, as it is directly related to the number, charge and mobility of the ions present in electrolyte solutions.

Polarisation effects within the conductivity cell are minimised by the use of symmetrically alternating current. The circuit of the audio frequency signal generator used here (32) is shown in Fig.1-A; the output voltage was rendered smoothly sinusoidal by adjustment of the grid potentiometer, while simultaneously monitoring the waveform on a cathode ray oscilloscope.

The output of the audio frequency generator was fed via a 6AQ5 power amplifier (33), to the bridge circuit (Fig.1-B). The maximum audio frequency output voltage across the conductivity cell, with distilled water in situ, was 30 volts. This fell to low fractions of a volt on replacing the water with urine, an effect attributable to the high conductivity of the latter. A mercury thermometer placed within the conductivity cell showed no alteration in urinary temperature during the course of conductivity measurements.

The bridge circuit is straightforward. Three standard resistances, of 53 ohms, 250 ohms, and 500 ohms (wire-wounnd, and accurate to 1%) were found sufficient to encompass the range of urinary resistance encountered in this study.

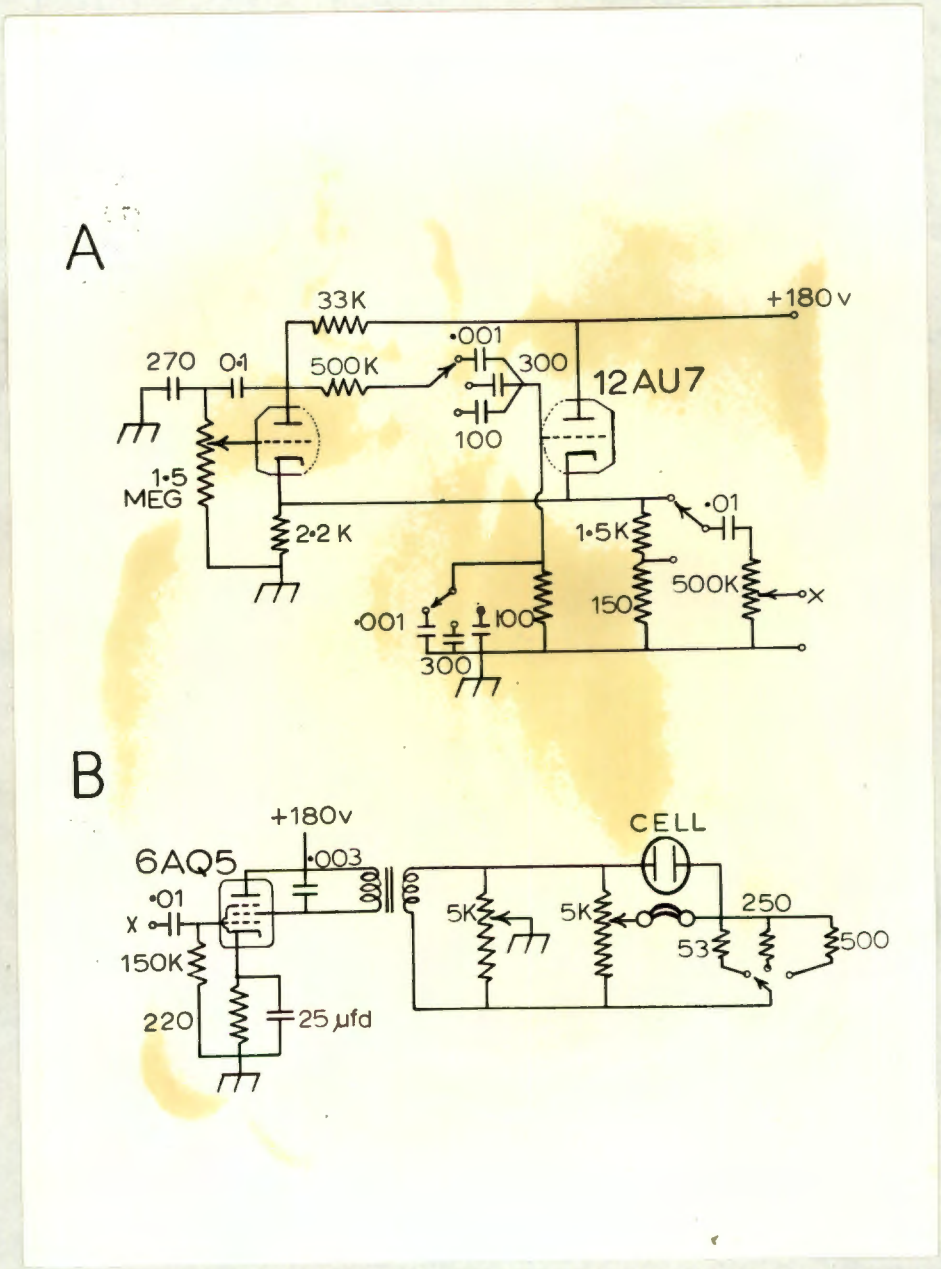

Fig. 1

Circuit of Apparatus for measurement of Urinary Specific Conductivity.

(A) Variable pitch, variable output, audio-frequency signal generator(32). Sinusoidal waveform obtained by adjustment of the grid potentiometer.

(B) Power amplifier and Wheatstone bridge.

Circuit constants are in ohms and microfarads; capacitor values NOT prefixed by decimal points, are in picofarads.

Earphones were used as a null detector; an audio tone of about 2000 c/s was found to be optimum.

The conductivity of urine was so high as to totally overshadow reactance effects; a sharp null point was obtained on all occasions. Introduction of a variable capacitor into the circuit was therefore not necessary. Similarly, balanced earthing of the bridge, although provided, was found to be redundant.

Small resistances introduced by poor circuit connections can introduce large errors in the determination of urinary specific conductivity. It was found necessary to clean out the side-arms of the conductivity cell at regular intervals (every few weeks), with very dilute HCl. The photograph of the complete apparatus (Fig.2) shows the wires leading to the side-arms of the conductivity cell, and to the ear-phones, as connected to the bridge by jack-plug and feed-through terminals, respectively; these connections were later soldered into place. Similarly, the platinum wires emerging from the mercury in the conductivity cell side-arms, were soldered to the wires coming from the bridge.

Conventional practice demands the siting of the conductivity cell in a constant temperature bath. As the ionic concentrations, and relative proportions of various ions, may differ by several orders of magnitude in different urines, and as temperature variation has been said to cause an alteration of specific conductivity of only some 2% per degree Centigrade (13), urinary specific conductivity was initially measured at room temperature. Similarly, where urine was diluted prior to measurement of its conductivity ordinary glass-distilled rather than 'conductivity' water was felt to be quite adequate.

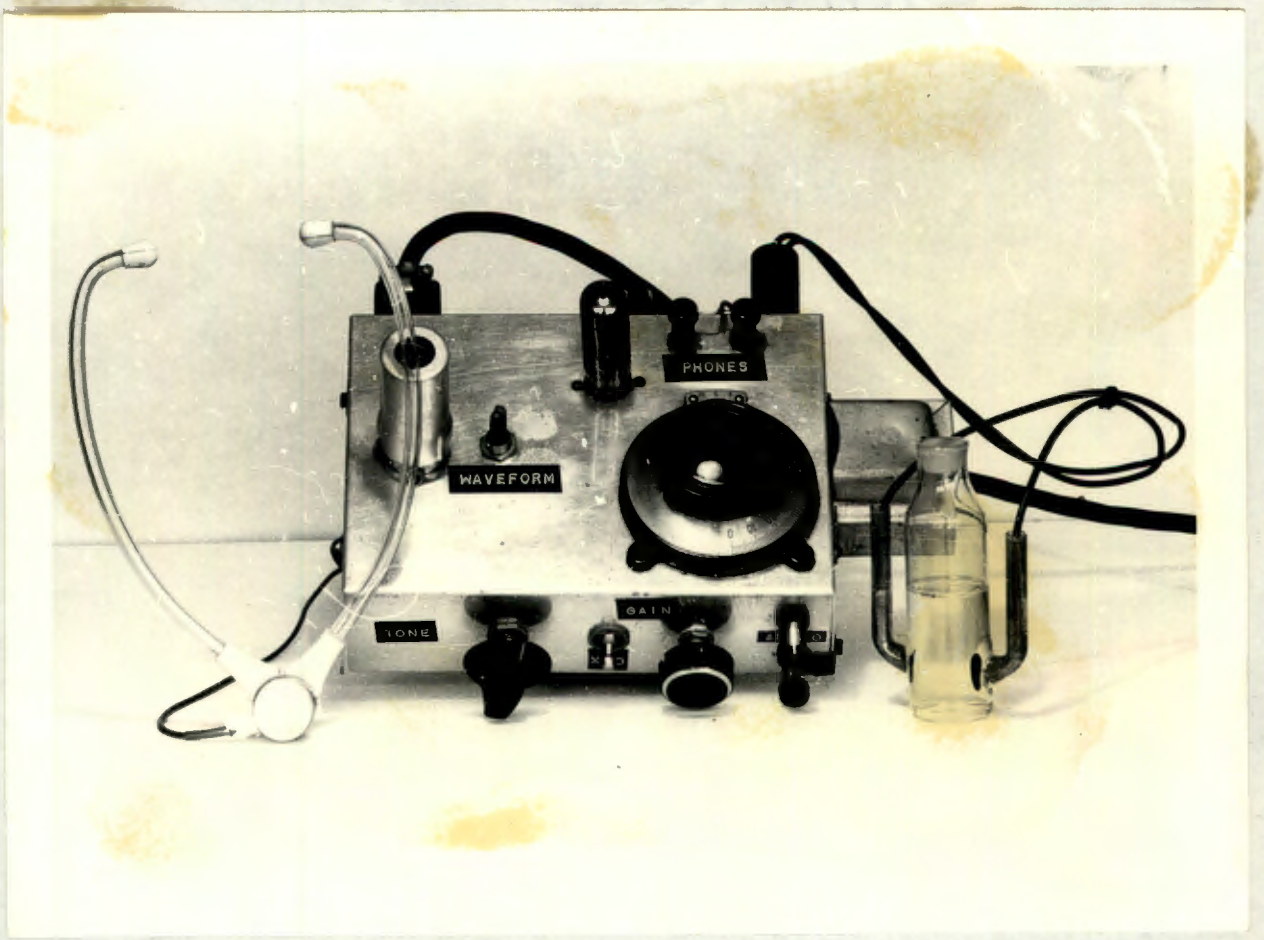

Fig. 2

Apparatus for measuring urinary Specific Conductivity.

The conductivity cell was of simple 'student' type, with circular platinum electrodes of approximately 1 cm. diameter, placed a little over 1 cm. apart from each other. The electrodes were platinised in the usual way (13). When not in use, the cell was kept filled with distilled water. A mark was made on the wall of the cell, near the top, and all measurements of conductivity were made with the cell filled to this level.

A vernier slow-motion dial was attached to the bridge potentiometer. The actual resistance of this potentiometer was measured on an accurate volt-ohm meter (Heathkit V-7A). Calibration graphs were made whereby the resistance (in ohms) of the fluid within the conductivity cell could be obtained directly from the dial reading.

The cell constant was determined from time to time, using 0.1 and 0.01 N KCl solutions. During these procedures the cell was kept at 25° C. by immersion in a water-bath. The equivalent conductivities of 0.1 and 0.01 N KCl solutions at 25°C are 128.96 and 141.27, respectively (23); during calculation of the cell constant the specific conductivities of these solutions were taken as .0129 and .001413. The cell constant was calculated as: $C = k.R$ where C = cell constant, k = specific conductivity of the standard solution, and R = the observed resistance. Typical results are given below:

Solution	Resistance at 25°C. (ohms)	Sp.K at 25° (=k)	Calculated cell constant (=C)
0.1 N KCl	33.15	01290	.427
0.01 N KCl	298.5	.001413	.422

Mean: .4245

All subsequently measured specific conductivities were then obtained by the same equation, substituting the calculated cell constant for C.

Specific conductivity is expressed in milliMhos, throughout this work.

APPENDIX C

Measurement of the Dielectric Constant of Urine.

Dielectric constants of non-conducting fluids are usually measured by taking advantage of the relationship (16) :

$$\frac{D_1}{D_2} = \frac{C_1}{C_2} \qquad (1)$$

where D_1 and D_2 are the dielectric constants of the test and standard fluids, respectively, and C_1 and C_2 are the respective capacitances of a given condenser filled alternately with each of these fluids.

In practice, measurement of the dielectric constant therefore hinges on the accurate measurement of capacitance. This maybe accomplished by inclusion of the condenser containing the fluid - the 'test' condenser - in a resonant circuit, loosely coupled to a fixed-frequency oscillator(6). Change in the capacity of the test condenser, as induced by the unknown fluid, throws the circuit out of resonance. Adjustment of a calibrated air-dielectric condenser connected in parallel with the test condenser, will nov restore the circuit to resonance; the change in capacitance required equals that induced in the test condenser.

This method is applicable only to fluids of low conductivity. As conductivity rises, so recognition of resonance becomes more and more difficult; the capacitance of the test condenser becomes a smaller and smaller part of the effect measured (10). With fluids

of conductivity approaching that of urine, the condenser is completely short-circuited.

It is therefore necessary to insulate the condenser from the urine. This immediately introduces a new problem. Insulation placed between a condenser plate and the urine effectively constitutes a second condenser placed in series with the first (4). The overall capacity, C , of the insulated condenser then becomes

$$C = \frac{C_1 C_2}{C_1 + C_2} \qquad \text{(ii)}$$

Where C_1 and C_2 are the capacitances of the effective condensers across the insulation and the urine, respectively. As almost all insulators have very low dielectric constants, of the order of 1 to 4 or 5, (2), while that of water is about 80, it is clear that even major changes in urinary dielectric constant would hardly affect C, the capacity of the entire, urine-filled insulated condenser.

This difficulty has been overcome, quite empirically, as follows. A solution of 'Perspex' shavings dissolved in chloroform, was applied to the condenser plates. Once dry, this effectively insulated the condenser for periods of minutes to several hours, despite its immersion in concentrated salt solutions or urine. During this period, changes of capacitance induced by the immersion of the condenser in various fluids, could readily be measured. Fluids of high conductivity gave small capacity changes; those of low conductivity, much larger changes. Where test and standard fluids were of identical conductivity, the dielectric constant of the former could be obtained by the simple relationship

given above(i).

Thus, in what follows, the term 'dielectric constant' refers to a figure obtained by comparison of the effective capacity of the (insulated) condenser when immersed in urine,as contrasted to that obtained in a salt mixture of identical low-frequency conductivity. The latter is assumed, whatever its salt content, to have a dielectric constant equal to that of water. In so far as dilute electrolyte solutions in themselves have lower dielectric constants than pure water alone (35), all the estimates are of course fractionally too high, and in effect are a measure only of the alteration of 'bulk' dielectric constant brought about by the non-electrolyte urinary particles.

The mode of action of the 'Perspex' -chloroform insulation is not clear. Pure 'perspex' behaves as do any of the other insulators of low dielectric constant. Preliminary experiments using polyethylene, glass and methyl-methacrylate polymers also yielded only the results to be anticipated from equation (ii) above. Superficially, the Perspex-chloroform insulation behaves as if it were permeable only to water,and not to ions.

Measurement of the dielectric constant was performed at an oscillator frequency of 5 mc/s. No attempt was made to study dielectric dispersion. While this frequency is too high to register the dielectric increment of particles of large relaxation time, eg. proteins,it is well within the upper limit of frequency for the detection of the dielectric effect of amino-acids and peptides (5).(over 100 mc/s).

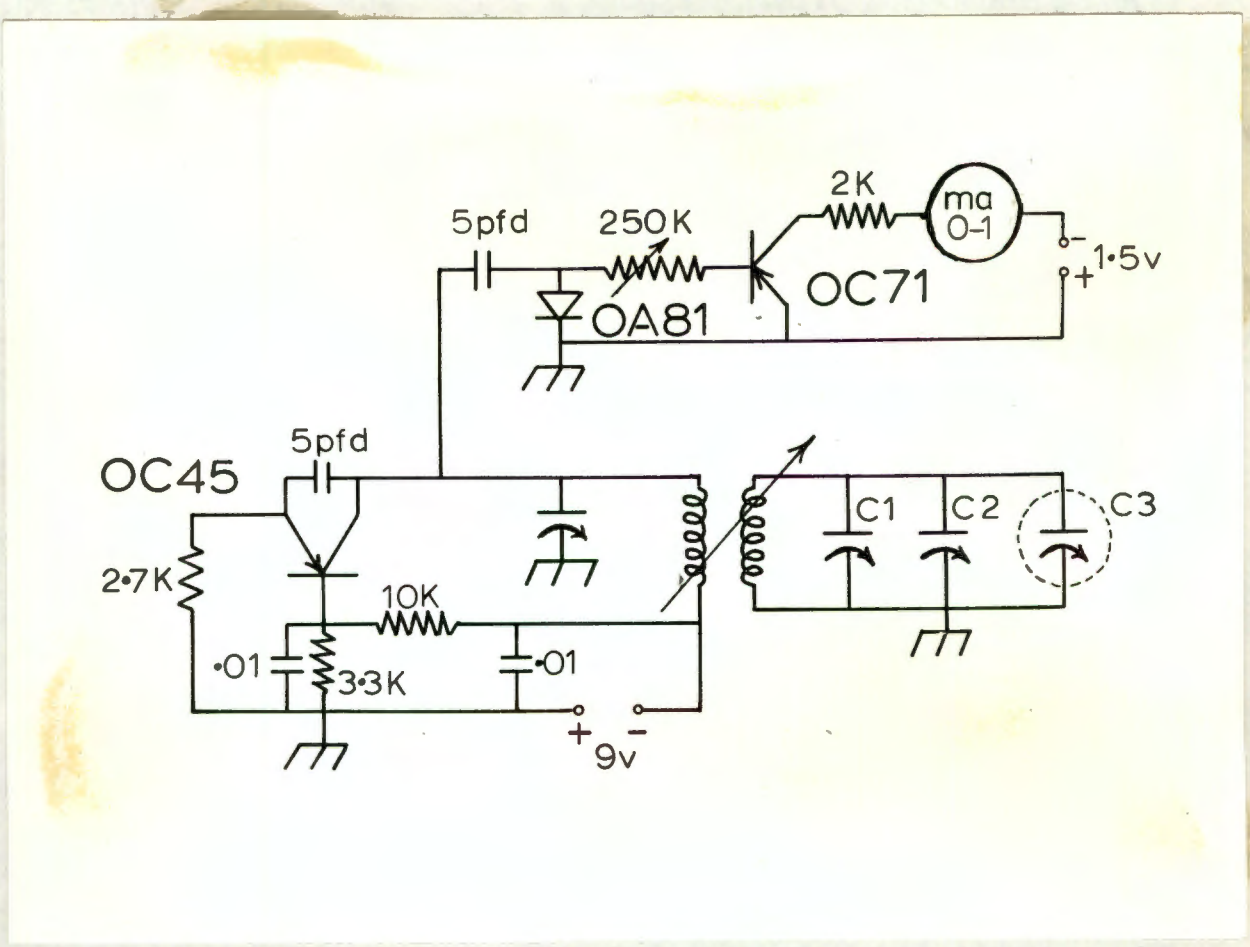

Fig. 1 ; 5 mc/s oscillator, radio-frequency output meter, and coupled resonant circuit, for measurement of the dielectric constant.

The dielectric increment of glycine varies from 23.4 at 20°C., to 22.3 at 30° C.;this is constant over a pH range of 4.5 to 7.8 and is independent of frequency upto about 100 mc/s (5).Accuracy of the measurement of dielectric constant as performed here may be gauged by noting the apparent dielectric increment of glycine when added to various urines (section 17);it is clear that ,while the 'recoveries' are not good, they suffice to confirm the validity of the relationship shown in Fig.21 .

Technique: The circuit diagram of the complete apparatus is shown in Fig.1 , and is seen to be simply a slightly modified version of a transistorised 'grid-dip' oscillator (32) to which a resonant circuit has been coupled. C3 represents the test condenser. The frequency of the oscillator was set initially at 5 mc/s and then left unaltered. Auditory monitoring of the signal on a communications receiver showed no frequency shift during dialectric constant measurements.

Fig. 2 shows the assembled apparatus.The test condenser is seen on the right,suspended in a glass beaker.All measurements were made with the condenser at a constant depth in the fluid tested.

Adequacy of the insulation was tested frequently;the D.C. resistance across the plates of the condenser when immersed in urine was over 200 megohms when the insulation was still intact.Readings became quite unreliable (as judged by glycine 'recovery' experiments) when the resistance fell even fractionally below this.

The coupling between the resonant circuit and the

Fig. 2: Apparatus for measurement of dielectric constant.

oscillator was found to be highly critical. Optimum coupling was the least that would give definite indication of resonance. As the conductivity of each fluid tested differed, the coupling needed readjustment with every reading.

All readings were made at room temperature.

B I B L I O G R A P H Y

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SUMMARY

This thesis is composed of two parts, each related to the problem of the mode of regulation of the renal excretion of inorganic phosphate.

Part One: Demonstration of secretion of inorganic phosphate in the dog kidney.

Each of ten dogs was given a large dose of 'Parathormone'; interrupted stop-flow studies were then performed. The results favour the hypothesis of distal tubular secretion of inorganic phosphate, but also reveal this to be quantitatively insignificant in contrast to the simultaneously induced inhibition of proximal tubular reabsorbtion.

Part TWo: The ionic structure of urine.

