THE ACTION OF CALCIUM SALTS.

BY

CHARLES O. JONES, M.D., M.Sc., M.R.C.S.

(From the Biochemical Laboratories, University of Liverpool.)

THERE is at the present time a certain vagueness as to the powers of the animal organism to excrete calcium salts, some authorities even prohibiting milk as a diet in certain conditions, supposing that the calcium is liable to accumulate owing to faulty excretory powers.

The work here described was undertaken to endeavour to estimate the excretory powers of animals for calcium salts, and also to find out the channels whereby the animal is enabled to protect itself against any excess. Rabbits were used in all the experiments, and all doses were given intravenously, as it was found that when given by the mouth there was some vagueness as to how much had been absorbed, while hypodermic injections were unsatisfactory owing to slow absorption and consequent abscess formation.

The salt used was pure calcium chloride in 10 per cent. solution; the calcium was in all cases estimated gravimetrically.

The first rabbit was given 1 gram of calcium chloride intravenously; death was instantaneous. Clotting was found to have occurred from the point of injection to the heart, which had stopped in diastole. A second rabbit was given the same dose, and died at once with a convulsion. Coagulation was found extending from the point of injection to the heart. The other vessels were found normal.

It was found that 0.5 gram of calcium chloride was a maximum dose; this is equal to 0.252 gram of calcium oxide. All results are calculated to calcium oxide.

Each column in the tables shows a daily excretion in cubic centimetres or grams.

Experiment: Excess Excreted by Intestine.

A rabbit was given an injection of 0.5 gram of calcium chloride, the urine and faeces being examined daily to estimate its excretion.

Before Injection: Normal.				After Injection.							
<i>Urine:</i>											
Volume ...	45	Nil	10	Nil	Nil	13	Nil	8			
Calcium ...	0.03	Nil	0.04	Nil	Nil	0.05	Nil	0.3			
<i>Faeces:</i>											
Weight ...	21	Nil	10.5	7	6.5	Nil	1.5	2.5			
Calcium ...	0.181	Nil	0.361	0.093	0.157	Nil	0.04	0.051			

It will be seen that the calcium excess is nearly all excreted by the intestine. One other point was noticed, namely, the gradual diminution in quantity and also the increasing dryness of the faeces which follows. This will be dealt with later. It is also evident that in the above example the calcium has a marked effect on metabolism; this was further investigated, and another rabbit injected with the same dose.

Experiment: Renal Irritation and Paresis.

Before Injection: Normal.				After Injection.							
Volume ...				45	Nil	Nil	Nil	10	Nil	Nil	40
Urea ...				0.385	Nil	Nil	Nil	0.25	Nil	Nil	0.796
Chlorides ...				0.155	Nil	Nil	Nil	0.02	Nil	Nil	0.036
Microscopic examination				Nil	Nil	Nil	Nil	A few casts	Nil	Nil	Carbonates, phosphates, oxalates.

In this example the injection had a powerful effect, and it is to be noted that the variation in the effect was very marked. There was in this case complete anuria for three days, with symptoms of marked renal irritation, and finally the excretion of insoluble calcium salts.

This renal irritation and paresis explains why calcium is excreted by the bowel. The kidney is only able to deal with a certain concentration of calcium. This limitation point of kidney efficiency towards calcium differs in every

animal, and probably varies at different times in the same animal's life.

When the accumulation of calcium exceeds this point it throws the kidneys out of action, and the excretion is then taken on by the intestine, and when the calcium accumulation has been lessened the kidney is once again enabled to take on its duties and sweep the excess of the salt out of the blood.

This calcium "toleration point" varies very considerably from animal to animal, as the next example shows. The rabbit was given the same injection as the previous one, namely, 0.5 gram.

Experiment: Toleration Point.

Before Injection: Normal.				After Injection.			
<i>Urine:</i>							
Amount in c.cm. ...	50	58	110	115			
Calcium as oxide ...	0.025	0.123	0.369	0.143			
<i>Faeces:</i>							
Amount in grams ...	26	40	23	27			
Calcium as oxide ...	0.208	0.312	0.415	0.356			

Here it will be noticed the kidneys and intestines both excreted the calcium. The toleration point was higher in this animal than in the previous case, and was just above the amount injected. If the injection had been larger the dose would have put the kidneys out of action; if smaller the kidneys alone would have dealt with the excess.

