Acta vet. scand. 1963, 4, 97—112.

From the Medical Department of the Royal Veterinary College,
Stockholm.

THE VOLUME OF DISTRIBUTION OF SODIUM THIOSULPHATE AS A MEASURE OF THE EXTRA-CELLULAR FLUID SPACE IN SUCKLING PIGS

By
Gunnar Tollerz

Piglets raised under the conditions of modern animal husbandry are frequently exposed to factors that tend to disturb their fluid balance. The consequences are not seldom manifest disease and death. It can be safely presumed that although usually secondary to an initiating change of the environment or to a primary disease of some other kind, such disturbances contribute substantially to the great losses among piglets below weaning age.

The essential reason for this sensitivity seems to be that fluid homoeostasis is not established in the newborn piglet but develops gradually in the growing young animal. The observation that oral administration of 0.5 % sodium-chloride solution causes salt and water retention in piglets (11) is a reflection of an elimination inability. Newborn piglets which are not fed milk lose as much as 10 % of their body-weight per day (12). This is probably mainly an effect of water loss depending on the inability of the kidneys to concentrate urine.

These conditions emphasise the importance of knowing the normal distribution of water in baby pigs. *Engelhardt et al.* (5) determined the extracellular fluid space (EFS) in pigs weighing between 13 and 100 kg. In the available literature I have not found any examination of the EFS in baby pigs however.

In the present work the EFS was determined at about weekly intervals in piglets between 4 days and 6 weeks old.

MATERIAL AND METHODS

Experimental animals: A litter of 8 piglets, 6 females and 2 males, of the Swedish Land Breed was used. During the time of the experiment they were kept together with the sow. On the 2nd and 21st days each piglet was given 2 ml. of an iron-dextran preparation ("Imposil", Pharmacia) intramuscularly. The dose corresponds to 150 mg. of Fe^{+++}. When they were 3 weeks old a commercial solid food for young pigs (Smågrisfoder, Forss) was given ad lib. in a separate pen, to which only the piglets had access.

Unless otherwise stated, all the pigs appeared to be in good health during the experimental period.

Experimental procedure: The thiosulphate (TS) method of *Cardozo et al.* (2) was used with some modifications.

The piglets were taken from the sow immediately before an experiment, without previous starvation. They were anaesthesized by inhalation of trichlorethylene. A polyethylene tube (no. 50) was introduced as an indwelling catheter into the anterior vena cava at the thoracic aperture by means of an injection cannula and a nylon guide. After withdrawal of a 2 ml. blood specimen for preparation of serum for blank determination the anaesthesia was continued by "Mebumal"[1]) intravenously. The anaesthesia was kept as light as possible; therefore, an additional small dose of the anaesthetic had to be given every 10—15 minutes in order to maintain sleep. The toe reflexes were almost always present. TS solution ($Na_2 S_2 O_3 \cdot 5 H_2O$, 15.8 g.; $Na_2 HPO_4$, 6 g.; sterile water to make a 10 % solution. Danish Pharmacopoeia) was purchased in packages, each containing 10 ampoules. One ampoule per package was tested by iodometric titration. Recovery from water averaged 98.6 %, with a range of 96.5—99.1 at 12 determinations.

The TS solution was infused into an ear vein at an amount of 2.25—2.51 ml. per kg. body-weight from a calibrated burette, which was connected with the cannula via a 2-way valve (6). An infusion time of 3.5 minutes was aimed at. Isotonic sodium-

---

[1]) Mebumal consists of 5:ethyl-5 (1-methylbutyl)-malonyl carbamide (Pentobarbitone), 1.8 g.; pentobarbitone sodium, 4.0 g.; urethane, 25.0 g.; 96 % ethanol, 15.0 g.; glycerol, 125 g.; sterile water to make 100 ml.

chloride solution in an amount, not exceeding 0.5 % of the body-weight, was infused through the other canal of the 2-way valve before and after the infusion of TS.