The physico-chemical structure of urine has been investigated here by a study of variations in urinary specific conductivity, ionic strength and dielectric constant, throughout the physiological range of urinary osmolality. Clear-cut inter-relationships have emerged between these parameters.

The overall ionic mobilities, activity and osmotic coefficients were compared to those of equivalent inorganic salt solutions. The former appear to be identical in urine and salt solutions. There is reason to suspect that the osmotic coefficients differ, however. Dielectric constants fell appreciably with increasing urinary osmolality. Synthesis of osmotic coefficient and dielectric constant data suggests that the particulate content of urine may be arranged in micellar form.

The inter-relationships derived from the various parameters above can be used as bases for the rapid estimation of both urinary ionic strength and urea concentration. The data also suggest that the

urinary osmolar output, in normal individuals in a steady state, is a function of diet.

ACKNOWLEDGEMENTS

Dr. W.P.U.Jackson, Head of the Endocrine Research Group, Dept. of Medicine, University of Cape Town, gave me every facility and constant encouragement throughout the course of this work.

Professors J.H.Louw and C.N.Barnard very kindly placed the Experimental Surgical Laboratory at my disposal .The dog experiments could not have been done without their support;their laboratory staff were most helpful.

The latter half of this Thesis arose directly from the comprehensive investigations into the aetiology of renal stone developed by Mr.M.Modlin. His dauntless forays into the realms of advanced physical chemistry were a constant stimulus. Many of the initial urinary analyses were carried out at his instigation.

The material presented here demanded the painstaking analysis of countless urine specimens. I am most grateful to Mr.J.Grapouw and Mr.A.Bruins for their patience and good humour while engaged on this Herculean task.

The photographs were prepared by Mr.I.O'Reilly and Mr.A.Bruins.

Financial support came from the Wellcome Trust, the Council for Scientific and Industrial Research, the University of Cape Town Staff Research Fund, and the Dr.C.L.Herman Research Fund.

APPENDIX D

Methods of Chemical Estimations

All urines were collected under toluene, and stored at 4° while awaiting analysis.

Osmolality was determined by observation of depression of freezing point. A 'Fiske' osmometer, calibrated with NaCl standards, and accurate to 2%, was used.

Na and K were determined by flame photometry.

Ca and Mg were determined by flame spectro-photometry; the methods were developed locally. Details have been published elsewhere (20)(18).

Inorganic Phosphate and Ammonium concentrations were determined as described by King and Wootton (21)

Inorganic Sulphate was determined by the technique evolved by Dodgson (8)

Creatinine was determined by the method of Folin and Wu (21). This is based on the Jaffe reaction ,i.e. creatinine when mixed with an alkaline picrate solution, gives rise to a reddish bron colour.

Both serum and urine samples in the dog experimen contained large amounts of glucose. Glucose itself reacts with alkaline picric acid mixture to produce a dark brown colour.To reduce this interfering effect 3% NaOH was used in place of the more usual 10% NaOH, and the solutions were read precisely 10 minutes after preparation.

APPENDIX E

Statistical Methods

All statistical methods applied in this work were derived from references (4) and (28). The most frequently used equations were:

(i) The constants, m and C, of regression equations of the form $y=mx + C$, were calculated by:

$$m = \frac{\Sigma xy - \frac{(\Sigma x)(\Sigma y)}{N}}{\Sigma x^2 - \frac{(\Sigma x)^2}{N}}$$

$$C = \frac{(\Sigma x)(\Sigma yx) - (\Sigma y)(\Sigma x^2)}{(\Sigma x)^2 - N(\Sigma x^2)}$$

(ii) Correlation coefficients(r):

$$r = \frac{\Sigma xy}{N} - \bar{x} \cdot \bar{y} \Big/ \sigma x \cdot \sigma y$$

(iii) Standard Error of an Estimate;

$$S_x = \sigma_x \sqrt{1 - (r^2)}$$

(iv) Standard Deviation (S.D.)

$$S.D. = \sqrt{\Sigma x^2 - (\bar{x})^2}$$

Bessels correction was applied where the number analysed was less than 30. Thus

$$\sigma^2 = \frac{n}{n-1} (S.D.^2)$$

(v) Significance was tested by the Student t test:

$$d = \frac{|\bar{x}_1 - \bar{x}_2|}{\sqrt{\frac{\sigma^1}{N_1} + \frac{\sigma^2}{N_2}}}$$

APPENDIX F

Raw Data.

"And so we see that the poetry fades out of the problem, and by the time the serious application of exact science begins we are left with only pointer readings".

Eddington.

Experiment 1

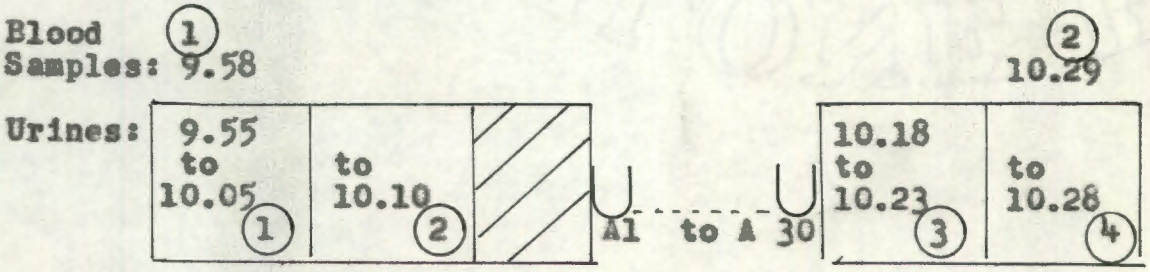
Infusions: (1) 10% dextrose-water. Rate adjusted ad lib to give urinary flow rate of 2 - 5 ml./minute.

(2) 'Normal' saline, containing 1.5 G. creatinine per litre. Commenced at 9.25 a.m. Infused at rate of about 1 ml./minute.

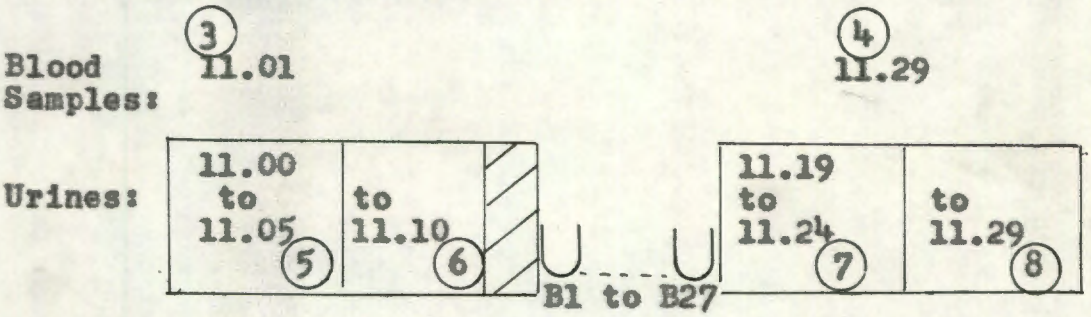
Priming Dose of 0.5 G. creatinine, given I.V. at 9.25 a.m.

Equilibration Period: 30 minutes.

Times of Blood and Urine Collections:



300 u. Parathormone given I.V. at 10.30 a.m.



Note: (1) The 10% dextrose-water infusion ran dry at 10.40 a.m.; replaced immediately by 5% dextrose-water.

(2) In this and subsequent experiments, the circled figures refer to sample numbers; the other figures refer to times of collection. The figures pertaining to blood samples are given above the interrupted series of squares; the latter represent control urine collections. Shaded squares represent the

tubes in which urine samples were collected immediately following cessation of stopped flow.

R E S U L T S

(A) Observed Results:

Sera:

No.	1	2	3	4
Cr (mg./100 ml.)	5.00	4.76	3.94	4.41
P (mg./100 ml.)	7.7	7.0	8.3	8.7

Control Urines:

No.	1	2	3	4	5
Vol. (ml.)	31.0	15.8	21.5	20.0	11.0
Cr (mg./100 ml)	32.5	24.1	16.9	16.6	32.3
P (mg./100 ml)	2.23	1.55	1.55	2.01	13.6

No.	6	7	8
Vol.(ml.)	11.4	10.4	10.4
Cr (mg./100 ml.)	32.3	33.6	34.1
P (mg./100 ml.)	15.7	19.2	20.3

Stop-Flow Urines:

Tube No.	Urine Volume(ml.)	Cr mg/100 ml.	P	Na mEq/l	Cumulative Volume (ml.)
A1	.70	45.0	1.47	40.0	0.70
A2	.77	-	2.19	-	1.47
A3	.71	-	3.08	-	2.18

Tube No.	Urine Volume(ml.)	Cr mg/100	P ml.	Na mEq/l	Cumulative Volume (ml.)
A4	.69	55.0	2.53	32.0	2.87
A5	.73	-	2.70	-	3.60
A6	.86	59.0	-	16.0	4.46
A7	.64	-	-	-	5.10
A8	.63	52.5	-	28.0	5.73
A9	.66	-	1.94	-	6.39
A10	.51	50.0	-	32.0	6.90
A11	.76	72.5	-	48.0	7.66
A12	.81	-	-	-	8.47
A13	.60	-	0.86	-	9.07
A14	.56	45.0	-	56.0	9.63
A15	.67	-	0.74	-	10.30
A16	.61	42.5	-	56.0	10.91
A17	.58	-	0.58	-	11.49
A18	.50	43.8	-	64.0	11.99
A19	.55	-	1.27	-	12.54
A20	.57	-	-	32.0	13.11
A21	.58	-	1.19	-	13.69
A22	.58	35.0	-	36.0	14.27
A23	.65	-	1.37	-	14.92
A24	.54	37.5	-	64.0	15.46
A25	.50	-	2.29	-	15.96
A26	.59	35.0	-	80.0	16.55
A27	.53	-	2.05	-	17.08
A28	.74	28.8	-	64.0	17.82
A29	.70	-	2.19	-	18.52
A30	2.30	35.0	1.57	88.0	20.82

Tube No.	Urine Volume(ml.)	Cr mg/100	P ml.	Na mEq/l	Cumulative Volume (ml.)
B1	.88	37.0	17.9	40.0	0.88
B2	.77	-	-	-	1.65
B3	.59	38.2	19.6	32.0	2.24
B4	.63	-	-	-	2.87
B5	.68	63.3	33.9	24.0	3.55
B6	.47	-	-	-	4.02
B7	.41	48.9	30.4	16.0	4.43
B8	.40	-	-	-	4.83
B9	.49	47.8	21.4	16.0	5.32
B10	.39	-	-	-	5.71
B11	.43	32.6	19.6	25.4	6.14
B12	.48	-	-	-	6.62
B13	.43	41.9	14.1	45.6	7.05
B14	.48	-	-	-	7.53
B15	.51	37.6	15.9	40.8	8.04
B16	.46	-	-	-	8.50
B17	.47	43.3	12.5	38.4	8.97
B18	.38	-	-	-	9.35
B19	.50	37.6	12.0	42.0	9.85
B20	.57	-	-	-	10.42
B21	.45	35.5	13.1	38.4	10.87
B22	.38	-	-	-	11.25
B23	.49	41.6	17.2	43.2	11.74
B24	.52	-	-	-	12.26
B25	.50	40.8	20.4	48.0	12.76
B26	.59	-	-	-	13.35
B27	.58	42.6	24.3	39.6	13.93

(B) Derived Results:

Urine Controls:

	No.	1	2	3	4	5
	Vol.(ml./min.)	3.10	3.16	4.30	4.00	2.20
@	Ccr (ml./min.)	20.2	15.3	15.2	13.9	18.0
@	% excretion P:	4.5	4.2	6.2	8.2	20.1

	No.	6	7	8
	Vol.(ml./min.)	2.28	2.08	2.08
@	Ccr (ml./min.)	18.7	15.8	16.1
@	% excretion P:	23.4	28.6	38.5

@ Note: Serum concentrations of creatinine and inorganic phosphate necessary for these calculations, estimated from observed values by simple proportion.

DOG A

Experiment 2

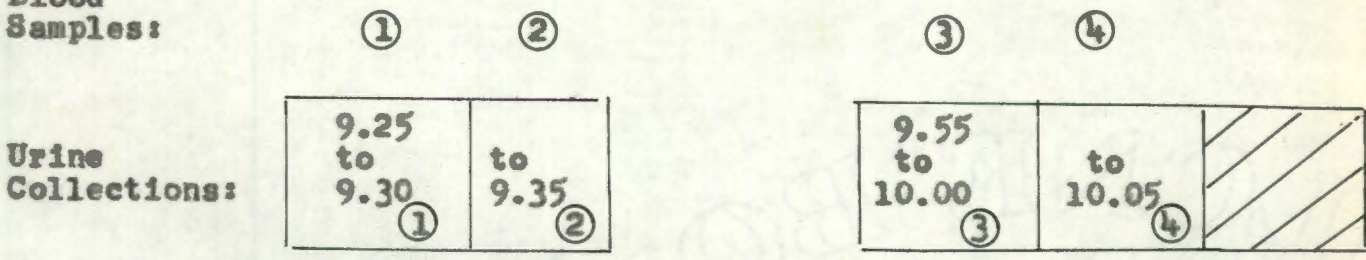
Infusions: (1) 5% dextrose-water. Rate adjusted ad lib to give urine flow of 3-5 ml./minute.

(2) 5% dextrose-water, containing 1.0 G. creatinine per litre. Commenced at 9.00 a.m. infused at rate of about 1 ml./minute.

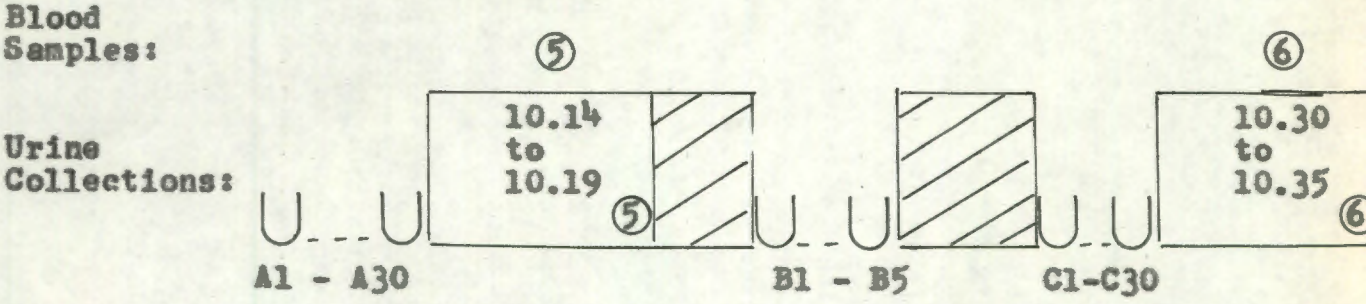
Priming Dose: 0.5 G. creatinine, given at 9.00 a.m., I.V.

Equilibration Period: 25 minutes.

Times of Blood and Urine Collections:



200 u.Parathormone,
0.5 ml. Sr^{85},
Both given I.V.
at 9.37 a.m.



Note: (1) Times of collection of blood samples not given, as these were at exact midpoints in time of the corresponding control urine collections.

(2) Dogs A and B were the only dogs in which control urine collections were made between stop-flow periods A,B, and C.

RESULTS

(A) Observed Results:

Sera:

No.	1	2	3	4	5	6
Cr (mg/100ml)	2.69	2.15	2.06	1.91	1.91	1.91
P (mg/100ml)	3.83	3.85	3.65	3.75	3.55	3.55
Na (mEq/l.)	139	139	139	137	137	138
Sr^{85} (c/s/G)	-	-	117	110	91	84

Control Urines:

No.	1	2	3	4	5	6
Cr (mg/100ml.)	11.05	10.75	10.15	9.55	8.96	7.76
P (mg/100ml.)	3.02	2.92	3.34	2.40	3.02	2.20
Na (mEq/l.)	20.9	18.3	13.5	14.8	13.9	13.0
Sr^{85} (c/s/G)	-	-	33.6	35.5	26.7	18.5
Vol.(ml.)	17.2	17.1	16.1	16.0	18.9	17.3

Stop-Flow Urines:

Tube No.	Urine Weight(G.)	Cr mg/100ml.	P	Na mEq/l.	Sr^{85} c/s/G.	Cumulative Volume(ml.)
A1	.607	8.21	7.07	18.0	34.7	.607
A2	.855	8.05	7.51	11.2	30.4	1.462
A3	.429	9.14	7.83	15.2	32.1	1.891
A4	.635	8.65	7.07	10.3	27.5	2.526
A5	.581	9.24	6.89	6.0	19.3	3.107
A6	.517	9.41	5.72	3.6	12.4	3.624
A7	.491	9.08	6.03	2.3	6.4	4.115
A8	.754	8.27	6.23	3.4	4.5	4.869
A9	.574	9.17	6.05	6.5	3.8	5.443
A10	.646	9.12	5.35	10.6	5.9	6.089
A11	.556	9.39	4.90	18.8	14.1	6.645
A12	.535	10.30	3.99	25.5	25.7	7.180
A13	.522	10.15	2.22	34.8	41.9	7.702
A14	.509	10.27	1.85	39.9	46.8	8.211
A15	.567	10.16	1.37	35.8	47.3	8.778
A16	.630	9.98	3.00	30.5	47.2	9.408
A17	.516	11.12	4.25	25.0	42.0	9.924
A18	.591	9.16	5.41	21.9	35.4	10.515
A19	.604	9.02	5.66	20.2	34.1	11.119
A20	.662	8.00	5.95	21.3	32.3	11.781

Dog A iv

Tube No.	Urine Weight(g.)	Cr mg/100ml.	P	Na mEq/l	Sr^{85} c/s/G.	Cumulative Volume(ml.)
A21	.593	8.35	6.58	22.5	34.3	12.374
A22	.603	7.93	6.68	21.8	32.6	12.977
A23-A30:data not given, as irrelevant.						
B1	.911	8.20	6.84	10.6	24.9	0.911
B2	.716	8.85	7.21	10.5	24.0	1.627
B3	.527	9.08	7.44	10.5	23.6	2.154
B4	.644	9.20	7.41	7.2	20.0	2.798
B5	.783	10.46	7.05	2.8	12.7	3.581
C1	.838	9.10	6.42	5.6	7.2	0.838
C2	.579	9.96	6.50	6.8	6.7	1.417
C3	.459	10.10	5.23	7.7	6.7	1.876
C4	.466	9.97	5.62	7.0	10.1	2.342
C5	.489	9.82	5.46	4.3	11.8	2.831
C6	.345	10.95	4.71	3.0	9.2	3.176
C7	.434	10.14	3.98	1.3	8.9	3.610
C8	.456	10.15	3.67	1.7	8.1	4.066
C9	.558	9.61	3.33	2.9	6.4	4.624
C10	.429	9.56	3.50	3.7	3.7	5.053
C11	.423	9.83	3.69	6.4	1.8	5.476
C12	.368	9.55	3.66	8.8	2.5	5.844
C13	.418	8.19	3.90	10.9	4.0	6.262
C14	.462	8.10	4.11	16.6	9.1	6.724
C15	.443	8.58	4.06	21.1	16.6	7.167
C16	.494	7.70	3.30	26.6	24.9	7.661
C17	.418	8.43	2.60	33.2	30.3	8.079
C18	.506	8.42	1.65	33.6	33.9	8.585
C19	.542	8.44	1.82	35.3	38.0	9.127
C20	.421	9.35	2.01	34.6	38.7	9.548
C21	.424	9.36	2.01	34.0	38.9	9.972

Dog A v

Tube No.	Urine Weight(G.)	Cr mg/100ml.	P	Na mEq/l	Sr^{85} c/s/G.	Cumulative Volume(ml.)
C22	.436	9.98	2.35	29.4	34.5	10.408
C23	.504	9.10	2.88	26.7	31.3	10.912
C24	.470	8.39	4.06	23.7	29.1	11.382

C25 - C30:data not given as irrelevant.

(B) Derived Results:

Urine Controls:

No.	1	2	3	4	5	6
Vol.(ml/min.)	3.44	3.42	3.22	3.20	3.78	3.55
Cer (ml/min.)	14.2	17.1	15.9	16.0	17.7	14.4
% excretion P	19.2	15.2	18.6	12.8	18.1	15.2

Stop-Flow Urines:

Tube No.	% Total Volume	Urinary P as @ fraction of that filtered
A1	6.9	.445
A2	16.7	.484
A3	21.5	.445
A4	28.8	.425
A5	35.4	.386
A6	41.3	.316
A7	46.9	.345
A8	55.5	.356
A9	62.0	.342
A10	69.4	.304
A11	75.7	.271

@ Note: Values of Cr_P and P_P needed for this calculation got by simple proportion.