Another point is to be noticed. The organism does not confine itself to throwing out the calcium excess; along with it go reserve supplies of calcium, which often, as will be seen later, amount to far more than the amount injected. It is possible that the toleration point depends largely on the amount of reserve calcium.

The next example, given the same amount (namely, 0.5 gram), shows again the injection passing the toleration point of calcium.

Experiment: Toleration Point.

Before Injection: Normal.				After Injection.			
<i>Urine:</i>							
Volume ...	45	Nil	50	50	32		
Calcium ...	0.04	Nil	0.169	0.175	0.135		
<i>Faeces:</i>							
Weight ...	27	17	22	40	20		
Calcium ...	0.150	0.261	0.165	0.495	0.403		

It will be seen that during the next day the kidneys were inactive, and that the bowel excreted a quantity of calcium. The toleration point was now reached by decrease in calcium salts, and henceforward kidneys and intestine excreted large quantities of calcium.

Chemical Form of Excretion.

An attempt was now made to find in what form the calcium was excreted into the intestine. The faeces were dried, and one part was used to estimate calcium gravimetrically; another part was extracted with ether in a Soxhlet apparatus. From this portion the fatty acid was estimated by dissolving in absolute alcohol and titration with N/10 caustic soda. The residue after ether extraction was titrated with hydrochloric acid, dried, and again extracted with ether.

The following series will show that in each case with a maximum injection of calcium salts there is excreted with it an extra quantity of soap, and this soap is an insoluble soap.

Experiment 1.

Before Injection: Normal Average.				After Injection.			
Neutral fat ...	0.690	0.405	0.336	0.762			
Fatty acid... ..	0.704	0.756	0.816	0.986			
Soaps	0.718	1.780	1.486	0.306			
Calcium oxide ...	0.767	1.544	1.251	0.276			

Experiment 2.

Before Injection: Normal Average.				After Injection.		
Neutral fat	...	...	0.726	1.028	1.599	0.889
Fatty acid...	...	...	1.153	0.879	1.349	0.862
Soaps	...	...	0.840	1.297	1.310	0.440
Calcium oxide	...	...	0.759	1.209	1.799	0.382

Experiment 3.

Before Injection: Normal Average.				After Injection.		
Neutral fat	...	...	0.484	1.27	0.931	0.735
Fatty acid ..	...	...	0.782	1.27	0.818	0.740
Soaps	...	...	0.584	1.512	0.622	0.335
Calcium oxide	...	...	0.566	1.462	0.654	0.427

Experiment 4.

Before Injection: Normal Average.				After Injection.		
Neutral fat	...	...	0.986	0.611	0.861	
Fatty acid...	...	...	0.778	0.902	0.854	
Soaps	...	...	0.526	0.714	0.706	
Calcium oxide	...	...	0.640	0.984	0.721	

Experiment 5.

Before Injection.				After Injection.			
Weight of faeces	...	30	28	24	29	28	36
Fat and fatty acid	...	3.018	2.285	1.928	2.221	0.728	1.206
Soaps		0.258	0.140	0.268	0.240	0.345	0.425
Calcium oxide	...	0.780	0.632	0.618	0.469	1.036	0.853

Experiment 6.

Before Injection: Normal.				After Injection.		
Neutral fat	...	...	0.300	0.405	0.336	0.662
Fatty acid	...	...	0.307	0.756	0.816	0.582
Soluble soaps	...	...	0.041	0.084	0.015	0.015
Insoluble soaps	...	...	0.272	1.696	1.456	0.276

From these tables it is observed that a maximum sublethal dose of calcium produced an extra excretion of soap. The results obtained in experiment 6 show that the soaps increased in quantity, and are almost entirely the insoluble soaps of calcium. But it is to be noted that the effect of a definite dose of calcium will have different effects on different animals. In one it will call forth a large increase in the soap excretion, while in another a large quantity of calcium is excreted, but with a relatively small accompanying amount of soap. It seems probable that it is only excessive amounts of calcium salts in the blood which throw out soap, and that increases, if they are not excessive, will simply be excreted as inorganic calcium salts through the intestine. This is demonstrated by the following experiment:

Experiment: Rabbit; Smaller Dose (2.5 c.cm. of 10 per cent. Solution of Calcium Chloride).

Before Injection.				After Injection.		
Weight of faeces	...	30	17	28	33	34
Fat and fatty acid	...	2.13	1.89	0.879	1.24	0.930
Soaps	...	0.258	0.150	0.123	0.277	0.279
Calcium oxide	...	0.432	0.371	0.330	0.713	0.514

Here there is little or no increase in the soaps, while the calcium excretion is largely increased. Consequently it would appear that calcium is usually excreted by the intestine as an inorganic salt, and that it is only when the amount in the blood is very great that fatty acid is dragged out with it and forms soaps.