Tube No.	% Total Volume	Urinary P as-fraction of that filtered.
A12	81.8	.199
A13	87.7	.109
A14	93.5	.093
A15	100.0	.070
A16	107.2	.156
A17	113.2	.198
A18	119.8	.306
A19	126.7	.324
A20	134.2	.387
A21	141.0	.408
B1	10.6	.449
B2	19.0	.438
B3	25.1	.441
B4	32.6	.433
B5	41.7	.363
C1	9.8	.379
C2	16.5	.351
C3	21.9	.279
C4	27.3	.303
C5	33.0	.299
C6	37.0	.231
C7	42.1	.211
C8	47.4	.195
C9	53.9	.187
C10	58.9	.197
C11	63.8	.202

Tube No.	% Total Volume	Urinary P as fraction of that filtered
C12	68.1	.206
C13	72.9	.256
C14	78.3	.273
C15	83.5	.254
C16	89.2	.231
C17	94.1	.166
C18	100.0	.105
C19	106.3	.116
C20	111.2	.116
C21	116.2	.116
C22	121.2	.127
C23	127.1	.171
C24	132.6	.260

Δ P	% Total Intra-tubular Volume	
(C - A)	of A	of C
+ .034	41.7 to 46.9	5.2
+ .023	51.5	9.8
- .005	55.5	13.8
+ .009	58.2	16.5
- .063	62.0	20.3
- .025	63.6	21.9
- .001	69.0	27.3
- .005	69.4	27.7
+ .028	74.7	33.0
- .040	75.7	34.0
+ .032	78.7	37.0
+ .012	81.8	40.1
+ .102	83.8	42.1
+ .086	87.7	46.0
+ .102	89.1	47.4
+ .034	93.5	51.8
+ .117	95.6	53.9
+ .127	100.0	58.3
+ .041	100.6	58.9
+ .046	105.5	63.8
+ .050	107.2	65.5
+ .008	109.8	68.1
+ .058	113.1	71.4
- .050	114.6	72.9
- .033	119.8	78.1
- .051	120.0	78.3

DOG B

Experiment 3

Infusions: (1) 5% dextrose-water.

(2) 'Normal' saline, containing 1.0 G.creatinine/litre.

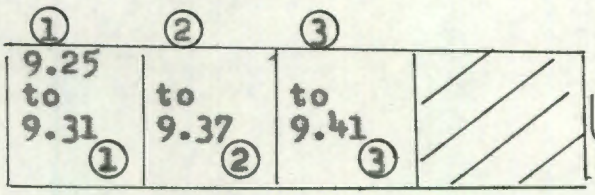
Priming Dose: 0.1 G creatinine, given I.V. at 8.50 a.m.

Equilibration Period: 35 minutes.

Times of Urine and Blood Collections:

Blood samples:

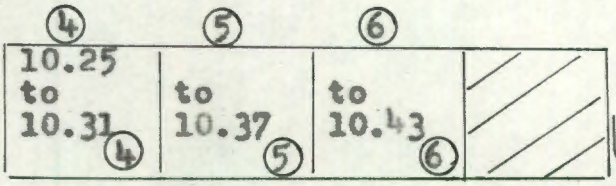
Urines:



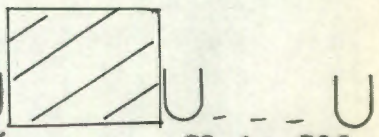
A1 to A30 100 u.Parathormone. I.V. at 9.51 a.m.

Blood samples:

Urines:



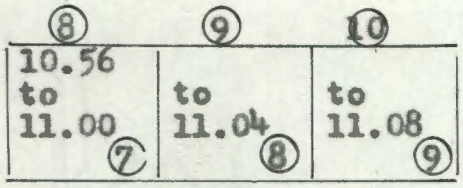
B1 to B6



C1 to C30

Blood samples:

Urines:



Note: Urine collection 7 begun immediately after C30.

RESULTS

(A) Observed Results:

Sera:

No.	1	2	3	4	5	6
Cr (mg/100 ml.)	2.84	2.60	2.62	1.89	1.75	1.34
P (mg/100 ml.)	5.12	4.91	4.91	3.44	3.00	2.91
Na (mEq/l.)	126	130	130	-	126	126

No.	7	8	9	10
Cr (mg/100 ml.)	1.31	1.43	1.60	1.60
P (mg/100 ml.)	2.73	2.73	2.71	2.53
Na (mEq/l.)	122	116	-	119

Urine Controls:

No.	1	2	3	4	5	6	7
Vol.(ml.)	22.5	31.0	16.5	10.0	14.8	26.5	37.7
Cr (mg/100 ml.)	33.8	24.5	24.4	37.5	33.1	19.3	9.6
P (mg/100 ml.)	13.6	10.1	10.2	12.1	9.2	4.6	2.3
Na (mEq/l.)	71	73	71	51	50	49	53

No.	8	9
Vol.(ml.)	35.5	33.3
Cr (mg/100 ml.)	9.5	10.4
P (mg/100 ml.)	2.1	1.9
Na (mEq/l.)	51	49

Stop-Flow Urines:

Tube No.	Urine Weight(G.)	Cr mg/100ml.	P	Na mEq/l.	Cumulative Volume (ml.)
A1	.585	31.7	9.55	30.3	0.585
A2	.278	35.4	6.67	35.6	0.863
A3	.483	44.0	10.89	25.5	1.346
A4	.452	41.4	12.27	25.8	1.798
A5	.528	43.5	13.50	25.0	2.326
A6	.594	45.9	14.92	22.6	2.920
A7	.779	52.0	15.14	16.8	3.699
A8	.655	55.6	16.20	10.4	4.354
A9	.605	58.0	15.69	8.7	4.959
A10	.513	58.8	14.03	8.4	5.490
A11	.552	57.3	11.60	12.7	6.042
A12	.592	57.2	8.08	16.9	6.634
A13	.636	53.6	7.93	27.0	7.270
A14	.600	45.8	5.94	35.8	7.870
A15	.594	43.2	5.63	41.1	8.464
A16	.595	42.7	4.31	40.2	9.059
A17	.596	43.6	4.06	38.0	9.655
A18	.549	46.0	3.71	37.2	10.204
A19	.634	48.0	4.67	35.1	10.838
A20	.595	43.5	6.06	35.0	11.433
A21	.601	43.4	8.44	36.5	12.034
A22	.559	38.7	7.80	36.9	12.593
A23	.556	39.7	7.76	37.3	13.149
A24	.786	36.1	7.16	30.9	13.935
A25	.534	35.4	7.20	35.1	14.469

A26 to A30:data not given as irrelevant.

Stop-Flow Urines:

Tube No.	Urine Weight(G.)	Cr Mg/100ml.	P	Na mEq/l.	Cumulative Volume (ml.)
B1	.973	17.3	3.14	19.9	0.973
B2	.529	25.6	1.72	17.2	1.502
B3	.515	25.1	3.60	24.2	2.017
B4	.487	27.3	2.26	21.8	2.504
B5	.690	29.7	5.41	17.8	3.194
B6	.717	35.8	5.46	13.0	3.911
C1	1.010	32.4	5.34	6.9	1.010
C2	.569	36.0	2.33	10.8	1.579
C3	.469	39.6	2.60	16.7	2.048
C4	.615	35.4	2.32	15.4	2.663
C5	.881	40.0	3.17	12.9	3.544
C6	.954	40.2	3.56	7.8	4.498
C7	.856	37.2	2.40	5.3	5.354
C8	.783	33.2	1.74	5.5	6.137
C9	.799	30.3	1.62	6.9	6.936
C10	.764	29.1	1.40	11.6	7.700
C11	.873	27.2	0.65	16.0	8.573
C12	.885	27.1	0.79	27.9	9.458
C13	.896	22.0	0.40	39.3	10.354
C14	.952	19.7	0.22	46.8	11.306
C15	.857	18.1	0.20	51.0	12.163
C16	.726	17.6	0.32	55.4	12.889
C17	.697	18.2	0.42	56.3	13.586
C18	.721	16.0	0.27	53.3	14.307

C19 to C30:data not given as irrelevant.

(B) Derived Results:

Control Urines:

No.	1	2	3	4	5
Vol.(ml/min.)	3.75	5.17	4.13	1.67	2.47
Ccr (ml/min.)	44.6	48.7	38.5	33.1	46.7
% excretion P:	22.3	21.8	22.3	17.7	16.2

No.	6	7	8	9
Vol.(ml/min.)	4.42	9.43	8.88	8.33
Ccr (ml/min.)	63.7	64.4	52.7	54.1
% excretion P:	11.0	12.5	9.5	11.6

Stop-Flow Urines:

Tube No.	% Total Volume	Urinary P as fraction of that filtered
A1	5.7	.161
A2	8.5	.101
A3	13.2	.132
A4	17.6	.158
A5	22.8	.166
A6	28.6	.173
A7	36.3	.155
A8	42.7	.155
A9	48.6	.144
A10	53.8	.127
A11	59.2	.108
A12	65.0	.075
A13	71.2	.079
A14	77.1	.069
A15	82.9	.070
A16	88.8	.054
A17	94.6	.050
A18	100.0	.043
A19	106.2	.052
A20	112.0	.074
A21	117.9	.104
A22	123.4	.108
A23	128.9	.104
A24	136.6	.106
A25	141.8	.109
B1	8.0	.084
B2	12.3	.031
B3	16.6	.066

Stop-Flow Urines:

Tube No.	% Total Volume	Urinary P as fraction of that filtered
B4	20.6	.038
B5	26.3	.084
B6	32.2	.070
C1	8.3	.079
C2	13.0	.031
C3	16.8	.032
C4	21.9	.031
C5	29.1	.038
C6	37.0	.043
C7	44.0	.031
C8	50.5	.025
C9	57.0	.026
C10	63.3	.023
C11	70.5	.011
C12	77.8	.014
C13	85.1	.009
C14	93.0	.005
C15	100.0	.005
C16	106.0	.009
C17	111.7	.011
C18	117.6	.008

ΔP (C - A)	% Total Intra-tubular Volume of A	of C
- .076	32.2 to 36.3	4.1
- .076	40.5	8.3
- .124	42.7	10.5
- .113	45.2	13.0
- .112	48.6	16.4
- .095	49.0	16.8
- .096	53.8	21.6
- .077	54.1	21.9
- .070	59.2	27.0
- .037	61.3	29.1
- .032	65.0	32.8
- .036	69.2	37.0
- .048	71.2	39.0
- .038	76.2	44.0
- .044	77.1	44.9
- .045	82.7	50.5
- .044	82.9	50.7
- .028	88.8	56.6
- .024	89.2	57.0
- .027	94.6	62.4
- .020	95.5	63.3
- .032	100.0	67.8
- .041	102.7	70.5
-.038	106.2	74.0
- .060	110.0	77.8
- .065	112.0	79.8
- .095	117.3	85.1
- .099	117.9	85.7
- .103	123.4	91.2
- .099	125.2	93.0

DOG C

Experiment 4

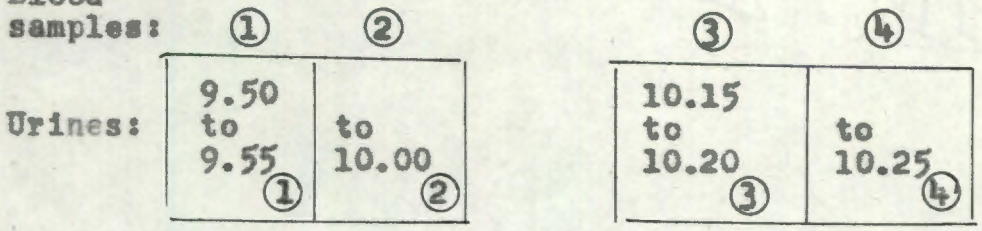
Infusions: (1) 10% dextrose-water.

(2) 'Normal' saline, containing 1.0G creatinine per litre. Commenced at 9.25 a.m.

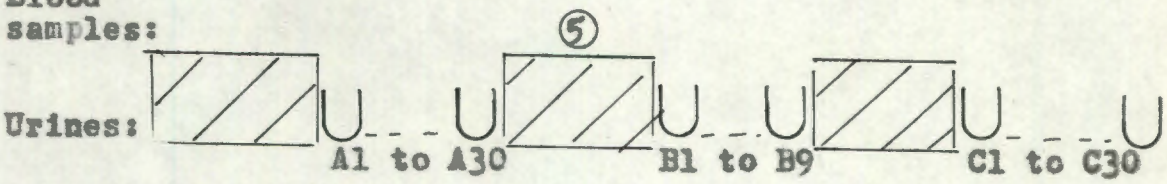
Priming Dose of 0.1 G creatinine given I.V. at 9.25 a.m.

Equilibration Period: 25 minutes.

Times of Blood and Urine Collections:



Parathormone
200 u. given I.V.
at 10.01 a.m.



Note: (1)Blood samples taken at midpoint in time of corresponding urine collections.

(2) Period of ureteric occlusion prior to collection of urines A1 to A30, follows immediately after control urine collection 4.

R E S U L T S

A. Observed Results:

Sera:

No. -	1	2	3	4	5
Cr(mg/100 ml.)	2.06	1.71	1.60	1.49	1.54
P (mg/100 ml.)	4.50	4.20	3.90	3.73	4.10
Na (mEq/l.)	138	138	134	128	128

Control Urines:

No.	1	2	3	4
Vol.(ml.)	16.6	17.8	26.6	35.0
Cr (mg/100 ml.)	9.43	9.43	7.14	6.00
P (mg/100 ml.)	4.17	4.08	3.50	3.08
Na (mEq/l.)	3.2	3.3	1.8	1.8

Stop-Flow Urines:

Tube No.	Urine Weight(G)	Cr mg/100ml	P mg/100ml	Na mEq/l.	Cumulative Volume(ml.)
A1	.573	4.89	3.28	17.5	0.573
A2	.538	4.88	3.40	21.4	1.111
A3	.411	5.29	3.59	18.7	1.522
A4	.410	5.52	3.95	18.5	1.932
A5	.336	6.07	4.05	16.8	2.268
A6	.437	5.75	3.92	14.5	2.705
A7	.436	6.21	4.46	12.4	3.141
A8	.479	6.27	4.40	10.4	3.620
A9	.478	6.28	4.31	8.6	4.098
A10	.538	6.08	4.08	7.0	4.636
A11	.562	5.48	3.39	-	5.198
A12	.799	5.31	3.74	4.6	5.997

Stop-Flow Urines:

Tube No.	Urine Weight(C)	Cr mg/100ml	P	Na mEq/l.	Cumulative Volume(ml.)
A13	.684	5.47	3.60	4.1	6.681
A14	.809	4.93	3.53	3.7	7.490
A15	.616	5.42	3.48	4.1	8.106
A16	.601	5.31	3.14	4.2	8.707
A17	.611	5.19	2.93	5.2	9.318
A18	.611	5.17	3.13	6.7	9.929
A19	.603	4.94	3.00	8.2	10.532
A20	.606	5.20	2.79	10.4	11.138
A21	.616	4.64	2.69	12.2	11.754
A22	.601	4.71	2.45	15.4	12.355
A23	.670	4.09	1.80	16.1	13.025
A24	.661	4.61	1.99	21.9	13.686
A25	.715	4.61	1.71	24.4	14.401
A26	.665	4.36	1.73	26.4	15.066
A27	.719	4.12	1.45	27.2	15.785
A28	.675	4.31	1.51	27.8	16.460
A29	.641	4.48	1.57	28.9	17.101
A30	.695	4.22	1.48	28.6	17.796
B1	.666	3.33	3.08	16.5	0.666
B2	.609	3.90	3.66	17.7	1.275
B3	.813	4.44	4.09	14.6	2.088
B4	.762	4.67	4.46	12.6	2.850
B5	.780	5.41	4.83	10.1	3.630
B6	.815	5.05	4.60	5.3	4.445
B7	.783	4.88	4.32	3.1	5.228
B8	.718	4.31	4.19	4.9	5.946
B9	.655	3.99	3.79	3.5	6.601

Tube No.	Urine Weight(G)	Cr mg/100 ml.	P	Na mEq/l.	Cumulative Volume(ml.)
C1	.841	5.21	3.94	6.8	0.841
C2	.635	6.18	4.11	7.7	1.476
C3	.402	6.93	5.52	5.8	1.878
C4	.524	6.63	4.35	5.4	2.402
C5	.490	6.98	4.58	3.5	2.892
C6	.425	7.19	4.67	5.8	3.317
C7	.511	7.25	4.39	4.7	3.828
C8	.551	6.91	4.34	4.2	4.379
C9	.555	6.30	4.14	2.2	4.934
C10	.471	6.60	3.94	3.9	5.405
C11	.473	6.57	3.66	1.6	5.878
C12	.402	6.48	3.68	1.2	6.280
C13	.541	6.18	3.61	1.9	6.821
C14	.443	6.24	3.64	1.4	7.264
C15	.448	6.56	3.65	2.1	7.712
C16	.368	6.63	3.54	1.7	8.080
C17	.442	6.63	3.41	1.9	8.522
C18	.441	6.63	3.41	2.4	8.963
C19	.507	6.78	3.30	2.6	9.470
C20	.510	6.49	3.21	3.2	9.980
C21	.454	7.09	3.16	3.5	10.434
C22	.421	7.26	3.27	3.5	10.855
C23	.433	7.06	3.18	4.2	11.288
C24	.340	8.22	3.31	5.1	11.628
C25	.411	7.05	3.23	4.9	12.039
C26	.431	7.38	2.90	5.1	12.470
C27	.433	7.36	-	5.8	12.903
C28	.439	7.26	2.85	6.2	13.342
C29	.411	7.39	2.65	7.0	13.753
C30	.417	7.28	2.80	7.1	14.170

(B) Derived Results:

Control Urines:

No.	1	2	3	4
Vol.(ml./min.)	3.32	3.56	5.32	7.00
Ccr (ml./min.)	15.2	19.6	23.7	27.3
% excretion P	20.2	17.6	20.1	20.5

Stop-Flow Urines:

Tube No.	% Total Volume	Urinary P as-fraction of that filtered.
A1	3.2	.264
A2	6.2	.274
A3	8.6	.267
A4	10.9	.282
A5	12.7	.263
A6	15.2	.269
A7	17.7	.283
A8	20.3	.277
A9	23.0	.270
A10	26.1	.264
A11	29.2	.244
A12	33.7	.277
A13	37.5	.259
A14	42.1	.282
A15	45.5	.253
A16	48.9	.233
A17	52.4	.222
A18	55.8	.239
A19	59.2	.239
A20	62.6	.211
A21	66.0	.228

Tube No.	% Total Volume	Urinary P as fraction of that filtered.
A22	69.4	.205
A23	73.2	.173
A24	76.9	.170
A25	80.9	.146
A26	84.7	.156
A27	88.7	.139
A28	92.5	.138
A29	96.1	.138
A30	100.0	.138
B1	5.2	.348
B2	9.9	.353
B3	16.2	.346
B4	22.1	.359
B5	28.1	.336
B6	34.4	.342
B7	40.5	.333
B8	46.1	.366
B9	51.2	.357
C1	6.5	.284
C2	11.4	.250
C3	14.6	.299
C4	18.6	.247
C5	22.4	.247
C6	25.7	.244
C7	.29.7	.228
C8	33.9	.236
C9	38.2	.247
C10	41.9	.224
C11	45.6	.209
C12	48.7	.214
C13	52.9	.220
C14	56.3	.219
C15	59.8	.209
C16	62.6	.201
C17	66.0	.193
C18	69.5	.193
C19	73.4	.183
C20	77.3	.186
C21	80.9	.167
C22	84.1	.169
C23	87.5	.169
C24	90.1	.151
C25	93.3	.172
C26	96.6	.148
C27	100.0	.133
C28	103.4	.148
C29	106.6	.135
C30	109.8	.145

ΔP (C - A)	% Total Intra-tubular Volume of A	of C
.062	51.2 to 52.4	1.2
.045	55.8	4.6
.045	57.7	6.5
.011	59.2	8.0
.039	62.6	11.4
.071	65.8	14.6
.021	66.0	14.8
.042	69.4	18.2
.074	69.8	18.6
.074	73.2	22.0
.077	73.6	22.4
.098	76.9	25.7
.082	80.9	29.7
.080	84.7	33.5
.097	85.1	33.9
.108	88.7	37.5
.109	89.4	38.2
.086	92.5	41.3
.086	93.1	41.9
.071	96.1	44.9
.071	96.8	45.6
.076	99.9	48.7
.082	100.0	48.8

DOG D

Experiment 5

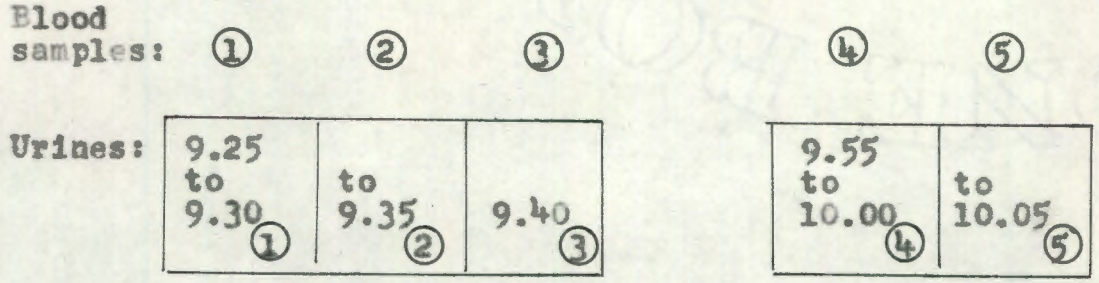
Infusions: (1) 5% dextrose-water.

(2) 5% dextrose-water containing 1.0 G creatinine.

Priming Dose of 0.5 G creatinine, given I.V. at 9.00 a.m.

Equilibration Period: 25 minutes.