An attempt was next made to find out the effect of accumulation of calcium salts after several injections at short intervals. It was noticed that following an injection, and more so after repeated injections, the faeces became dry and smaller in amount, and finally the animal died. The action of calcium salts as an intestinal astringent appears to occur after intravenous injection, and is, therefore, not altogether a local effect.

On examining an animal killed by repeated sublethal doses of calcium chloride at short intervals, extensive clotting was found to have taken place in the heart and vessels, and this clotting appeared *ante mortem*. The stomach was full of food; the appetite appeared almost unimpaired. The small intestine was full of food; the large intestine, and more especially its lower third, was almost empty, containing only a very few small and dry scybala.

A second rabbit gave similar *post-mortem* results.

The explanation appears to be as follows: The calcium equilibrium is kept constant normally by the kidneys, excess being thrown out as phosphate, carbonate, and oxalate. Calcium as inorganic salt, probably as phosphate, is normally excreted by the large intestine, and probably many cases of constipation are due to excessive excretion by the gut. If the calcium increases in the blood, the kidneys and intestine work harder to throw it out. When a certain point of accumulation occurs (which may be called the animal's calcium toleration point) the kidney is thrown out of action; the intestine is still able to excrete it, and does so, though less and less actively owing to the astringent effect.

The calcium content of the blood is now high, and finally fatty acid is combined with the calcium and excreted by the bowel as calcium soap. The intestine is now working slower, owing to intestinal paresis from astringent action of lime salts. The calcium is increasingly dammed back till the calcium causes clotting of the blood and the animal dies.

If this is so, what protection has the animal organism against a sudden invasion of calcium salts? Is immunity confined to the organic world, or does the same result occur in the inorganic?

Experiment: Increasing Doses.

A rabbit was injected with 5 c.cm. of 2.5 per cent. solution of calcium chloride. There was no appreciable increase in the excretion, calcium salts, or soaps. After an interval of five days the injection was increased to 5 c.cm. of 5 per cent. solution of calcium chloride. Again there was only a very slight increase, if any. A few days were again allowed to elapse, and a full dose (5 c.cm. of 10 per cent. solution) was injected. Neither the calcium excretion nor the soaps were increased as a result, showing clearly that the organism can accommodate itself to increasing doses of calcium salts as long as the animal is allowed to excrete one before the second arrives, and in this way it is able to neutralize a large dose, which, without such artificial chemical immunity, would have profound effects on the animal.

Weight before Injection.					Injection, 5 c.cm. of 2% Sol.		Injection, 5 c.cm. of 5% Sol.		Injection, 5 c.cm. of 10% Sol.	
					After First Injection.		After Second Injection.		After Third Injection.	
Faeces...	...	21	22	18	24	17	21	16	15	20
Fat	...	0.735	0.488	0.472	0.621	0.484	0.567	0.432	0.483	0.528
Soaps	...	0.290	0.207	0.155	0.184	0.164	0.277	0.192	0.156	0.140
Calcium oxide		0.235	0.321	0.144	0.210	0.186	0.256	0.173	0.136	0.128

Conclusions.

1. Calcium salts, when injected into the blood in small quantities, are excreted by the kidneys as phosphates, carbonates, and oxalates.

2. In larger quantities the bowel also takes part in the excretion, and the calcium is excreted as inorganic salt.

3. At a fixed concentration of calcium in the blood

greater than the above, the kidneys are thrown out of action and all the excretion is performed by the intestine, until a point is reached where the quantity in the blood is again brought below the "toleration point," when the kidney again takes on its excreting function.

4. If the concentration in the blood is greater still, the calcium is excreted also as calcium soap by the intestine.

5. The excretion of large quantities of calcium through the intestinal walls has an astringent action, and causes diminished action and paresis of the intestinal movements. The faeces cease to be excreted so freely, and if more calcium arrives in the blood the increased concentration of the calcium ion produces spontaneous intravascular clotting and death.

6. The calcium "toleration point," or the point of concentration of calcium in the blood above which the kidneys are unable to act, can be raised by injecting increasing doses of calcium chloride into the blood, provided time is given for the animal to complete the excretion of one injection before the next is given. This action appears to extend the theory of immunity into the inorganic world, and shows that the body can react to calcium salts much in the same way that it reacts to an organic toxin.