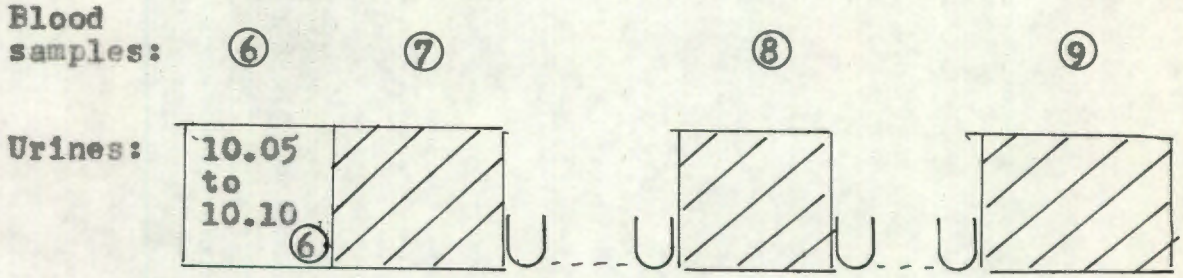
Times of Blood and Urine Collections:

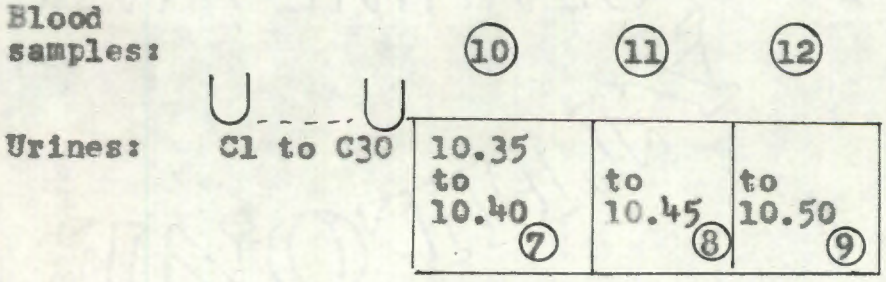


Parathormone

200 u., given I.V.

at 9.40





Note: Urine collection C, follows immediately after the third period of ureteric occlusion.

R E S U L T S

(A) Observed Results:

Sera:

No.	1	2	3	4	5	6
Cr (mg/100 ml.)	4.80	4.68	4.57	4.37	4.34	4.43
P (mg/100 ml.)	2.50	2.50	2.60	2.00	1.85	2.18

No.	7	8	9	10	11	12
Cr (mg/100 ml.)	4.34	4.40	4.49	4.46	4.49	4.86
P (mg/100 ml.)	2.40	2.40	2.28	2.40	2.53	2.55

Control Urines:

No.	1	2	3	4	5
Vol. (ml.)	27.0	32.0	32.0	18.5	23.5
P (mg/100 ml.)	1.75	1.25	1.17	1.96	1.58
Cr (mg/100 ml.)	43.1	35.7	30.6	47.4	38.4

No.	6	7	8	9
Vol. (ml.)	26.0	35.5	37.0	38.0
P (mg/100 ml.)	1.67	1.42	1.42	1.58
Cr (mg/100 ml.)	33.4	20.3	17.7	17.4

Stop-Flow Urines:

Tube No.	Urine Weight(G.)	Cr mg/100 ml.	P mg/100 ml.	Na mEq/l.	Cumulative Volume (ml.)
A1	.641	27.5	1.64	3.3	0.641
A2	.616	29.8	1.78	10.1	1.257

Tube No.	Urine Weight(G.)	Cr	P	Na	Cumulative Volume (ml.)
		mg/100 ml.		mEq/l.	
A3	.679	30.7	1.72	4.7	1.936
A4	.596	37.1	2.27	4.5	2.532
A5	.553	40.6	2.63	4.0	3.085
A6	.552	40.8	2.59	4.1	3.637
A7	.512	40.2	2.55	3.1	4.149
A8	.590	38.4	2.62	2.8	4.739
A9	.605	37.7	2.37	2.9	5.344
A10	.526	39.2	2.68	3.0	5.870
A11	.533	37.1	2.30	3.0	6.403
A12	.720	35.0	1.99	2.7	7.123
A13	.857	33.8	1.75	2.8	7.980
A14	.554	37.4	1.63	3.6	8.534
A15	.694	35.0	1.76	2.7	9.228
A16	.768	34.5	1.45	2.8	9.996
A17	.608	36.0	1.40	3.1	10.604
A18	.649	35.9	1.18	3.3	11.253
A19	.547	36.2	0.87	3.5	11.800
A20	.582	35.0	0.87	3.7	12.382
A21	.661	35.2	0.15	3.6	13.043
A22	.410	40.9	0.11	4.2	13.453
A23	.771	34.6	0.27	3.6	14.224
A24	.681	36.9	0.69	4.0	14.905
A25	.704	36.0	0.57	3.9	15.609
A26	.642	36.8	0.46	3.7	16.251

A27 to A30:data not given as irrelevant.

Tube No.	Urine Weight(G.)	Cr	P	Na	Cumulative Volume (ml.)
		mg/100 ml.		mEq/l.	
B1	.703	25.4	1.70	4.7	0.703
B2	.775	25.6	1.82	9.2	1.478
B3	.755	26.6	1.85	3.7	2.233
B4	.658	29.5	1.78	2.7	2.891
B5	.661	35.9	2.24	2.7	3.552
B6	.471	38.3	2.02	2.6	4.023
C1	1.048	29.2	2.00	6.6	1.048
C2	.489	34.2	2.14	4.8	1.537
C3	.596	31.5	1.88	3.1	2.133
C4	.534	34.4	2.38	3.0	2.667
C5	.534	41.2	2.30	2.8	3.201
C6	.533	38.0	2.22	2.7	3.734
C7	.521	39.5	1.74	2.2	4.255
C8	.424	40.7	1.71	2.7	4.679
C9	.402	40.5	1.46	2.4	5.081
C10	.476	38.2	1.51	2.0	5.557
C11	.529	37.9	1.38	2.8	6.086
C12	.590	37.7	1.44	2.9	6.676
C13	.538	39.4	1.50	2.4	7.214
C14	.561	40.0	1.36	2.6	7.775
C15	.510	39.0	1.20	2.8	8.285
C16	.542	40.4	1.05	2.6	8.827
C17	.479	40.9	1.26	2.9	9.306
C18	.437	38.1	1.36	2.7	9.743
C19	.567	35.7	1.18	3.3	10.310
C20	.515	36.0	1.00	3.0	10.825
C21	.436	37.6	0.83	3.0	11.261

Tube No.	Urine Weight(G.)	Cr mg/100 ml.	P	Na mEq/l.	Cumulative Volume (ml.)
C22	.528	34.4	0.94	2.6	11.789
C23	.550	36.2	0.87	2.8	12.339
C24	.571	34.5	0.84	2.8	12.910
C25	.566	34.6	0.68	3.3	13.476
C26	.514	36.0	1.00	3.2	13.990

C27 to C30:data not given as irrelevant.

(B) Derived Data.

Urine Controls:

No.	1	2	3	4	5
Vol.(ml./min.)	5.40	6.40	6.40	3.70	4.70
Ccr (ml./min.)	48.5	48.8	42.8	40.2	41.6
% excretion P:	7.8	6.6	6.9	9.0	9.7

No.	6	7	8	9
Vol.(ml./min.)	5.20	7.10	7.40	7.60
Ccr Iml./min.)	39.2	32.3	29.1	27.2

Stop-Flow Urines:

Tube No.	% Total Volume	Urinary P as fraction of that filtered	Tube No.	% Total Volume	Urinary P as fraction of that filtered
A1	4.8	.108	A6	27.0	.115
A2	9.3	.108	A7	30.8	.115
A3	14.4	.101	A8	35.2	.123
A4	18.8	.111	A9	39.7	.114
A5	22.9	.117	A10	43.6	.124

Tube No.	% Total Volume	Urinary P as fraction of that filtered
A11	47.6	.103
A12	52.9	.103
A13	59.3	.094
A14	63.4	.079
A15	68.6	.091
A16	74.3	.076
A17	78.8	.070
A18	83.6	.059
A19	87.7	.043
A20	92.0	.045
A21	97.0	.008
A22	100.0	.005
A23	105.7	.014
A24	110.8	.034
A25	116.0	.029
A26	120.8	.023
B1	5.2	.123
B2	11.0	.130
B3	16.6	.127
B4	21.4	.111
B5	26.4	.114
B6	29.9	.097
C1	7.8	.135
C2	11.4	.123
C3	15.8	.118
C4	19.8	.136
C5	23.8	.110
C6	27.7	.115

Tube No.	% Total Volume	Urinary P as fraction of that filtered
C7	31.6	.087
C8	34.7	.083
C9	37.7	.071
C10	41.3	.078
C11	45.2	.072
C12	49.6	.075
C13	53.6	.075
C14	57.7	.067
C15	61.5	.061
C16	65.5	.051
C17	69.1	.061
C18	72.3	.070
C19	76.5	.065
C20	80.4	.055
C21	83.6	.044
C22	87.5	.054
C23	91.6	.047
C24	95.8	.048
C25	100.0	.039
C26	103.9	.055

Δ P (C - A)	% Total Intra-tubular Volume of A	of C
+ .020	29.9 to 30.8	0.9
+ .012	35.2	5.3
+ .021	37.7	7.8
+ .009	39.7	9.8
- .001	41.3	11.4
- .006	43.6	13.7
+ .015	45.7	15.8
+ .033	47.6	17.7
+ .033	49.7	19.8
+ .007	52.9	23.0
+ .016	53.7	23.8
+ .021	57.6	27.7
- .007	59.3	29.4
+ .008	61.5	31.6
+ .004	63.4	33.5
- .008	64.6	34.7
- .020	67.6	37.7
- .013	68.6	38.7
+ .002	71.2	41.3
- .004	74.3	44.4
- .002	75.1	45.2
+ .005	78.8	48.9
+ .016	79.5	49.6
+ .016	83.5	53.6
+ .008	83.6	53.7
+ .024	87.6	57.7
+ .018	87.7	57.8
+ .016	91.4	61.5

△ P (C - A)	% Total Intra-tubular Volume of A	of C
+ .006	92.0	62.1
+ .043	95.4	65.5
+ .053	97.0	67.1
+ .056	99.0	69.1
+ .065	100.0	70.1
+ .056	102.2	72.3
+ .051	105.7	75.8
+ .031	106.4	76.5
+ .021	110.3	80.4
+ .010	110.8	80.9
+ .015	113.5	83.6
+ .025	116.0	86.1
+ .031	117.4	87.5
+ .024	120.8	90.9

DOG E

Experiment 6

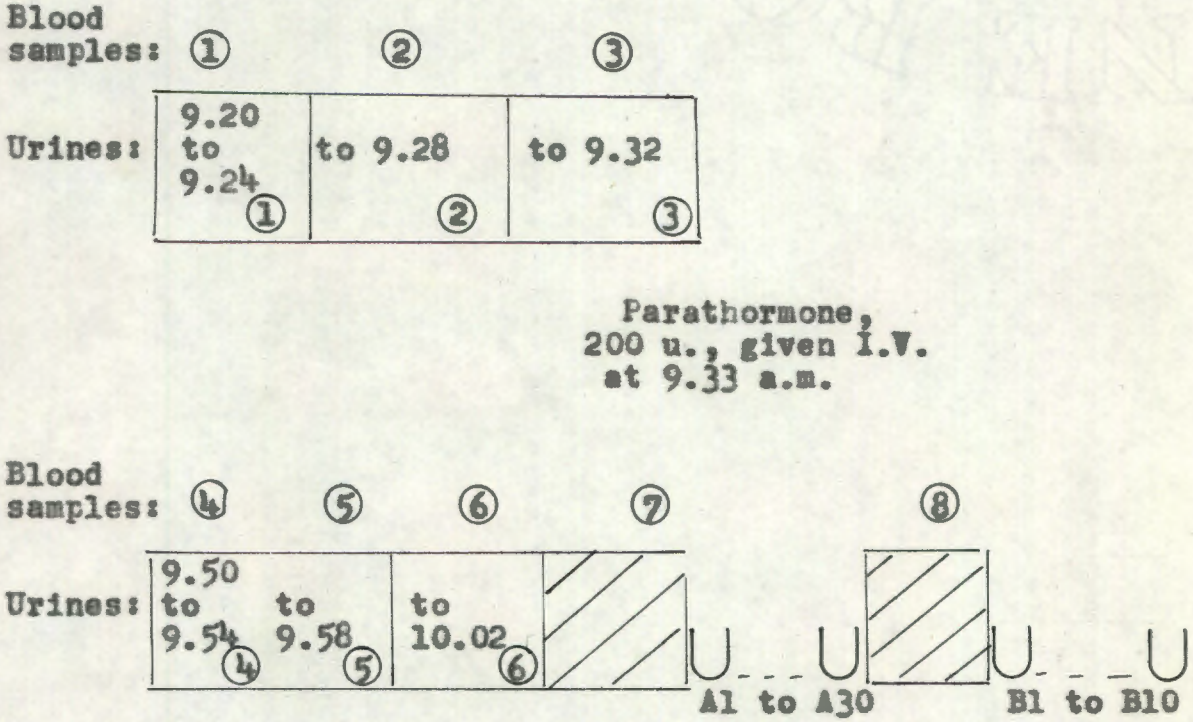
Infusions: (1) 10% dextrose-water.

(2) 5% dextrose-water, containing 1.0 G. creatinine per litre.

Priming Dose of 0.5 G. creatinine, given I.V. at 9.00a.m.

Equilibration Period: 20 minutes.

Times of Blood and Urine Collections:



Note: Third period of ureteric occlusion follows immediately after collection of B10.

R E S U L T S

(A) Observed Results

Sera:

No.	1	2	3	4	5	6
Cr (mg/100ml)	4.63	4263	4.11	3.89	3.60	3.60
P (mg/100 ml)	4.07	4.25	3.89	3.78	4.02	3.86

No.	7	8	9	10	11
Cr (mg/100 ml.)	3.31	3.49	3.43	3.43	3.43
P (mg/100 ml.)	3.86	3.83	3.55	3.27	2.86

Control Urines:

No.	1	2	3	4	5
Vol. (ml.)	47.0	41.5	42.5	42.5	42.0
Cr (mg/100 ml.)	17.4	16.5	15.6	13.8	13.4
P (mg/100 ml.)	2.43	2.43	2.43	3.13	3.00
Na (mEq/1.)	19.1	18.7	18.5	17.0	17.0

No.	6	7	8	9
Vol. Iml.)	48.5	43.0	45.0	45.0
Cr (mg/100 ml.)	13.0	10.3	10.3	10.3
P (mg/100 ml.)	2.96	2.78	2.52	2.17
Na (mEq/1.)	17.0	15.2	14.1	14.1

Stop-Flow Urines:

Tube No.	Urine Weight(G.)	Cr mg/100 ml.	P	Na mEq/1.	Cumulative Volume (ml.)
A1	1.271	10.4	3.27	11.2	1.271
A2	.663	11.6	3.43	12.1	1.934

Tube No.	Urine Weight(G.)	Cr mg/100 ml.	P	Na mEq/l.	Cumulative Volume (ml.)
A3	.715	11.7	3.58	8.0	2.649
A4	.657	12.4	3.59	3.6	3.306
A5	.813	12.2	3.65	1.6	4.119
A6	.637	13.7	3.28	1.0	4.756
A7	.726	13.4	3.35	1.2	5.482
A8	.576	12.7	3.45	3.1	6.058
A9	.579	12.8	3.25	4.0	6.637
A10	.580	13.4	3.12	5.7	7.217
A11	.726	13.3	2.61	7.7	7.943
A12	.562	13.9	2.32	9.9	8.505
A13	.558	14.1	1.73	11.9	9.063
A14	.566	13.2	1.47	13.5	9.629
A15	.576	16.4	0.84	16.0	10.205
A16	.592	14.2	1.03	16.3	10.797
A17	.565	15.2	1.02	17.6	11.362
A18	.621	14.8	.0.50	18.0	11.983
A19	.509	16.2	0.51	19.3	12.492
A20	.562	15.2	0.58	18.8	13.054
A21	.414	16.6	0.14	17.3	13.468
A22	.763	13.1	1.06	16.9	14.231
A23	.566	13.5	1.17	17.8	14.797
A24	.574	11.9	1.74	17.4	15.371
A25	.479	10.9	1.86	18.6	15.850
A26	.682	11.0	1.98	16.7	16.532
A27	.463	11.5	2.04	18.8	16.995
A28	.725	10.5	2.18	16.4	17.720
A29	.694	10.5	2.47	17.1	18.414
A30	.540	11.3	2.02	17.4	18.954

Tube No.	Urine Weight(G.)	Cr mg/100 ml.	P	Na mEq/l.	Cumulative Volume (ml.)
B1	1.450	9.9	2.78	14.3	1.450
B2	.809	10.1	2.12	14.3	2.259
B3	.582	12.0	2.74	8.9	2.841
B4	.642	11.7	2.63	3.9	3.483
B5	.613	11.2	2.62	2.3	4.096
B6	.530	11.8	1.92	2.1	4.626
B7	.556	12.4	2.25	1.5	5.182
B8	.500	11.3	2.35	2.2	5.682
B9	.597	10.8	2.49	3.1	6.279
B10	.861	11.4	2.40	4.6	7.140
C1	1.519	10.6	2.77	7.7	1.519
C2	.752	12.0	2.88	11.7	2.271
C3	.411	13.0	2.58	6.7	2.682
C4	.373	14.2	3.26	3.5	3.055
C5	.440	12.9	2.25	4.4	3.495
C6	.492	12.3	1.97	2.2	3.987
C7	.464	12.7	1.90	1.4	4.451
C8	.528	13.3	2.10	1.5	4.979
C9	.540	13.6	2.06	1.2	5.519
C10	.458	14.1	2.01	1.9	5.977
C11	.523	13.3	2.06	3.0	6.500
C12	.506	12.3	2.01	4.4	7.006
C13	.511	11.9	2.03	5.7	7.517
C14	.621	11.3	2.00	7.5	8.138
C15	.471	12.5	2.04	9.3	8.609
C16	.685	11.7	1.98	11.0	9.294
C17	.553	11.8	2.10	13.0	9.847
C18	.613	11.9	1.95	14.3	10.460

Tube No.	Urine Weight (G.)	Cr mg/100 ml.	P	Na mEq/l.	Cumulative Volume(ml.)
C19	.600	11.2	1.17	16.7	11.060
C20	.617	11.7	0.95	18.0	11.677
C21	.656	12.3	0.83	17.9	12.333
C22	.726	12.5	0.64	18.0	13.059
C23	.551	11.9	0.47	20.4	13.610
C24	.675	12.0	0.60	18.6	14.285
C25	.697	12.5	0.78	17.7	14.982
C26	.496	12.0	1.11	18.7	15.478
C27	.696	10.8	1.38	17.1	16.174
C28	.570	11.2	1.60	17.1	16.744
C29	.739	11.0	1.85	16.4	17.483
C30	.638	10.6	1.89	16.8	18.121

(B) Derived Results:

Control Urines:

No.	1	2	3	4	5
Vol.(ml./min.)	11.75	10.38	10.63	10.63	10.50
Ccr (ml./min.)	44.2	37.0	40.4	37.7	39.1
% excretion P :	15.9	16.1	16.5	23.3	20.1

No.	6	7	8	9
Vol.(ml/min.)	12.13	10.75	11.25	11.25
Ccr (ml/min.)	43.8	32.3	33.8	33.8
% excretion P :	21.2	25.3	27.9	25.3

Stop-Flow Urines:

Tube No.	% Total Volume	Urinary P as fraction of that filtered.	Tube No.	% Total Volume	Urinary P as fraction of that filtered.
A1	9.4	.270	B1	10.7	.256
A2	14.4	.254	B2	16.6	.191
A3	19.7	262	B3	20.9	.208
A4	24.5	.248	B4	25.6	.205
A5	30.6	.257	B5	30.1	.213
A6	35.3	.205	B6	34.0	.148
A7	40.7	.214	B7	38.1	.165
A8	45.0	.233	B8	41.7	.190
A9	49.3	.218	B9	46.1	.210
A10	53.6	.200	B10	52.5	.192
A11	59.0	.168			
A12	63.1	.143	C1	11.2	.252
A13	67.3	.105	C2	16.7	.232
A14	71.5	.108	C3	19.7	.192
A15	75.8	.044	C4	22.4	.222
A16	80.2	.062	C5	25.7	.169
A17	84.4	.058	C6	29.3	.155
A18	89.0	.029	C7	32.7	.145
A19	92.8	.027	C8	36.6	.153
A20	96.9	.033	C9	40.6	.146
A21	100.0	.007	C10	43.9	.138
A22	105.7	.069	C11	47.8	.150
A23	109.9	.074	C12	51.5	.158
A24	114.1	.125	C13	55.2	.165
A25	117.7	.146	C14	59.8	.171
A26	122.8	.154	C15	63.3	.157
A27	126.2	.152	C16	68.3	.163

Tube No.	% Total Volume	Urinary P as fraction of that filtered.
C17	72.4	.172
C18	76.9	.158
C19	81.3	.101
C20	85.8	.078
C21	90.6	.065
C22	96.0	.049
C23	100.0	.038
C24	105.0	.048
C25	110.1	.060
C26	113.7	.089
C27	118.8	.123
C28	123.0	.138
C29	.28.5	.163
C30	133.1	.172

△ P (C - A)	% Total Intra-tubular Volume of A	of C
.052	52.5 to 53.6	1.1
.084	59.0	6.5
.109	63.1	10.6
.149	63.7	11.2
.142	67.3	14.8
.116	69.2	16.7
.084	71.5	19.0
.148	72.2	19.7
.178	74.9	22.4
.125	75.8	23.3
.093	80.2	27.7
.097	81.8	29.3
.087	84.4	31.9
.116	85.2	32.7
.124	89.0	36.5
.126	89.1	36.6
.119	92.8	40.3
.113	93.1	40.6
.105	96.4	43.9
.117	96.9	44.4
.143	100.0	47.5
.081	100.3	47.8
.089	104.0	51.5
.096	105.7	53.2
.091	107.7	55.2
.097	109.9	57.4
.046	112.3	59.8
.032	114.1	61.6
.011	115.8	63.3

△ P (C - A)	% Total Intra-tubular Volume of A	of C
.017	117.7	65.2
.009	120.8	68.3
.018	122.8	70.3
.020	124.9	72.4
.006	126.2	73.7
.006	129.4	76.9

Dog F

Experiment 7

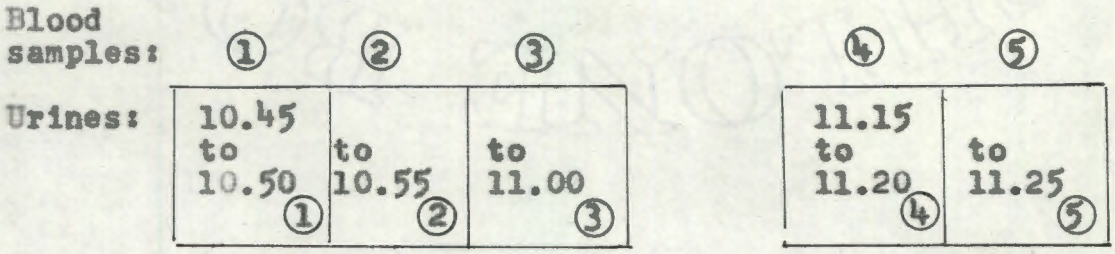
Infusions: (1) 10% dextrose-water.

(2) 5% dextrose-water, containing 1.0 G. creatinine per litre.

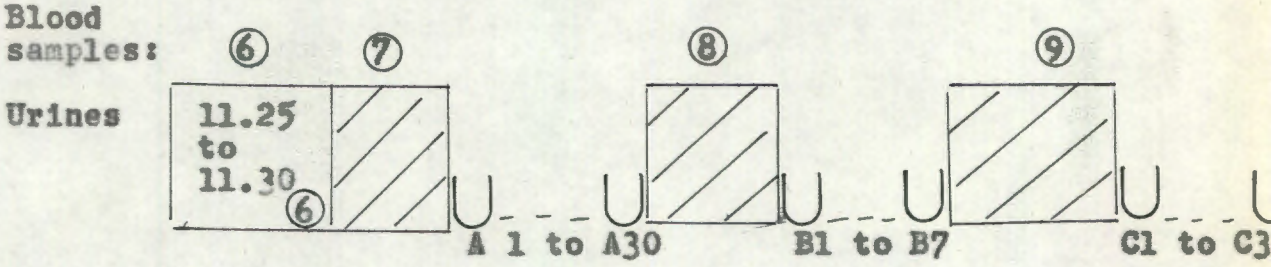
Priming Dose of 0.5 G. creatinine, given I.V. at 10.25 a.m.

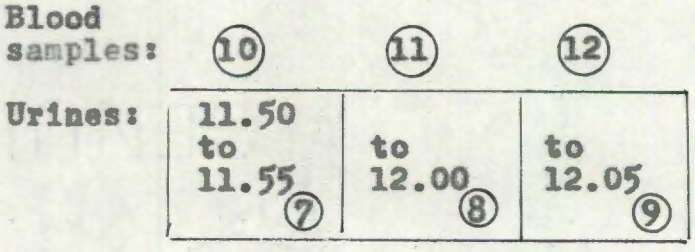
Equilibration Period: 20 minutes.

Times of Blood and Urine Collections:



Parathormone
200 u. I.V., at 11.01





Note: Blood samples taken at midpoint in time of each urine collection period, as shown.

R E S U L T S

(A) Observed Results:

Sera:

No.	1	2	3	4	5
Cr (mg/100 ml.)	8.12	8.12	7.88	7.75	7.05
P (mg/100 ml.)	2.90	-	2.85	2.85	3.15

No.	6	7	8	9	10	11	12
Cr (mg/100 ml.)	6.95	6.89	6.89	6.89	6.89	6.89	6.89
P (mg/100 ml.)	2.95	3.10	3.20	3.20	3.25	2.90	2.90

Urine Controls:

No.	1	2	3	4	5	6
Vol.(ml.)	10.9	14.7	15.7	14.8	15.8	13.6
Cr (mg/100 ml.)	65.2	51.7	43.1	38.2	35.7	35.7
P (mg/100 ml.)	4.79	3.85	3.54	3.96	4.38	4.58
Na (mEq/l.)	13.3	15.4	16.7	15.2	17.0	16.1

No.	7	8	9
Vol.(ml.)	19.2	18.6	20.2
Cr (mg/100 ml.)	25.9	25.9	25.9
P (mg/100 ml.)	3.54	3.13	3.13
Na (mEq/l.)	16.1	16.5	17.0

Stop-Flow Urines:

Tube No.	Urine Weight(G.)	Cr mg/100 ml.	P	Na mEq/l.	Cumulative Volume(ml.)
A1	.419	35.7	4.52	11.0	.419
A2	.304	40.8	4.68	10.6	.723
A3	.620	36.4	4.96	7.8	1.343
A4	.591	37.8	5.14	4.2	1.934
A5	.551	38.3	5.04	3.2	2.485
A6	.495	38.5	4.61	4.4	2.980
A7	.551	39.1	4.24	7.4	3.531
A8	.535	38.6	3.75	11.4	4.066
A9	.298	42.5	3.48	16.2	4.364
A10	.353	39.6	2.55	17.9	4.717
A11	.341	40.9	2.29	21.5	5.058
A12	.328	42.5	1.79	23.9	5.386
A13	.371	44.3	1.59	24.6	5.757
A14	.530	41.5	1.35	23.3	6.287
A15	.369	45.4	2.02	24.0	7.029
A16	.373	45.1	2.02	24.0	7.029
A17	.523	41.0	2.42	21.5	7.552
A18	.419	40.4	2.89	21.7	7.971
A19	.324	38.6	3.35	21.8	8.295
A20	.317	34.4	3.43	22.3	8.612
B1	.406	27.1	4.32	21.2	0.406
B2	.325	28.5	4.15	18.2	0.731
B3	.269	27.6	4.38	14.2	1.000
B4	.501	28.6	4.80	9.8	1.501
B5	.432	32.3	5.07	5.2	1.933
B6	.508	31.7	5.03	3.5	2.441
B7	.494	32.5	4.94	4.7	2.935

Tube No.	Urine Weight(G.)	Cr mg/100 ml.	P	Na mEq/l.	Cumulative Volume(ml.)
C1	.556	30.3	4.27	7.6	.556
C2	.502	33.0	3.73	9.5	1.058
C3	.483	38.1	3.25	4.7	1.541
C4	.730	38.1	3.15	2.4	2.271
C5	.494	41.3	2.93	3.1	2.765
C6	.622	38.1	2.67	5.7	3.387
C7	.466	37.4	2.64	8.7	3.853
C8	.544	36.3	2.49	11.6	4.397
C9	.457	35.5	2.32	16.1	4.854
C10	.350	33.7	1.57	19.5	5.204
C11	.447	32.3	1.45	22.0	5.651
C12	.509	33.3	1.23	24.0	6.160
C13	.460	34.1	1.16	25.0	6.620
C14	.462	34.1	1.24	24.5	7.082
C15	.322	34.6	1.92	25.1	7.404
C16	.462	32.6	2.05	24.3	7.866
C17	.456	30.2	2.24	23.4	8.322
C18	.397	29.0	2.71	23.1	8.719

C19 to C30: data not given as irrelevant.

(B) Derived Results:

Urine Controls:

No.	1	2	3	4	5	6
Vol.(ml/min.)	2.18	2.94	3.14	2.96	3.16	2.72
Ccr (ml/min.)	17.5	18.7	17.2	14.6	16.0	14.0
% excretion P:	20.5	21.0	22.7	28.2	27.5	30.3

No.	7	8	9
Vol.(ml/min.)	3.84	3.72	4.04
Ccr (ml/min.)	14.4	14.0	15.2
% excretion P:	29.0	28.7	28.7

Stop-Flow Urines:

Tube No.	% Total Volume	Urinary P as fraction of that filtered.
A1	6.7	.281
A2	11.5	.255
A3	21.4	.303
A4	30.8	.302
A5	39.5	.293
A6	47.4	.266
A7	56.2	.241
A8	64.7	.216
A9	69.4	.182
A10	75.0	.143
A11	80.5	.124
A12	85.7	.094
A13	91.6	.080
A14	100.0	.072
A15	105.9	.084
A16	111.8	.100
A17	120.1	.131
A18	126.8	.159
A19	131.9	.193
A20	137.0	.222
B1	6.1	.342
B2	11.0	.313
B3	15.1	.342
B4	22.7	.361
B5	29.2	.337
B6	36.9	.342
B7	44.3	.327
C1	2.4	.303
C2	16.0	.243
C3	23.3	.184
C4	34.3	.178
C5	41.8	.153
C6	51.2	.151
C7	58.2	.152
C8	66.4	.148
C9	73.3	.141
C10	78.6	.100
C11	85.4	.097
C12	93.1	.087
C13	100.0	.073
C14	107.0	.078
C15	111.8	.119
C16	118.8	.135

△P (C - A)	% Total Intra-tubular Volume of A	of C
+ .037	44.3 to 47.7	3.1
+ .062	52.7	8.4
+ .002	56.2	11.9
+ .027	60.3	16.0
- .032	64.7	20.4
+ .002	67.6	23.3
- .004	69.4	25.1
+ .035	75.0	30.7
+ .054	78.6	34.3
+ .029	80.5	36.2
+ .059	85.7	41.4
+ .073	86.1	41.8
+ .071	91.6	47.3
+ .079	95.5	51.2
+ .080	100.0	55.7
+ .068	102.5	58.2
+ .064	105.9	61.6
+ .048	110.7	66.4
+ .041	111.8	67.5
+ .010	117.6	73.3
- .031	120.1	75.8
- .059	122.9	78.6

DOG G

Experiment 8

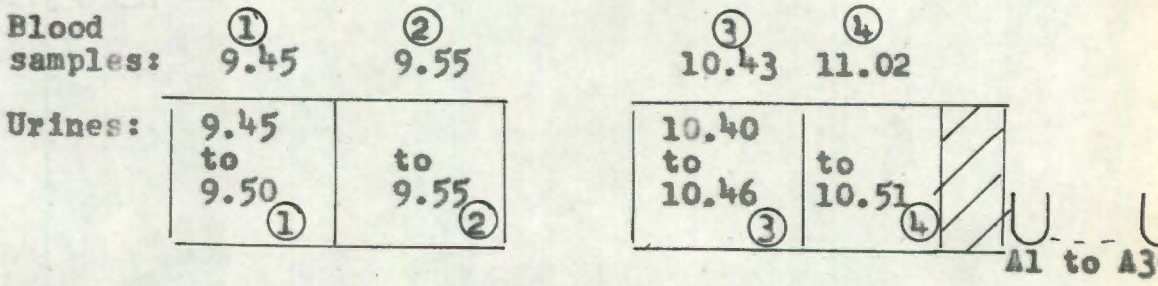
Infusions: (1) 5% dextrose-water.

(2) 'Normal' saline, containing 1.0 G. creatinine per litre. Commenced at 9.01 a.m. Infusion rate about 1 ml./minute.

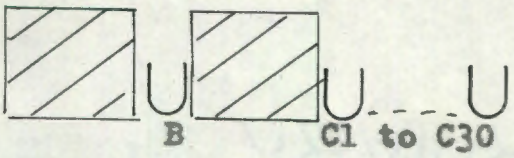
Priming Dose of 0.5 G creatinine, given I.V. at 9.00 a.m.

Equilibration Period: 44 minutes.

Times of Blood and Urine collections:



Parathormone, 100 u., given I.V. at 10.30 a.m.



Note: (1) Period of ureteric occlusion prior to B urine collection, followed a few minutes after urine A30 collected.

(2) Only Dogs C and G lack post-stopflow control urine collections. These dogs were the first two of the series. Dog G was the only dog in which the B urine was collected in one tube.

R E S U L T S

(A) Observed Results:

Sera:

No.	1	2	3	4
Cr (mg/100 ml.)	4.13	3.38	2.84	3.81
P (mg/100 ml.)	4.56	4.18	3.57	4.06

Control Urines:

No.	1	2	3	4
Vol.(ml.)	10.4	8.1	8.2	11.7
Cr (mg/100 ml.)	34.8	40.3	40.0	28.7
P (mg/100 ml.)	7.2	8.4	18.1	13.1
Na (mEq/l.)	11.3	9.6	18.3	26.1

Stop-Flow Urines:

Tube No.	Urine Weight (G.)	Cr mg/100 ml.	P	Na mEq/l	Cumulative Volume (ml.)
A1	1.020	33.5	18.8	30.0	1.020
A2	.596	44.9	22.6	33.0	1.616
A3	.467	53.6	29.9	25.0	2.083
A4	.418	56.9	31.8	20.2	2.501
A5	.496	47.7	27.2	13.3	2.997
A6	.383	37.7	17.7	9.3	3.380
A7	.683	24.4	11.9	7.9	4.063
A8	.470	22.2	10.1	12.6	4.533
A9	.404	24.1	9.9	18.1	4.937
A10	.415	22.0	8.7	19.8	5.352
A11	.428	21.5	7.9	27.9	5.780
A12	.550	21.2	8.3	38.5	6.330
A13	.601	20.5	8.1	50.5	6.931

Tube No.	Urine Weight(G.)	Cr mg/100 ml.	P	Na mEq/l	Cumulative Volume (ml.)
A14	.619	18.3	7.4	50.3	7.550
A15	.544	20.2	7.4	50.0	8.094
A16	.625	26.0	7.2	42.6	8.719
A17	.540	19.2	7.1	45.9	9.259
A18	.480	17.5	7.5	41.6	9.739
A19	.534	16.6	7.3	40.3	10.273
A20	.655	16.6	6.3	39.7	10.928
A21	.513	16.8	7.8	39.9	11.441
A22	.446	16.3	7.4	40.7	11.887
A23	.482	17.1	7.1	41.9	12.369
A24	.525	16.6	8.0	39.2	12.894
A25	.521	17.2	7.9	40.0	13.415
A26	.483	16.7	8.2	39.5	13.898
A27	.458	16.8	8.4	39.8	14.356
A28	.493	17.8	8.3	41.7	14.849
A29	.455	16.2	8.3	38.6	15.304
A30	.560	16.8	8.6	39.6	15.864
B	4.800	-	-	-	4.800
C1	1.295	27.6	13.3	30.5	1.295
C2	.696	40.1	17.2	41.2	1.991
C3	.945	45.2	23.7	33.3	2.936
C4	.784	46.8	22.3	22.8	3.734
C5	.763	31.8	15.1	12.2	4.497
C6	.540	25.3	10.9	9.6	5.037
C7	.484	22.1	9.0	9.9	5.521
C8	.418	22.0	8.3	12.2	5.939
C9	.476	21.5	8.2	14.2	6.475

Tube No.	Urine Weight(G.)	Cr mg/100 ml.	P	Na mEq/l	Cumulative Volume (ml.)
B10	.686	19.1	7.2	18.4	7.101
C11	.477	19.2	7.5	27.3	7.578
C12	.449	19.4	6.8	36.9	8.027
C13	.450	18.8	7.4	50.5	8.477
C14	.445	17.7	6.7	61.8	8.922
C15	.466	17.1	6.4	68.9	9.388
C16	.510	15.1	6.0	71.5	9.898
C17	.528	16.4	5.8	74.4	10.426
C18	.554	16.1	5.6	70.1	10.980
C19	.465	16.0	5.5	68.1	11.445
C20	.523	18.3	5.5	77.1	11.968
C21	.492	15.7	5.8	56.4	12.460
C22	.448	17.0	5.9	53.9	12.908
C23	.529	15.4	6.1	48.5	13.437
C24	.537	14.6	6.7	47.1	13.974
C25	.538	15.9	6.9	46.4	14.512
C26	.612	15.2	7.1	44.1	15.124
C27	.529	15.3	7.6	46.8	15.653
C28	.619	14.5	7.7	43.9	16.272
C29	.510	13.8	7.7	47.0	16.782
C30	.538	16.3	7.7	46.7	17.320

(B) Derived Results:

Urine Controls:

No.	1	2	3	4
Vol.(ml./min.)	2.08	1.62	1.37	2.34
Ccr(ml./min.)	18.4	18.3	19.3	19.5
% excretion Pi	18.2	17.4	36.0	40.4

Note: Mid-period Serum concentrations of Cr and P needed fo these calculations, derived by simple proportion.

Stop-Flow Urines:

Tube No.	% Total Volume	Urinary P as fraction of that filtered.	Tube No.	% Total Volume	Urinary P as fraction of that filtered
A1	11.7	.526	B	40.2	-
A2	18.5	.472	C1	10.8	.452
A3	23.9	.524	C2	16.6	.402
A4	28.7	.524	C3	24.5	.492
A5	34.4	.535	C4	31.2	.446
A6	38.8	.440	C5	37.5	.446
A7	46.6	.457	C6	42.1	.404
A8	52.1	.426	C7	46.1	.382
A9	56.6	.385	C8	49.6	.354
A10	61.4	.371	C9	54.1	.358
A11	66.3	.367	C10	59.3	.354
A12	72.7	.367	C11	63.4	.367
A13	79.6	.395	C12	67.1	.329
A14	86.6	.379	C13	70.9	.369
A15	92.8	.344	C14	74.6	.355
A16	100.0	.260	C15	78.4	.351
A17	106.2	.347	C16	82.6	.372
A18	111.6	.402	C17	87.3	.332
A19	117.8	.412	C18	91.7	.326
A20	125.3	.380	C19	95.6	.323

Tube No.	% Total Volume	Urinary P as fraction of that filtered.
C20	100.0	.282
C21	104.1	.346
C22	108.0	.325
C23	112.5	.396
C24	116.9	.430
C25	121.4	.407
C26	126.4	.438

Note: Serum Cr and P concentrations needed for these estimations assumed equal to those of blood sample 4

ΔP (C - A)	% Total Intra-tubular Volume of A	of C
- .005	46.6	6.4
+ .026	51.0	10.8
- .024	52.1	11.9
+ .017	56.6	16.4
+ .031	56.8	16.6
+ .121	61.4	21.2
+ .125	64.7	24.5
+ .079	66.3	26.1
+ .079	71.4	31.2
+ .079	72.7	32.5
+ .051	77.7	37.5
+ .009	79.6	39.4
+ .025	82.3	42.1
+ .003	86.3	46.1
- .025	86.6	46.4
+ .010	89.8	49.6

ΔP (C - A)	% Total Intra-tubular Volume of A	of C
+ .014	92.8	52.6
+ .098	94.3	54.2
+ .084	99.5	59.3
+ .107	100.0	59.8
+ .020	103.6	63.4
- .018	106.2	66.0
- .073	107.3	67.1

DOG H

Experiment 9

Infusions: (1) 5% dextrose-water.

(2) 'Normal' saline, containing 1.0 G. creatinine per litre.

Priming Dose of 0.1 G. creatinine, given I.V. at 10.43 a.m.

Equilibration Period: 33 minutes.

Times of Blood and Urine Collections:

Blood samples: ① ② ③ ④ ⑤ ⑥

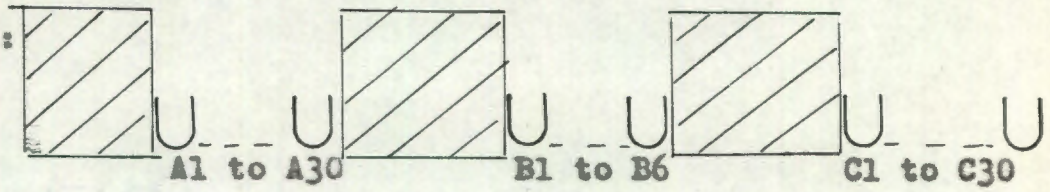
Urines:

9.16 to 9.20 ①	to 9.24 ②	to 9.28 ③	9.53 to 9.57 ④	to 10.01 ⑤	to 10.05 ⑥

Parathormone, 400 u. given I.V. at 9.33 a.m.

Blood samples: ⑦

Urines:



Blood samples: ⑧ ⑨ ⑩

Urines:

10.35 to 10.39 ⑦	to 10.43 ⑧	to 10.47 ⑨

Note: First period of ureteric occlusion follows immediately after urine control number 6; similarly urine control number 7 follows immediately after collection of C30.