AN APPARATUS FOR X-RAY LOCALIZATION.

BY

WILLIAM COTTON, M.D.,
BISHOPSTON, BRISTOL.

IN view of the present interest in this matter I have sketched (in isometric perspective) an apparatus with many familiar and some novel details. This is adapted for almost any of the prevailing methods of localization and for any part of the body, except perhaps the orbit. Any form of upright tube stand, if not too elaborate, will do; nor is any special table required, provided it is level, narrow, long, straight-edged, and transparent to x-rays. More particularly I would call attention to the plate-holder, which consists of an upper and a lower deck, connected similarly as in the case of the two beams of the ordinary parallel rulers, and capable either of being clamped in any position or of being used free. The lower deck can be slid along either edge of any straight table, and, being reversible, can be applied to the table from either side or end, and is not any obstacle to the passage of x-rays. The upper deck can, by means of adapters, support any plate or fluorescent screen, so as to slide from either side of the table to the other. On the fluorescent screen and in close contact with its surface can be placed a widely overlapping sliding protective glass shield (in sections if preferred) of lead-glass, slightly sand-blasted or otherwise roughened on its upper surface, and sufficiently optically transparent to act as a temporary recording surface for outlining the shadows by means of a lead pencil when the screen is lit up. This recording surface being much more extensive than the fluorescent screen, permits the position of the points of the plumb-bob upon it to be marked irrespective of the actual place of a, perhaps, small fluorescent screen, and at the same time provides some protection for the hands of the observer; the pencil marks can afterwards be washed off.

O_1 and O_2 are the first and second positions of the x-ray centre of emission, constituting the Base and parallel to the plane of the fluorescent screen, which plane is always horizontal if the surface of the table is so; x_1 and x_2 are the two points indicated by the successive positions of the point of the plumb-bob, where the vertical x-rays cut the picture plane, constituting the base on the plate; and m_1 and m_2 are respectively the first and second positions of the shadow of a foreign body thrown from O_1 and then from O_2 . If on the recording surface of the shield when the light is turned on we mark the points x_1 and x_2 and join x_1 with m_1 and x_2 with m_2 we get a sort of x-shaped figure; the point of intersection is the crucial point p . If the plane of the upper deck is truly horizontal and the plumb-line correctly centred over the x-ray centre of emission (as can be done once for all in various ingenious ways), then we know that the centre of the geometrical space occupied (but probably not completely filled) by any foreign body M is always in the vertical line $P M$ below p . The distance $p M$ is the depth of this "meta-

centre" of the foreign body below p and within the patient. By means of a free plumb-line we can now mark the point on the patient vertically below p , noticing carefully at the time the depth (if any) between the surface of the patient and the point p at the level of the upper deck. We can now dismiss the patient until he is wanted for operation.

To get the depth $p M$ we have only to plot out one or other of the triangles $O x m$, and mark in the position of p in some of the ordinary well-known ways. It is wise always for the radiographer to add half an inch or more

to the depth $p M$, once he is sure of his vertical direction, when he knows he is dealing with any irregularly shaped foreign body of any size much larger than a small shot or fragment. With an undistorted service bullet the surgeon may be safely left to make his own correction.

A good deal of the apparatus depicted can be improvised with the resources necessarily present when an x-ray installation can be installed and worked. As a rule existing practice prefers to get the point x and m , over each other and to ignore p as a separate entity; this also can fairly easily be done by means of this apparatus. I and II indicate the first and second positions of the brackets bearing the tube box and the plumb-line.

SANITATION OF CAMPS (SAND AND WATER).

BY

MAJOR T. FORREST, R.A.M.C.(T.),
S.M.O., GAILES CAMP, AYRSHIRE.

AN outbreak of diarrhoea in two companies of the 16th (S.) Battalion H.L.I. on December 16th, 1914, when ninety men were affected, caused an investigation to be made. Complaints as to the quality of the water supply had already been noted, and the valuable assistance of Dr. R. M. Buchanan, City Bacteriologist, Glasgow, was obtained. The water was, however, ruled out, as the number of men affected was only a fraction of the whole number using the same water supply. The same process eliminated the food supplies, which are daily inspected, and invariably of excellent quality.

In the search for evidence of local contamination it was found that the camp kettles were being scrubbed with sand picked up indiscriminately. Clean sand was provided, and orders issued that it only was to be used for scrubbing purposes. Thereafter no further cases occurred.