R E S U L T S

(A) Observed Results:

Sera:

No.	1	2	3	4	5
Cr (mg/100 ml.)	6.32	5.86	5.56	5.07	4.95
P (mg/100 ml.)	4.45	4.39	4.48	3.52	3.41

No.	6	7	8	9	10
Cr (mg/100 ml.)	.13	4.52	4.19	4.03	3.91
P (mg/100 ml.)	3.44	2.91	2.71	2.57	2.57

Control Urines:

No.	1	2	3	4	5
Vol.(ml.)	11.8	13.0	13.0	14.5	14.5
Cr (mg/100 ml.)	26.1	23.0	21.4	20.6	19.5
P (mg/100 ml.)	4.49	4.56	4.86	5.23	5.12
Na (mEq/l.)	3.0	2.8	2.8	4.4	5.8

No.	6	7	8	9
Vol.(ml.)	15.3	14.5	13.0	14.8
Cr (mg/100 ml.)	18.7	15.2	14.4	13.6
P (mg/100 ml.)	4.98	4.37	4.23	4.11
Na (mEq/l.)	7.8	14.0	15.3	17.2

Stop-Flow Urines:

Tube No.	Urine Weight(G.)	Cr mg/100 ml.	P mg/100 ml.	Na mEq/l.	Cumulative Volume(ml.)
A1	.606	23.2	4.75	9.0	0.606
A2	.660	23.0	4.57	14.0	1.266

Tube No.	Urine Weight(G.)	Cr mg/100 ml.	P	Na mEq/l.	Cumulative Volume(ml.)
A3	.569	24.1	4.76	8.6	1.835
A4	.610	24.3	4.82	7.2	2.445
A5	.633	25.4	4.96	4.8	3.078
A6	.603	25.3	5.04	2.9	3.681
A7	.605	25.2	4.97	1.8	4.286
A8	.582	25.8	5.13	1.8	4.868
A9	.622	23.9	5.25	1.9	5.490
A10	.564	25.3	5.10	2.2	6.054
A11	.670	24.8	5.17	2.5	6.724
A12	.596	25.4	5.14	3.1	7.320
A13	.566	25.0	5.12	3.4	7.886
A14	.617	24.7	4.95	4.7	8.503
A15	.565	26.0	4.82	6.4	9.068
A16	.577	33.0	4.26	7.4	9.645
A17	.572	34.0	3.94	9.3	10.217
A18	.613	34.8	3.52	10.4	10.830
A19	.573	36.0	3.37	11.5	11.403
A20	.617	29.6	3.32	12.5	12.020
A21	.565	30.4	3.42	13.2	12.585
A22.	.574	29.2	3.60	13.0	13.159
A23	.567	28.4	3.72	13.4	13.726
A24	.545	27.7	3.94	14.2	14.271
A25	.569	25.5	4.04	14.4	14.840
A26	.570	24.5	4.13	13.5	15.410
A27	.489	24.1	4.04	14.3	15.899
A28	.559	23.6	4.30	14.6	16.458
A29	.567	23.0	4.25	14.3	17.025
A30	.604	22.5	4.36	13.6	17.629

Tube No.	Urine Weight(G.)	Cr mg/100 ml.	P	Na mEq/l.	Cumulative Volume(ml.)
B1	.720	18.4	4.52	6.7	0.720
B2	.706	18.6	4.49	9.1	1.426
B3	.659	19.5	4.58	12.1	2.085
B4	.704	20.1	4.61	5.2	2.789
B5	.662	20.7	4.54	2.7	3.451
B6	.714	20.5	4.89	1.5	4.165
C1	.588	21.0	4.87	1.5	.588
C2	.324	19.9	4.60	12.0	.912
C3	.626	19.7	4.71	5.4	1.538
C4	.583	20.3	4.80	2.6	2.121
C5	.625	21.1	4.87	2.4	2.746
C6	.526	23.0	4.89	1.7	3.272
C7	.522	23.1	4.74	2.7	3.794
C8	.524	23.0	4.56	1.3	4.318
C9	.568	22.3	4.25	2.2	4.886
C10	.580	23.6	4.13	1.2	5.466
C11	.562	24.2	4.15	1.6	6.028
C12	.524	24.4	3.88	1.8	6.552
C13	.527	24.1	3.94	2.5	7.079
C14	.532	24.4	4.05	3.0	7.611
C15	.605	24.4	4.00	5.0	8.216
C16	.502	25.0	4.17	5.6	8.718
C17	.523	23.8	4.12	6.0	9.241
C18	.485	22.9	3.92	8.3	9.726
C19	.565	22.8	3.79	10.1	10.291
C20	.482	23.6	3.60	11.0	10.773
C21	.574	23.3	3.31	11.8	11.347

Tube No.	Urine Weight(G.)	Cr mg/100 ml.	P	Na mEq/l.	Cumulative Volume(ml.)
C22	.539	23.7	2.96	12.8	11.886
C23	.527	23.6	3.12	12.8	12.413
C24	.522	22.6	3.36	13.5	12.935
C25	.534	19.7	3.75	13.3	13.469
C26	.504	17.6	4.03	13.4	13.973
C27	.538	18.6	3.83	13.0	14.511
C28	.526	16.7	4.11	12.9	15.037
C29	.527	17.9	4.14	12.8	15.564
C30	.538	17.9	4.04	12.7	16.102

(B) Derived Results:

Control Urines:

No.	1	2	3	4	5
Vol(ml./min.)	2.95	3.25	3.25	3.63	3.63
Ccr(ml./min.)	12.2	12.8	12.5	14.7	14.3
% excretionP:	24.4	26.	28.1	36.8	38.1

No.	6	7	8	9
Vol(ml./min.)	3.83	3.63	3.25	3.70
Ccr(ml/min.)	14.0	13.2	11.6	12.9
% excretion P:	39.8	45.4	46.2	45.9

Stop-Flow Urines:

Tube No.	% Total Volume	Urinary P as fraction of that filtered.	Tube No.	% Total Volume	Urinary P as fraction of that filtered.
A1	5.3	.308	B1	6.1	.382
A2	11.1	.299	B2	12.0	.375
A3	16.1	.297	B3	17.5	.365
A4	21.4	.298	B4	23.5	.356
A5	27.0	.294	B5	29.0	.341
A6	32.3	.300	B6	35.0	.370
A7	37.6	.297			
A8	42.7	.299	C1	4.9	.360
A9	48.1	.330	C2	7.7	.359
A10	53.1	.303	C3	12.9	.372
A11	59.0	.314	C4	17.8	.368
A12	64.2	.305	C5	23.1	.359
A13	69.2	.308	C6	27.5	.330
A14	74.6	.302	C7	31.9	.319
A15	79.5	.279	C8	36.3	.308
A16	84.6	.194	C9	41.1	.296
A17	89.6	.174	C10	46.0	.272
A18	95.0	.152	C11	50.7	.267
A19	100.0	.141	C12	55.1	.247
A20	105.4	.169	C13	60.0	.254
A21	110.4	.169	C14	64.0	.258
A22	115.4	.186	C15	69.1	.255
A23	120.4	.197	C16	73.3	.259
A24	125.2	.219	C17	77.7	.269
A25	130.1	.238	C18	81.8	.266
A26	135.1	.254	C19	86.6	.258

Tube No.	% Total Volume	Urinary P as fraction of tthat filtered.
C20	90.6	.237
C21	95.5	.221
C22	100.0	.194
C23	104.4	.205
C24	108.8	.231
C25	113.3	.296
C26	117.6	.242
C27	122.1	.320
C28	126.5	.383
C29	130.9	.360
C30	135.5	.351

△P (C - A)	% Total Intra-tubular Volume of A	of C
+ .063	35.0 to 37.6	2.6
+ .061	39.9	4.9
+ .060	42.7	7.7
+ .042	47.9	12.9
+ .038	48.1	13.1
+ .065	52.8	17.8
+ .056	53.1	18.1
+ .045	58.1	23.1
+ .016	59.0	24.0
+ .025	62.5	27.5
+ .014	64.2	29.2

ΔP (C - A)	% Total Intra-tubular Volume of A	of C
+ .011	66.9	31.9
.000	69.2	34.2
+ .006	71.3	36.3
- .006	74.6	39.6
+ .017	76.1	41.1
- .007	79.5	44.5
+ .078	81.0	46.0
+ .073	84.6	49.6
+ .093	85.7	50.7
+ .073	89.6	54.6
+ .095	90.1	55.1
+ .102	95.0	60.0
+ .117	99.0	64.0
+ .114	100.0	65.0
+ .086	104.1	69.1
+ .090	105.4	70.4
+ .090	108.3	73.3
+ .100	110.4	75.4
+ .083	112.7	77.7
+ .080	115.4	80.4
+ .069	116.8	81.8
+ .061	120.4	85.4
+ .039	121.6	86.6
+ .018	125.2	90.2
- .001	125.6	90.6
- .017	130.1	95.1
- .033	130.5	95.5
- .060	135.0	100.1

DOG I

Experiment 10

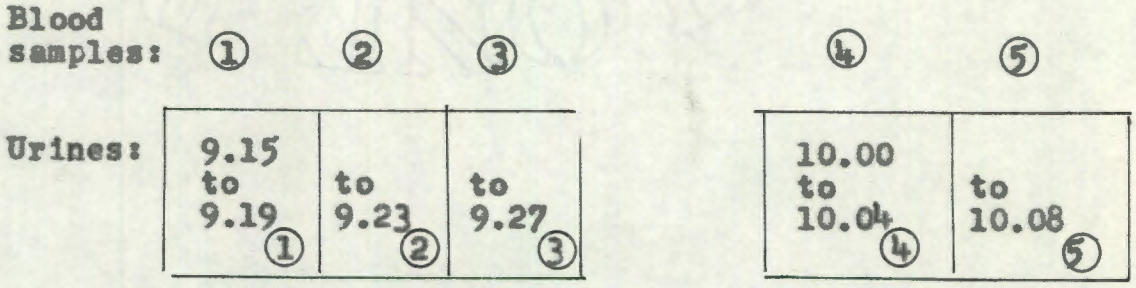
Infusions: (1) 5% dextrose-water.

(a) 'Normal' saline containing 1.0 G. creatinine per litre. Commenced at 8.30 a.m.

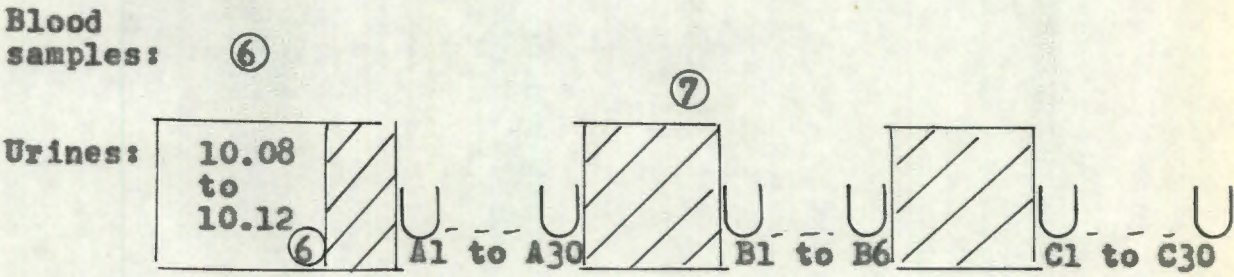
Priming Dose of 0.5 G. creatinine, given I.V. at 8.30 a.m.

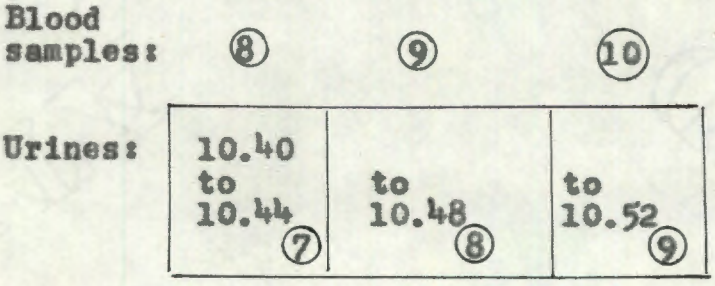
Equilibration Period: 45 minutes.

Times of Blood and Urine Collections:



400 u. Parathormone given I.V. at 9.28 a.m.





Note: (1) Blood samples taken at exact midperiod in time of corresponding urine collection.

(2) Urine collection 8 follows immediately after C30.

R E S U L T S

(A) Observed Results:

Sera:

No.	1	2	3	4	5
Cr (mg/100 ml.)	6.31	6.48	6.42	5.90	5.96
P (mg/100 ml.)	3.90	3.84	3.81	3.49	3.44
Na (mEq/l.)	131	129	129	124	123

No.	6	7	8	9	10
Cr (mg/100 ml.)	5.84	5.84	5.96	5.72	5.72
P (mg/100 ml.)	3.41	3.22	3.17	3.03	3.14
Na (mEq/l.)	123	124	122	121	121

Control Urines:

No.	1	2	3	4	5
Vol.(ml.)	14.0	13.0	12.5	15.8	15.0
Cr (mg/100 ml.)	35.2	35.8	35.6	27.9	27.8
P (mg/100 ml.)	8.18	8.36	7.73	9.09	9.36
Na (mEq/l.)	12.0	8.8	6.4	4.4	3.9

No.	6	7	8	9
Vol.(ml.)	15.0	16.0	15.5	14.5
Cr (mg/100 ml.)	27.5	23.1	23.4	23.1
P (mg/100 ml.)	8.86	6.27	6.27	6.09
Na (mEq/l.)	3.4	2.6	2.2	1.7

Stop-Flow Urines

Stop-Flow Urines:

Tube No.	Urine Weight(G.)	Cr mg/100 ml.	P	Na mEq/l.	Cumulative Volume(ml.)
A1	.525	32.9	10.18	4.9	0.525
A2	.428	33.0	10.26	4.3	0.953
A3	.348	35.0	10.80	6.4	1.301
A4	.409	35.6	9.98	4.2	1.710
A5	.611	35.1	11.17	3.5	2.321
A6	.658	35.9	11.90	3.3	2.979
A7	.524	37.4	11.15	2.8	3.503
A8	.719	33.7	10.29	2.2	4.222
A9	.663	31.8	9.85	1.6	4.885
A10	.651	30.9	10.16	1.4	5.536
A11	.610	30.6	9.73	2.2	6.146
A12	.610	29.9	8.94	3.4	6.756
A13	.619	29.4	8.99	5.1	7.375
A14	.561	29.6	9.28	6.7	7.936
A15	.552	29.6	9.16	8.5	8.488
A16	.595	30.0	7.73	10.5	9.083
A17	.516	30.1	7.39	9.2	9.599
A18	.524	30.6	7.69	10.4	10.123
A19	.541	30.7	7.22	11.3	10.664
A20	.535	32.5	7.13	12.8	11.199
A21	.582	33.2	5.90	12.7	11.781
A22	.529	33.8	5.75	12.1	12.310
A23	.531	35.5	5.24	12.4	12.841
A24	.572	36.0	5.32	11.3	13.413
A25	.500	37.5	5.10	10.2	13.913
A26	.534	36.7	4.94	8.2	14.447
A27	.543	38.3	4.11	7.6	14.990
A28	.540	39.8	5.60	6.7	15.530

Tube No.	Urine Weight(G.)	Cr mg/100 ml.	P	Na mEq/l.	Cumulative Volume(ml.)
A29	.525	39.1	5.18	6.0	16.055
A30	.537	38.3	5.49	5.9	16.592
B1	.560	32.0	8.27	3.3	0.560
B2	.385	32.8	8.14	4.2	0.945
B3	.615	33.2	8.71	3.5	1.560
B4	.600	36.0	9.77	5.6	2.160
B5	.800	36.1	10.51	3.2	2.960
B6	.774	36.0	10.56	1.6	3.734
C1	.550	36.1	10.01	0.9	0.550
C2	.431	35.3	9.21	1.3	0.981
C3	.547	35.1	8.52	3.3	1.528
C4	.471	34.9	9.18	2.3	1.999
C5	.816	34.6	10.14	1.6	2.815
C6	.728	34.9	10.68	1.6	3.543
C7	.628	35.7	9.95	1.1	4.171
C8	.551	35.1	8.89	0.8	4.722
C9	.584	33.3	8.46	0.9	5.306
C10	.520	33.2	8.17	1.0	5.826
C11	.580	32.3	7.85	1.4	6.406
C12	.644	31.8	7.68	2.5	7.050
C13	.527	32.1	7.61	3.4	7.577
C14	.598	31.9	7.32	5.2	8.175
C15	.565	32.0	7.13	5.6	8.740
C16	.464	32.4	7.21	6.5	9.204
C17	.510	32.2	7.18	6.5	9.714
C18	.542	32.0	7.03	6.9	10.256

Tube No.	Urine Weight(G.)	Cr mg/100 ml.	P	Na mEq/l.	Cumulative Volume(ml.)
C19	.465	32.4	6.74	7.4	10.721
C20	.533	32.1	6.50	8.2	11.254
C21	.500	32.4	6.52	9.2	11.754
C22	.495	33.1	6.20	9.6	12.249
C23	.493	32.6	6.13	10.9	12.742
C24	.487	32.8	5.77	12.7	13.229
C25	.549	32.7	5.58	12.2	13.778
C26	.511	33.2	5.35	11.3	14.289
C27	.512	33.5	5.28	9.9	14.801
C28	.512	33.7	5.55	11.7	15.313
C29	.515	34.8	5.52	7.9	15.828
C30	.516	34.3	5.41	7.5	16.344

(B) Derived Results:

Control Urines:

No.	1	2	3	4	5
Vol.(ml./min.)	3.50	3.25	3.13	3.95	3.75
Ccr (ml./min.)	19.5	18.0	17.4	18.7	17.5
% excretion P:	37.7	39.4	36.6	55.2	58.3

No.	6	7	8	9
Vol.(ml./min.)	3.75	4.00	3.88	3.63
Ccr (ml./min.)	17.6	15.5	15.8	14.7
% excretion P:	55.2	51.2	50.4	48.2

Stop-Flow Urines:

Tube No.	% Total Volume	Urinary P as fraction of that filtered.
A1	3.5	.536
A2	6.4	.539
A3	8.7	.535
A4	11.4	.486
A5	15.5	.551
A6	19.9	.574
A7	23.4	.517
A8	28.2	.529
A9	32.6	.537
A10	36.9	.570
A11	41.0	.551
A12	45.1	.518
A13	49.2	.530
A14	52.9	.543
A15	56.6	.536
A16	60.6	.447
A17	64.0	.425
A18	67.5	.436
A19	71.1	.408
A20	74.7	.380
A21	78.6	.308
A22	82.1	.295
A23	85.7	.256
A24	89.5	.256
A25	92.8	.236
A26	96.4	.233
A27	100.0	.186
A28	103.6	.244

Tube No.	% Total Volume	Urinary P as fraction of that filtered.
A29	107.1	.230
A30	110.7	.248
B1	3.4	.469
B2	5.8	.450
B3	9.5	.476
B4	13.2	.492
B5	18.1	.528
B6	22.8	.532
C1	3.4	.510
C2	6.0	.479
C3	9.3	.446
C4	12.2	.483
C5	17.2	.539
C6	21.7	.562
C7	25.5	.512
C8	28.9	.465
C9	32.5	.467
C10	35.6	.452
C11	39.2	.447
C12	43.1	.444
C13	46.4	.436
C14	50.0	.422
C15	53.5	.409
C16	56.3	.409
C17	59.4	.410
C18	62.7	.404
C19	65.6	.382
C20		

Tube No.	% Total Volume	Urinary P as fraction of that filtered.
C20	68.9	.372
C21	71.9	.370
C22	74.9	.338
C23	78.0	.345
C24	80.9	.338
C25	84.3	.313
C26	87.4	.296
C27	90.6	.290
C28	93.7	.303
C29	96.8	.291
C30	100.0	.290

Note: C30 taken as 100% of total intra-tubular volume despite vague end-point, as (i) this is in fact the most proximal and lowest P concentration present, and (ii) this gives the site of minimal Na concentration as 35.6% of the intra-tubular volume, which corresponds very closely to that of 36.9% in A.

Δ P (C - A)	% Total Intra-Tubular Volume of A	of C
- .007	22.8 to 23.4	0.6
- .019	26.2	3.4
- .050	28.2	5.4
- .058	28.8	6.0
- .091	32.1	9.3
- .054	32.6	9.8
- .087	35.0	12.2
- .031	36.9	14.1
- .012	40.0	17.2

△ P (C - A)	% Total Intra-Tubular Volume of A	of C
+ .011	41.0	18.2
+ .044	44.5	21.7
- .006	45.1	22.3
- .008	48.3	25.5
- .065	49.2	26.4
- .078	51.7	28.9
- .076	52.9	30.1
- .069	55.3	32.5
- .084	56.6	33.8
+ .005	58.4	35.6
0.000	60.6	37.8
+ .022	62.0	39.2
+ .019	64.0	41.2
+ .008	65.9	43.1
0.000	67.5	44.7
+ .028	69.2	46.4
+ .014	71.1	48.3
+ .042	72.8	50.0
+ .029	74.7	51.9
+ .101	76.3	53.5
+ .101	78.6	55.8
+ .114	79.1	56.3
+ .115	82.1	59.3
+ .154	82.2	59.4
+ .148	85.5	62.7
+ .126	85.7	62.9
+ .126	88.4	65.6
+ .116	89.5	66.7

ΔP (C - A)	% Total Intra-tubular Volume of A	of C
+ .136	9.17	68.9
+ .134	92.8	70.0
+ .137	94.7	71.9
+ .105	96.4	73.6
+ .152	97.7	74.9
+ .159	100.0	77.2
+ .101	100.8	78.0
+ .094	103.6	80.8
+ .108	103.7	80.9
+ .073	107.1	84.3
+ .048	110.2	87.4
+ .042	110.7	87.9

DOG J

Experiment 11

Infusions: (1) 5% dextrose-water

(2) 'Normal' saline, containing 1.0 G. creatinine per litre. Commenced at 8.40 a.m.

Priming Dose of 0.5 G. creatinine, given I.V. at 8.41 a.m.

Equilibration Period: 78 minutes.

Times of Blood and Urine collections:

Blood samples:	①	②	③	④	⑤
Urines:	9.59 to 10.03 ①	to. 10.07 ②	to 10.11 ③	10.31 to 10.35 ④	to 10.39 ⑤

Parathormone, 400 u., given I.V. at 10.11 a.m.

Blood samples:	⑥	⑦	
Urines:	10.39 to 10.43 ⑥	A1 to A30	B1 to B6 C1 to C30

Blood samples:	⑧	⑨	⑩
Urines:	11.10 to 11.14 ⑦	to 11.18 ⑧	to 11.22 ⑨

Note: (1) Urine collection 7 begun immediately after C30.
(2) Blood sample 5 broken soon after collection.

R E S U L T S

(A) Observed Results:

Sera:

No.	1	2	3	4	6
Cr (mg/100 ml.)	4.91	4.91	4.73	5.03	5.03
P (mg/100 ml.)	3.35	3.33	3.14	3.10	3.06

No.	7	8	9	10
Cr (mg/100 ml.)	5.03	5.03	5.03	5.09
P (mg/100 ml.)	3.03	3.13	3.16	3.09

Control Urines:

No.	1	2	3	4	5
Vol.(ml.)	22.0	24.0	27.0	22.5	22.5
Cr (mg/100 ml.)	14.3	13.2	12.6	12.0	11.5
P (mg/100 ml.)	1.60	1.62	1.62	2.53	2.68
Na (mEq/l.)	6.6	6.8	7.2	2.1	1.9

No.	6	7	8	9
Vol.(ml.)	22.5	21.0	19.0	17.5
Cr (mg/100 ml.)	11.0	10.2	10.4	10.7
P (mg/100 ml.)	2.79	3.66	3.83	4.04
Na (mEq/l.)	1.9	2.5	2.2	1.7

Stop-Flow Urines:

Tube No.	Urine Weight(G.)	Cr mg/100 ml.	P	Na mEq/l.	Cumulative Volume(ml.)
A1	.841	15.1	2.73	1.8	.841
A2	.696	18.3	2.90	2.7	1.537

Tube No.	Urine Weight(G.)	Cr mg/100 ml.	P	Na mEq/l.	Cumulative Volume(ml.)
A3	.604	18.4	2.91	3.8	2.141
A4	.510	18.1	2.89	5.0	2.651
A5	.623	17.9	2.90	6.6	3.274
A6	.467	17.6	2.73	8.0	3.741
A7	.512	17.7	3.06	7.5	4.253
A8	.546	20.0	3.66	7.2	4.799
A9	.597	21.2	4.02	2.8	5.396
A10	.509	21.5	3.86	1.7	5.905
A11	.634	20.5	3.81	1.2	6.539
A12	.549	20.2	3.70	1.4	7.088
A13	.499	20.0	3.63	1.7	7.587
A14	.557	18.9	3.52	-	8.144
A15	.591	19.0	3.57	1.8	8.735
A16	.544	18.8	3.42	1.7	9.279
A17	.496	18.5	3.24	1.9	9.775
A18	.576	18.3	3.43	2.2	10.351
A19	.488	17.9	3.28	2.8	10.839
A20	.531	17.7	3.18	2.9	11.370
A21	.569	17.3	3.21	3.0	11.939
A22	.490	16.8	2.94	2.2	12.429
A23	.528	16.7	2.85	2.3	12.957
A24	.504	16.9	2.76	2.2	13.461
A25	.565	16.5	2.63	2.3	14.026
A26	.489	16.2	2.60	2.8	14.515
A27	.527	16.4	2.46	2.2	15.042
A28	.488	20.4	3.07	4.7	15.530
A29	.523	15.4	2.37	2.5	16.053

A30:spilt.

Tube No.	Urine Weight (G.)	Cr mg/100 ml.	P	Na mEq/l.	Cumulative Volume (ml.)
B1	.784	15.6	2.77	-	0.784
B2	.782	18.5	2.65	-	1.566
B3	.683	18.8	3.13	-	2.249
B4	.628	17.5	2.48	-	2.877
B5	.587	18.1	2.13	-	3.464
B6	.512	17.9	2.75	-	3.976
C1	.778	18.4	3.50	6.1	0.778
C2	.705	22.3	3.32	3.4	1.483
C3	.749	22.0	3.58	2.5	2.232
C4	.551	22.2	3.96	2.7	2.783
C5	.540	22.6	3.33	3.4	3.323
C6	.575	21.8	3.48	3.8	3.898
C7	.646	22.0	4.03	4.4	4.544
C8	.576	22.8	4.08	3.8	5.120
C9	.615	23.7	4.26	2.0	5.735
C10	.535	23.6	4.31	1.4	6.270
C11	.578	22.4	4.08	0.9	6.848
C12	.568	22.2	4.05	0.8	7.416
C13	.525	22.0	4.18	0.7	7.941
C14	.537	22.6	3.94	1.0	8.478
C15	.495	21.6	3.75	-	8.973
C16	.538	21.8	3.71	-	9.511
C17	.532	21.6	3.66	-	10.043
C18	.559	19.6	3.09	-	10.602
C19	.490	21.8	3.66	-	11.092
C20	.502	21.8	3.36	-	11.594
C21	.571	21.4	3.87	-	12.165

Tube No.	Urine Weight(G.)	Cr mg/100 ml.	P	Na mEq/l.	Cumulative Volume (ml.)
C22	.515	21.3	3.40	-	12.680
C23	.523	21.1	2.92	-	13.203
C24	.571	20.8	3.02	-	13.774
C25	.561	-	-	-	14.335
C26	.481	19.8	3.23	-	14.816
C27	.569	19.8	3.05	-	15.385
C28	.489	18.3	3.07	-	15.874
C29	.525	19.6	3.10	-	16.399
C30	.522	19.3	3.04	-	16.921

(B) Derived Results:

Control Urines:

No.	1	2	3	4	5
Vol(ml./min.)	5.50	6.00	6.75	5.63	5.63
Ccr (ml./min.)	16.0	16.1	17.9	13.4	12.8
% excretion P:	16.4	18.1	19.4	34.2	38.1

No.	6	7	8	9
Vol.(ml./min.)	5.63	5.25	4.75	4.37
Ccr (ml./min.)	12.3	10.6	9.8	9.2
% excretion P:	41.7	57.6	58.7	62.1

Note: Serum Cr and P concentrations of blood sample 5 assumed intermediate between those of samples 4 and 6.

Stop-Flow Urines

Tube No.	% Total Volume	Urinary P as fraction of that filtered.	Tube No.	% Total Volume	Urinary P as fraction of that filtered.
A1	5.6	.298	B1	5.9	.295
A2	10.2	.261	B2	11.9	.238
A3	14.2	.261	B3	17.0	.276
A4	17.6	.263	B4	21.8	.235
A5	21.8	.267	B5	26.2	.195
A6	24.9	.256	B6	30.1	.255
A7	28.3	.285			
A8	31.9	.302	C1	5.9	.312
A9	35.9	.313	C2	11.2	.244
A10	39.3	.296	C3	16.9	.267
A11	43.5	.307	C4	21.1	.292
A12	47.1	.302	C5	25.2	.241
A13	50.4	.299	C6	29.5	.261
A14	54.1	.307	C7	34.4	.300
A15	58.1	.310	C8	38.8	.293
A16	61.7	.300	C9	43.4	.294
A17	65.0	.289	C10	47.5	.299
A18	68.8	.309	C11	51.9	.298
A19	72.1	.302	C12	56.2	.299
A20	75.6	.296	C13	60.1	.311
A21	79.4	.306	C14	64.2	.286
A22	82.6	.289	C15	68.0	.284
A23	86.1	.282	C16	72.0	.279
A24	89.5	.269	C17	76.1	.268
A25	93.2	.263	C18	80.3	.258
A26	96.5	.265	C19	84.0	.275
A27	100.0	.247	C20	87.8	.252
A28	103.2	.248	C21	92.1	.296
A29	106.7	.254	C22	96.0	.261

Tube No.	% Total Volume	Urinary P as fraction of that filtered.
C23	100.0	.227
C24	104.3	.238
C25	108.6	-
C26	112.2	.267
C27	116.5	.252
C28	-	.275
C29	-	.259
C30	-	.258

Δ P (C - A)	% Total Intra-tubular Volume of A	of C
+ .010	30.1 to 31.9	1.8
- .001	35.9	5.8
+ .016	36.0	5.9
- .052	39.3	9.2
- .063	41.3	11.2
- .040	43.5	13.4
- .035	47.0	16.9
- .010	47.1	17.0
- .007	50.4	20.3
- .015	52.2	22.1
- .066	54.1	24.0
- .069	55.3	25.2
- .049	58.1	28.0
- .039	59.6	29.5
0.000	61.7	31.6

Δ P (C - A)	% Total Intra-tubular Volume of A	of C
+ .011	64.5	34.4
+ .011	65.0	34.9
+ .016	68.8	38.7
- .009	68.9	38.8
- .008	72.1	42.0
- .002	73.5	43.4
- .003	75.6	45.5
- .007	77.6	47.5
- .008	79.4	49.3
+ .009	82.0	51.9
+ .010	82.6	52.5
+ .017	86.1	56.0
+ .030	86.3	56.2
+ .042	89.5	59.4
+ .048	90.2	60.1
+ .023	93.2	63.1
+ .021	94.3	64.2
+ .019	96.5	66.4
+ .037	98.1	68.1
+ .032	100.0	69.9
+ .031	102.1	72.0
+ .020	103.2	73.1
+ .014	106.2	76.1
+ .004	106.7	76.6

NORMAL 24-HOUR URINES - Section 1

(A) 'Whites'

Vol. (ml.)	Osm. mOsm/kg water	pH	Sp.$K^{u/25}_{rt}$ mMhos/cm.	Na	K	NH_4	Ca	Mg	SO_4	P	Ionic
						(mEq/l.)				mM/l.	Strength
1220	818	6.70	0.710	170.8	58.2	77.1	4.02	8.19	28.1	20.13	0.342
970	910	6.44	0.788	140.0	70.6	92.9	3.71	8.92	38.0	30.84	0.351
750	1418	6.28	1.175	210.0	88.0	118.6	10.80	21.20	53.1	37.42	0.500
1060	792	6.62	0.890	179.2	47.1	75.7	7.08	9.39	17.2	21.29	0.344
630	1014	6.61	0.939	162.4	79.8	100.0	11.90	16.10	37.0	19.62	0.410
1120	874	6.90	1.000	198.8	73.7	78.6	7.32	9.85	21.4	22.45	0.400
1270	1048	6.40	0.966	182.0	67.5	82.9	6.61	10.31	33.3	23.10	0.381
1080	1014	6.35	1.120	218.4	75.7	95.7	10.09	11.10	50.0	28.78	0.454
475	1160	5.80	0.991	176.4	72.7	155.7	6.84	14.50	52.1	35.26	0.466
930	1165	5.90	1.366	229.6	83.9	81.4	7.42	14.20	32.3	36.13	0.447
940	1252	6.68	1.088	151.2	122.8	67.1	4.20	15.00	70.8	49.04	0.427
566	1151	6.03	1.405	207.2	114.6	70.0	1.33	15.60	52.1	40.78	0.449
1570	866	6.27	0.833	156.8	60.4	71.4	0.04	9.55	39.1	20.00	0.327
570	1382	5.84	1.392	254.8	67.5	102.9	7.63	12.58	43.2	31.62	0.480
1380	767	6.50	0.855	145.6	66.5	70.0	4.31	9.30	21.4	25.29	0.322
840	1336	5.90	1.250	229.6	90.0	97.1	11.31	20.80	51.1	45.04	0.495
1070	781	5.83	0.655	156.8	53.2	97.1	4.58	7.71	9.38	24.28	0.333

(Section 1) 'Whites' - Continued.

Vol. (ml.)	Osm. mOsm/kg water	pH	Sp.K$^{u/25}$ mMhos/cm	Na	K	NH_4 (mEq/l.)	Ca	Mg	SO_4	P (mM/l.)	Ionic strength
1130	1079	5.74	1.212	229.6	61.4	105.7	11.81	11.95	30.2	33.04	0.450
2240	688	6.09	0.623	156.8	37.9	44.1	2.50	6.25	13.5	15.32	0.261
600	1314	6.10	1.491	260.4	87.0	128.2	5.67	12.39	30.2	39.73	0.524
1650	-	6.10	-	246.4	65.5	94.5	1.39	-	19.8	16.31	-
1900	647	6.40	0.667	165.2	34.8	60.9	3.29	6.51	17.7	15.60	0.289
1490	883	6.15	0.930	187.6	59.4	63.0	9.00	8.48	13.5	26.85	0.348
1390	797	6.20	0.787	156.8	45.0	84.0	6.40	8.39	3.1	21.56	0.314
2060	723	6.95	0.925	196.0	49.1	56.7	5.09	4.24	17.7	15.07	0.334
1070	1137	6.40	1.575	254.8	84.9	71.4	5.09	8.90	7.3	30.66	0.444
1360	1058	6.40	0.971	193.7	63.4	77.7	3.71	7.35	27.1	27.85	0.373
1140	790	6.70	0.949	182.0	51.2	77.7	7.02	6.66	17.7	17.57	0.790
1000	1080	6.18	1.266	238.0	76.7	94.5	9.00	9.95	4.2	26.84	0.445
1340	788	6.75	0.889	173.6	76.7	84.0	6.01	6.52	32.3	18.37	0.378
1890	765	6.45	0.820	162.4	47.1	88.2	2.30	5.94	20.3	14.15	0.324
1450	1015	6.20	1.205	235.2	70.6	75.6	3.69	5.58	23.4	23.78	0.412
1122	882	6.50	0.971	196.0	48.1	77.7	3.39	3.66	25.0	23.84	0.353
2540	614	6.60	0.699	170.8	33.8	56.7	4.80	5.05	4.2	14.43	0.284
750	1282	5.91	1.351	226.8	77.8	145.0	6.00	18.20	63.5	43.27	0.523
1070	1118	6.08	1.142	246.4	54.2	102.9	6.59	11.03	46.9	23.61	0.457
626	1304	6.39	1.162	212.8	83.9	161.8	3.87	16.60	87.5	39.70	0.544
940	1118	6.30	1.242	229.6	71.6	121.9	8.19	9.05	37.5	30.41	0.475
1240	827	6.50	0.909	198.8	62.4	65.1	7.18	6.60	28.7	21.07	0.368

Vol. (ml.)	Osm. (mOsm/kg. water)	pH	Sp.$K^{u/25}_{rt}$ (mMhos/cm.)	Na	K	NH_4	C_a (mEq/l.)	Mg	SO_4	P (mM/l.)	Ionic Strength
740	1054	6.50	1.316	243.6	88.0	102.9	4.00	7.80	25.5	23.72	0.470
1180	1024	6.00	1.162	238.0	52.2	102.9	12.00	10.60	34.4	27.70	0.448
820	1388	6.10	1.515	240.8	80.8	172.3	6.47	18.90	59.4	34.93	0.567
715	976	6.39	1.100	201.6	89.0	90.3	5.74	10.30	35.4	27.03	0.438
1450	904	6.42	1.043	210.0	68.6	84.0	3.59	5.27	20.8	22.07	0.393
1590	811	6.60	0.889	198.8	52.2	75.6	4.09	6.85	32.8	17.16	0.366
1150	1198	6.58	1.515	266.0	84.9	138.7	4.39	7.70	23.4	33.91	0.533
1070	938	5.82	1.042	193.2	73.7	111.4	5.00	9.42	35.4	30.36	0.420
1420	643	6.69	0.641	142.8	52.2	94.5	2.61	5.52	20.3	9.61	0.321
1110	818	6.01	0.794	196.0	45.0	77.3	4.41	4.40	33.3	19.70	0.351
1240	836	6.38	0.969	210.0	51.2	98.7	8.19	6.20	32.8	20.21	0.404
660	1224	6.50	1.235	224.0	68.6	149.2	6.90	11.80	59.4	42.88	0.514
1210	755	5.70	0.730	162.4	32.7	88.2	6.10	9.15	26.6	25.60	0.322
1890	542	6.75	0.465	114.8	38.9	67.2	3.40	4.26	29.2	11.65	0.259
930	1212	5.72	1.228	229.6	86.6	75.6	2.80	9.85	50.5	40.31	0.439

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2293	520	6.45	0.834	145.6	20.5	60.8	2.30	3.60	38.6	9.75	0.258
1875	754	5.21	1.016	201.6	37.9	63.8	1.60	8.60	62.0	13.13	0.350
18622	604	5.55	0.534	103.6	39.9	16.7	1.80	4.20	30.7	7.28	0.185
3046	761	6.18	0.698	154.0	31.7	51.7	2.80	7.40	46.4	5.33	0.277
1875	829	5.90	0.699	123.2	39.4	47.4	1.90	4.40	65.7	10.27	0.253
1385	933	6.02	0.929	184.8	34.3	39.5	4.40	10.50	70.9	22.62	0.320

Vol. ml.	Osm. (mOsm/kg water)	pH	Sp.$K^{u/25}_{rt}$ (mMhos/cm.)	Na	K	NH_4 (mEq/l.)	Ca	Mg	SO_4	P (mM/l.)	Ionic Strength
2275	574	7.25	0.597	154.0	11.8	23.6	5.60	3.00	38.0	3.51	0.224
1478	952	6.40	0.994	215.6	31.7	43.3	2.80	6.00	51.6	16.51	0.333
2786	775	6.95	0.968	226.8	35.8	33.4	2.00	3.70	51.6	4.03	0.333
2047	530	6.30	0.568	131.6	17.4	16.7	2.00	3.82	31.8	1.14	0.191
1999	603	7.40	0.638	154.0	25.6	19.8	3.00	3.104	36.5	7.30	0.228
1473	942	6.20	0.814	145.6	57.3	62.3	4.00	15.10	69.8	25.02	0.334
2555	708	6.10	0.796	179.2	26.6	31.9	3.10	6.40	52.6	5.97	0.297
2514	668	7.35	0.677	187.6	225	16.7	1.80	3.50	42.2	6.35	0.261
2095	701	5.50	0.711	162.4	35.8	21.3	0.70	6.90	48.5	11.18	0.256
2396	839	6.28	0.907	193.2	39.9	47.1	4.30	9.00	46.9	22.75	0.329
2959	561	6.00	0.537	126.0	28.1	36.5	0.50	5.20	26.1	6.92	0.213
1175	-	8.25	-	170.8	45.0	162.6	3.00	3.60	-	25.15	-
2995	481	6.20	0.442	114.8	23.0	31.9	1.00	3.20	16.2	6.10	0.185
2275	660	5.65	0.679	156.8	34.3	38.0	0.60	4.90	33.3	11.44	0.255
2475	578	7.30	0.644	140.0	25.1	48.6	0.50	2.70	20.8	10.66	0.237
2465	571	5.15	0.525	137.2	22.5	35.0	1.20	4.30	28.7	12.74	0.218
465	986	5.60	0.872	148.4	48.6	80.6	5.20	12.50	73.5	24.90	0.342
3294	-	5.82	-	95.2	13.8	16.7	1.20	3.80	-	6.37	-
1759	992	5.85	1.065	212.8	52.2	66.9	4.60	10.10	65.1	28.73	0.389
2131	821	5.45	0.732	173.6	41.4	48.6	3.10	5.80	57.3	16.38	0.306
1587	653	5.93	0.734	168.0	33.8	65.4	0.60	12.50	52.1	16.12	0.315

Vol. ml.	Osm. (mOsm/kg water)	pH	Sp.$K^{u/25}_{rt}$ (mMhos/cm.)	Na	K	NH_4	Ca	Mg	SO_4	P (mM/l.)	Ionic Strength
						(mEq/l.)					
2419	736	5.53	0.712	151.2	25.1	56.2	2.60	6.60	55.8	13.13	0.275
2575	963	5.10	1.005	207.2	23.0	60.8	3.60	7.60	57.3	3.25	0.337
2747	708	8.60	0.856	95.2	19.4	103.4	1.30	0.00	38.6	10.27	0.249
2376	709	6.15	0.702	165.2	38.4	44.1	1.10	3.90	36.5	17.55	0.277
3658	653	5.68	0.730	156.8	33.8	42.6	1.20	5.80	49.5	13.52	0.270
3236	552	6.72	0.604	140.0	28.1	33.4	4.00	4.60	29.7	11.44	0.235
2519	545	5.40	0.535	128.8	28.7	38.0	1.10	5.60	28.1	14.30	0.220
2201	680	8.20	0.804	156.8	34.3	65.4	0.80	0.09	36.0	8.58	0.284
1620	856	5.82	0.632	134.4	47.1	50.9	3.30	7.90	58.4	16.38	0.280
1250	980	6.00	0.882	207.2	39.9	48.6	2.20	8.00	56.8	13.78	0.341
1120	718	5.58	0.743	162.4	19.4	45.6	3.70	5.90	45.3	11.44	0.265
1250	811	5.25	0.535	117.6	27.6	66.1	4.80	6.30	70.3	9.62	0.263
1790	529	5.62	0.405	106.4	26.1	38.0	0.89	5.50	32.8	8.71	0.197
1125	667	6.50	0.654	145.6	27.6	43.6	0.90	8.20	35.4	7.54	0.250
1965	875	5.10	0.811	196.0	29.7	42.6	0.80	4.40	55.2	7.41	0.304
3686	552	6.82	0.496	123.2	14.3	20.5	1.90	3.20	49.5	2.47	0.192
2129	640	7.20	0.652	182.0	21.5	19.8	2.003	2.10	42.2	3.38	0.252
1925	893	5.60	1.006	201.6	38.4	41.0	2.80	5.10	55.8	7.02	0.330
2517	832	5.73	0.875	193.2	37.9	42.6	7.00	7.80	55.2	10.79	0.324
3032	783	5.85	0.758	168.0	38.4	42.6	1.10	4.20	59.4	5.20	0.287
1708	866	5.82	0.844	182.0	23.5	48.6	1.40	6.30	54.2	3.77	0.293

Vol. ml.	Osm. (mOsm/kg water)	pH	Sp.K$^{u/25}_{rt}$ (mMhos/cm.)	Na	K	NH_4	Ca	Mg	SO_4	P (mM/l.)	Ionic Strength.
						(mEq/l.)					
1537	932	5.80	0.933	190.4	54.2	35.0	1.30	11.80	63.6	24.96	0.334
1090	-	5.46	-	218.4	35.8	53.2	1.60	10.00	-	17.03	-
1112	1051	6.00	0.889	176.4	38.4	44.1	3.40	12.10	67.7	16.90	0.318
1975	-	7.82	-	148.4	16.4	39.5	2.45	2.20	-	1.95	-
1629	678	6.30	0.619	148.4	29.7	48.6	2.30	7.30	39.6	6.63	0.263
1249	900	6.50	1.023	212.8	46.0	53.2	0.80	7.70	51.1	10.66	0.354
2708	562	7.20	0.535	142.8	23.5	31.9	1.80	4.70	43.8	5.20	0.234
800	961	5.85	0.870	182.0	68.6	59.3	2.20	5.90	46.9	6.89	0.346
1625	876	5.70	0.841	168.0	36.8	86.1	1.60	2.27	55.8	6.93	0.325
2167	800	6.52	1.000	207.2	19.4	75.6	2.40	0.12	56.5	10.70	0.338
2500	663	6.50	0.685	179.2	21.5	52.5	1.80	0.04	48.5	7.19	0.283
1611	852	5.33	0.971	212.8	45.0	39.9	1.60	6.25	47.4	12.54	0.334

Osmolar/ Sp.K_{rt} Interrelationships in random normal urines. - Section 5

Osmolality as mOsm./kg water; Sp.K_{rt} as mMhos/cm.

'Abnormal' Urines -Section 3

Details of the analyses of these urines are not given here, as equations were not derived from these figures. The actual data can be inspected at any time in the Endocrine Laboratories' records.

66	2.06	58	2.07	72	4.24
91	3.53	812	20.80	411	15.15
125	4.98	357	11.84	860	22.30
170	5.90	221	7.66	798	23.40
298	10.91	81	4.15	879	30.00
252	8.83	41	2.02	652	17.67
92	3.85	510	15.37	703	20.00
288	9.36	229	7.44	332	12.02
239	7.06	106	4.24	429	14.46
220	7.79	42	1.94	926	31.40
154	6.05	864	26.45	689	25.70
149	4.81	469	16.95	559	19.60
926	27.70	248	9.63	252	7.66
410	13.43	120	5.37	295	9.10
195	7.06	56	3.02	443	16.34
98	4.32	477	13.66	332	10.64
48	2.42	193	6.05	551	14.40
928	29.78	106	4.08	257	7.66
402	11.93	41	1.78	804	23.52

Osm.	$Sp.K_{rt}$	Osm.	$Sp.K_{rt}$	Osm	$Sp.K_{rt}$
251	8.35	479	19.85	216	6.05
130	4.98	225	10.11	690	17.50
982	34.95	389	9.56	794	23.90
1160	37.90	904	23.50	930	26.70
288	10.15	402	11.23	798	19.30
661	18.10	946	25.61	778	20.70
927	30.00	791	20.70	47	1.62
644	29.20	918	25.70	982	27.91
788	24.80	971	30.20		
982	23.16	450	14.47		
420	14.70	682	23.82		
660	18.75	997	20.40		
1037	19.40	124	5.10		
352	14.11	106	3.92		
440	13.05	695	15.11		
282	8.38	361	11.20		
153	6.05	767	15.11		
202	8.62	126	4.24		
387	10.95	562	15.87		
520	18.81	968	35.30		
658	20.96	606	18.80		
579	18.01	819	21.60		
15	3.14	380	9.25		
118	3.62	221	7.06		
389	12.70	1146	29.00		
162	5.88	927	31.40		
123	3.75	886	24.85		
357	10.47	851	24.85		

Section 5.

TABLE 2

Progressive Dilution of Individual Urines.

No.	Osm. (mOsm/kg water)	Sp.Resist. (Ohms/cm.)	Sp.K (mMhos/cm.)	Log. Osm.	Log.Sp.Resist.
1	387	84.34	11.87	2.588	1.9260
	246	130.5	7.719	2.391	2.1154
	6o	494.8	2.027	1.786	2.694
2	510	73.04	13.71	2.708	1.864
	215	164.9	6.131	2.333	2.217
	61	560.7	1.788	1.786	2.749
3	512	50.18	19.99	2.709	1.701
	249	98.72	10.13	2.396	1.994
	46	530.1	1.887	1.662	2.724
4	457	91.18	10.99	2.660	1.960
	283	141.4	7.111	2.452	2.150
	78	483.0	2.070	1.892	2.684
5	998	36.05	27.40	2.999	1.557
	441	74.21	13.48	2.634	1.937
	218	141.4	7.111	2.339	2.150
	67	412.3	2.429	1.826	2.615

Osmolar / Sp.K_{20} Interrelationships in random normal urines. -Section 8

Osmolality in mOsm/kg. water; Sp.K_{20} in mMhos/cm.

Osm.	Sp.K_{20}	Osm.	Sp.K_{20}	Osm.	Sp.K_{20}
908	21.06	804	20.19	645	16.99
1088	28.10	613	16.54	838	21.02
443	10.73	1134	27.80	998	23.36
881	25.22	1172	26.41	1000	24.97
860	23.71	791	20.52	928	16.03
910	24.80	900	24.74	387	10.00
896	22.41	994	23.91	546	13.20
846	21.75	877	21.59	930	22.40
1070	26.25	1158	27.14	510	11.57
130	3.80	190	5.09	512	16.88
851	21.41	1000	29.53	729	22.55
695	18.60	480	7.54		
874	25.07	487	10.72		
550	13.18	703	22.78		
291	9.21	1018	25.03		
506	12.75	982	25.14		
679	14.64	830	24.67		
681	15.59	1200	29.12		
793	18.19	1106	27.77		
1080	30.00	1150	23.91		
1048	27.69	735	22.70		
662	19.93	596	15.16		
1290	23.32	617	16.63		
815	16.94	656	15.03		

Section 9

IONIC CONSTITUENT CONCENTRATIONS - NORMAL (random) URINES.

No.	Osm. (mOsm/kg water)	pH	Sp.$K^{u/10}_{20}$ (mMhos/cm.)	Na	K	NH_4	Ca	Mg	SO_4	P	Ionic strength
						(mEq/l.)				(mM/l.)	
1	860	5.50	2.963	178.0	55.0	72.6	7.30	9.77	27.4	51.29	0.348
2	923	6.40	3.344	100.0	87.5	65.0	5.18	8.33	27.8	17.42	0.289
3	498	5.40	1.213	62.0	21.3	36.3	1.30	3.70	15.0	11.07	0.135
4	405	5.30	1.237	46.0	32.5	59.5	2.23	2.72	17.7	11.81	0.154
5	260	5.26	0.766	39.5	20.0	13.6	0.95	2.33	11.4	7.86	0.084
6	261	5.00	0.766	38.5	13.8	23.0	2.40	4.76	10.7	12.42	0.092
7	580	5.43	1.845	97.0	42.5	65.6	3.18	3.97	24.9	32.32	0.229
8	492	6.65	1.789	81.0	72.5	29.4	1.85	3.30	13.2	6.27	0.199
9	1040	5.98	3.281	168.0	95.0	59.0	7.38	7.36	30.2	20.58	0.361
10	913	5.40	2.949	148.5	82.5	71.4	5.65	5.56	38.7	29.26	0.339
11	750	5.56	2.583	152.0	53.8	54.3	2.04	6.14	27.2	17.36	0.286
12	887	6.76	3.238	192.5	90.0	59.5	8.90	8.61	28.9	15.36	0.386
13	1084	5.40	3.441	235.0	42.5	93.0	4.33	6.97	37.5	16.57	0.406
14	525	6.95	2.368	132.5	66.3	44.6	1.85	3.76	9.9	3.33	0.258

Section 9 - Normal Urines, cont.

No.	Osm. (mOsm/kg water)	pH	Sp.$K^{u/10}_{20}$ (mMhos/cm.)	Na	K	NH_4	Ca	Mg	SO_4	P (mM/l.)	Ionic strength	Urea (mM/l.)
						(mEq/l.)						
15	558	6.60	2.075	167.5	35.0	35.3	2.58	4.82	15.4	4.99	0.258	-
16	435	5.90	1.601	97.5	27.5	29.8	2.82	4.04	14.6	5.76	0.173	-
17	956	6.50	3.446	245.0	58.8	70.7	8.15	9.56	30.2	10.37	0.418	-
18	836	6.35	2.768	162.5	52.5	100.4	10.45	8.34	41.4	14.34	0.366	-
19	1082	6.96	3.314	105.0	180.0	81.8	1.62	8.03	58.1	13.70	0.414	-
20	786	6.40	2.118	105.0	55.0	93.0	3.18	8.13	33.8	21.89	0.290	-
21	824	5.86	2.514	100.0	80.0	63.2	5.05	7.27	33.8	15.10	0.279	-
22	542	4.95	1.376	28.0	33.0	57.0	2.00	9.17	39.6	19.15	0.155	300
23	783	7.23	3.154	224.0	48.0	47.0	5.40	8.36	26.0	6.00	0.355	237
24	636	6.63	2.610	159.0	58.0	43.0	3.15	5.11	25.6	14.45	0.288	180
25	881	5.75	2.959	115.0	96.0	51.0	12.10	12.50	42.2	21.40	0.321	-
26	990	6.12	4.075	288.0	58.0	47.0	5.55	10.14	24.8	13.25	0.425	262
27	1140	5.60	3.859	215.0	73.0	55.0	10.20	11.69	38.0	24.90	0.396	-
28	1128	6.10	4.388	300.0	73.0	43.0	4.45	7.39	36.0	24.00	0.454	350
29	286	5.05	1.017	26.0	30.0	13.0	1.10	1.79	10.2	2.58	0.078	137
30	177	6.20	0.580	25.0	15.0	9.0	0.85	3.00	6.8	3.64	0.059	78
31	331	5.40	1.234	68.0	18.0	13.0	1.80	4.30	11.8	11.00	0.114	112
32	544	6.00	2.025	76.0	60.0	30.0	3.50	7.95	23.2	9.68	0.195	193
33	795	5.80	2.460	106.0	60.0	47.0	7.90	10.07	35.2	9.85	0.258	-

No.	Osm. (mOsm/kg water)	pH	Sp.$K^{u/10}_{20}$ (mMhos/cm.)	Na	K	NH_4	Ca	Mg	SO_4	P	Ionic Strength	Urea
						(mEq/l.)				(mM/l.)		(mM/l.)
34	929	6.00	3.511	220.0	35.0	81.0	9.60	10.71	44.0	10.01	0.389	302
35	730	6.90	2.218	119.0	60.0	43.0	10.60	8.77	33.0	20.30	0.273	308
36	829	5.23	3.129	142.0	88.0	60.0	2.65	7.63	26.8	19.60	0.319	250
37	876	5.80	3.410	156.0	80.0	55.0	5.30	9.74	31.0	12.20	0.330	280
38	1020	5.53	3.465	183.0	60.0	72.0	7.80	11.04	58.0	22.60	0.373	352
39	141	6.35	0.482	24.0	8.0	17.0	1.30	2.84	39.6	1.16	0.075	87
40	1023	5.43	3.016	129.0	55.0	85.0	5.60	15.90	53.6	30.30	0.329	440
41	509	7.00	1.848	112.0	38.0	21.0	2.10	3.25	21.4	7.14	0.192	208
42	894	5.80	2.786	155.0	53.0	47.0	2.75	9.25	46.4	17.60	0.297	300

Section 9

IONIC CONSTITUENT CONCENTRATIONS - ABNORMAL URINES

No.	Diagnosis	Osm. (mOsm/kg water)	pH	Sp.$K^{u/10}_{20}$ (mMhos/cm,)	Na	K	NH_4 (mEq/l.)	Mg	SO_4	P (mM/l.)	Urea
1	Hypertension; uraemia.	287	4.95	1.010	61.5	21.3	14.3	3.5	18.5	6.87	100
2	Nephrotic syndrome; ? cause.	370	4.80	1.001	5.0	45.0	50.1	0.1	41.6	30.72	133
3	Congestive cardiac failure;? cause	625	6.28	1.368	49.0	51.3	38.1	8.2	4.9	19.22	350
4	Hypertension	701	4.93	2.492	102.5	68.8	52.4	10.9	41.6	17.39	270
5	Infective hepatitis; jaundice.	106	6.40	0.039	10.5	18.8	8.0	2.4	1.9	1.19	53
6	Acute Renal failure	695	5.57	1.807	78.5	52.5	52.4	12.0	29.6	37.03	333
7	Rheumatoid arthritis, on Prednisone,	387	5.76	0.869	14.0	30.0	30.2	7.2	3.0	22.02	170
8	Nephrotic syndrome; ? cause.	490	7.36	1.708	109.0	42.5	36.6	8.9	15.6	17.95	163
9	Primary hepatic carcinima	251	7.70	0.927	48.5	32.5	9.5	3.8	13.3	12.20	93
10	Acute renal failure; ? cause.	446	7.63	1.915	138.0	47.5	54.0	1.9	11.0	4.35	100
11	Malignant hypertension	158	5.66	1.248	3.5	57.5	20.7	5.2	51.0	43.06	267

(A) Normal Infants

Subject	Weight (lbs.)	Volume (ml.)	Cr (mg/100 ml.)	Osm. (mOsm/kg water.)	Osm/Cr
A	7.5	124	14.8	2.7	1.47
		198	11.0	187	1.70
B	7.7	242	12.1	142	1.17
		198	9.3	105	1.13
		166	12.1	168	1.39
		167	12.4	160	1.29
		208	9.3	105	1.13
		352	5.5	63	1.15
C	5.9	125	13.4	206	1.54
		105	16.4	285	1.74
		81	19.0	342	1.80
		136	16.9	278	1.64
		100	20.4	305	1.50
D	7.9	126	16.5	166	1.01
		210	14.5	142	0.98
		108	10.2	82	0.80
		247	13.5	145	1.07
		223	11.1	116	1.05

(B) Normal Adults †

A	M	165	1421	89	576	0.65
B	M	165	1797	99	635	0.64

Subject	Weight (lbs.)	Volume (ml.)	Cr (mg/100 ml.)	Osm. (mOsm./kg water.)	Osm/Cr
C M	165	2461	71	431	0.61
D M	163	1823	90	458	0.51
E M	155	1074	140	844	0.60
F (M)	130	1215	96	508	0.53
G (M)	153	1266	125	669	0.54
H (F)	112	1020	80	368	0.46
I (M)	141	895	161	779	0.48
J (F)	140	454	206	1098	0.53
K (M)	155	656	270	1177	0.44
L (M)	178	831	143	752	0.53
M (M)	166	809	257	1162	0.45
N (M)	135	673	193	985	0.51
O (M)	150	915	148	929	0.63
P (M)	160	1100	191	872	0.46
		1010	211	1058	0.50
		1440	117	572	0.49
Q (M)	119	1402	115	688	0.60
R (M)	159	1527	234	1000	0.43
S (M)	175	1867	147	910	0.62
T (M)	165	1245	117	586	0.50
		2750	57	316	0.55
		1820	94	435	0.46
		1225	140	638	0.46
U (M)	145	1620	136	730	0.54
V (F)	148	-	80	417	0.52
W (M)	160	1120	140	851	0.61
X (M)	153	1560	132	727	0.55

(C) Obese Adults

Subject	Weight (lbs.)	Volume (ml.)	Cr (mg/100 ml.)	Osm (mOsm./kg water.)	Osm/Cr
1 (M) (5',3")	161	-	130	874	0.67
2 (M)	196	1650	37	252	0.69
3 (F) (4'10")	205	2150	56	432	0.77
4 (F)	205	-	147	1000	0.68
5 (F)	184	1480	99	894	0.90
6 (F)	240	-	82	750	0.92
7 (F) (5'3")	192	1350	64	509	0.80

(D) Diverse Clinical Conditions

Diagnosis	Weight (lbs.)	Vol. (ml.)	Cr (mg/100 ml.)	Osm. (mOsm/kg water)	Osm/Cr
(F) Thyrotoxicosis. Losing weight despite enhanced appetite	120	795	83	624	0.75
(F) Thyrotoxicosis. Obese. Lost 10 lbs in weight.	290	1670	64.8	568	0.88
(F) 43 years old. Dietary faddist. Vegetarian. Calorie intake estimated at 1000 cals. per day by dietitian.	105	1260	37.6	132	0.35
(M) Delayed development; bone age 8 years; chronological age 13 years. Height 41 inches.	33	-	42.5	650	1.53
		340	29.2	580	1.99
(M) ? Hypopituitary Undescended testes; absent pubic and axillary hair. Bone age 14 years, Chronological age 20 years. Height 5'2"	116	-	129	890	0.69
(M) Heavy manual labour. Quarry-worker	154	1575	110	832	0.75
(M) Heavy manual labour. Dock-worker. Stout.	-	550	125	1069	0.86
(M) 12 year old child. Ascending Paralysis. Immobile.	64	-	31.3	628	2.01
(M) Marasmus. 3 months old.	9¾	558	6.8	519	7.60
Infected Bronch-iectasis. Adult male Marked anorexia.	90	257	313	910	0.29

Diurnal Variation in Urinary Osmolar/Creatinine ratio in Normal Adults.

Subject	Urine No	Time of micturition	Vol. (ml.)	Cr (mg/100 ml.)	Osm. (mOsm/kg water)	Osm/Cr	24-Hour Osm/Cr
A	1	1100	284	84	721	.86	
	2	1230	176	64	508	.79	
	3	1410	236	55	389	.71	
	4	1740	252	90	528	.59	
	5	2045	251	84	472	.88	
	6	0645	200	158	819	.52	
	7	0715	22	136	786	.58	0.65
B	1	0810	257	91	514	.56	
	2	1415	167	138	626	.45	
	3	1945	383	88	728	.83	
	4	0015	465	90	617	.68	
	5	0720	525	94	568	.61	.064
C	1	1900	121	48	304	.64	
	2	1915	161	82	500	.61	
	3	2200	192	71	449	.63	
	4	2330	149	39	250	.64	
	5	0100	213	60	383	.64	
	6	0430	364	66	440	.66	
	7	0800	265	109	629	.58	
	8	1145	156	172	745	.43	
	9	1400	221	52	394	.76	
	10	1430	211	37	260	.70	
	11	1520	208	42	298	.71	
	12	1645	133	75	436	.58	
	13	1730	67	81	502	.62	0.61

Subject	Urine No	Time of micturition	Vol. (ml.)	Cr (mg/100 ml.)	Osm. (mOsm/kg. water)	Osm/Cr	24-Hour Osm/Cr
D	1	1410	283	71	512	.72	
	2	1725	327	74	450	.61	
	3	2115	323	51	317	.62	
	4	2320	382	51	326	.64	
	5	0830	351	158	556	.35	
	6	1120	157	180	752	.42	0.51
E	1	1201	206	140	991	.71	
	2	1730	314	98	602	.61	
	3	2348	240	151	800	.53	
	4	0715	314	164	963	.59	
F	1	1100	260	73	450	.614	
	2	1400	380	51	261	.510	
	3	1900	170	109	613	.560	
	4	2310	165	125	696	.556	
	5	0800	240	165	759	.461	0.53
G	1	1310	222	84	394	.47	
	2	1620	145	136	551	.41	
	3	1705	156	42	228	.55	
	4	1900	166	73	396	.54	
	5	2245	178	169	773	.46	
	6	0655	211	206	896	.43	
	7	0920	115	139	836	.60	
	8	1110	73	158	875	.56	0.54
H	1	1405	420	50	293	.58	
	2	2300	280	95	412	.43	
	3	0815	320	105	427	.41	0.46
I	1	1220	100	234	904	.39	
	2	1545	70	246	838	.34	
	3	2115	235	157	750	.48	
	4	0800	490	134	744	.55	0.48

Subject	Urine No.	Time of Micturition	Vol. (ml.)	Cr (mg/100 ml.)	Osm. (mOsm/kg water)	Osm/Cr	24-Hour Osm/Cr
J	1	0925	21	234	958	.41	
	2	1250	74	210	1092	.52	
	3	1600	72	213	1092	.51	
	4	1715	32	190	1066	.56	
	5	0800	255	204	1112	.55	0.53
K	1	2025	86	311	1183	.38	
	2	0730	159	387	1326	.34	
	3	1230	200	190	1038	.55	
	4	1830	211	223	1116	.50	0.44
L	1	0850	72	131	740	.57	
	2	1450	69	152	678	.45	
	3	1730	154	138	739	.54	
	4	0150	216	158	827	.52	
	5	0810	320	139	739	.53	0.53
M	1	0910	255	292	1154	.40	
	2	1645	272	241	1172	.49	
	3	1945	119	241	1178	.49	
	4	2345	163	223	1104	.50	0.45
N	1	1312	190	189	1016	.54	
	2	1700	93	204	942	.46	
	3	2315	220	196	982	.50	
	4	0614	170	188	974	.52	0.51
O	1	1155	168	147	990	.67	
	2	1710	238	126	850	.68	
	3	2110	161	142	899	.63	
	4	0800	348	164	1070	.65	0.63