Beginning 20 minutes after the injection of the TS solution had started, and at intervals of about 5 minutes, 8 to 10 samples of 2 ml. of blood were taken in tubes, each containing 2 standardized drips of 1 % heparin. The blood contents of the polyethylene catheter were discarded. The collection of the blood sample was done so that the midtime coincided as closely as possible with half a minute point. This point of time was recorded. The blood samples were centrifuged within 10 minutes after they had been drawn.

The pigs were weighed before and after the experiment with an accuracy of ± 5 g. The initial weight exceeded the final weight by more than 0.5 % on 3 occasions only. The initial weights were used in the calculations. Through the series of experiments the EFS was determined 51 times, i.e. each pig was examined approximately once a week. Duplicate determinations were performed in 11 of 51 experiments. The second determination was then made 4 hours after the beginning of the first one, when no TS was left in the blood. Four of the second determinations were preceded by ligation of the renal blood vessel. This was done under "Mebumal" anaesthesia with incision in the linea alba. Otherwise the same experimental procedure was followed.

Chemical determination. The TS content of blood plasma was determined by a micro-modification (2) of Newman's indirect iodometric macro-method (9). The standard error of a single determination was calculated from duplicate determinations on 30 specimens of plasma by the formula $\pm \sqrt{\frac{\Sigma c^2}{2n}}$, where c is the difference in concentration of TS (mg./ml.) between the duplicate determinations and n the number of specimens. The standard error was 0.0052 mg., which equals 1.2 % of the mean of the determinations. The determined plasma concentration of TS did not exceed 0.6 mg. per ml., except for the cases in which the renal vessels were ligated.

Calculation of the EFS. The EFS was calculated by the formula $V = \frac{TS_{inj.}}{C_o}$, where V is the apparent volume of distribution of TS in ml., $TS_{inj.}$ the amount of TS injected (mg.), and C_o the concentration of TS in plasma (mg. per ml.) at t_o, i.e. at zero time.

The TS-concentration value obtained were plotted against time on semilogarithmic paper.

The TS concentration at t_o was estimated by extrapolation. Correction for plasma protein and for the addition of heparin was done. The amount of plasma protein was taken as 5.0 g. per 100 ml. of plasma (13) and its probable volume was obtained by multiplying this weight by 0.73 (14). The overall correction factor (correction for recovery of TS from plasma included) is 92.71 %.

Of the total 62 EFS determinations 2 were excluded, because it was not possible to draw a straight line accurately through the plotted TS concentrations. In 11 cases it was uncertain how to draw the line correctly. Here the regression lines were calculated using the equation $\log C - \log C_m = k\ (t - t_m)$, where $\log C_m$ and t_m are the means of log concentrations and of times, respectively; k is calculated by $\frac{\Sigma\,[(t_i - t_m)\ (\log C_i - \log C_m)]}{(t_i - t_m)^2}$, where t_i are the consecutive time values and $\log C_i$ the consecutive logarithmic values of the concentrations.

In 49 cases, where a straight line was drawn by free hand, k was determined by the formula $k = \frac{\log_e C_1 - \log_e C_2}{t_1 - t_2}$ or 2.303. $\frac{\log_{10} C_1 - \log_{10} C_2}{t_1 - t_2}$. Thus, only two points on the line were used. k is the slope of the straight line, i.e. the disappearance rate of TS, expressed as per cent per minute.

In 14 cases chosen at random, but not including the cases in which the renal vessels were ligated, the regression line obtained by calculation was compared with the line drawn by free hand in order to estimate the error due to free-hand drawing. Standard error $(\varepsilon) = \pm\ 1.1\ \%$.

The error of C_o, due partly to varying situation of the points and partly to the extrapolation procedure, was calculated to be 3.34 % in the same 14 experiments (4).

Transformation of a standard error in log units, ε, into percentage of C_o, (ε), was made by the following calculation:

$$(\varepsilon) \text{ per cent} = 100.\ \varepsilon^{e} \log 10.$$

RESULTS

Equilibration time.

The distribution of the 20-minute plasma-concentration values (C_{20}) indicates that the equilibration time does not exceed 20 minutes. In 3 cases however, the C_{20}-values lay remarkably high above the calculated regression line. The equations of the regression lines without the C_{20}-values were therefore calculated. The

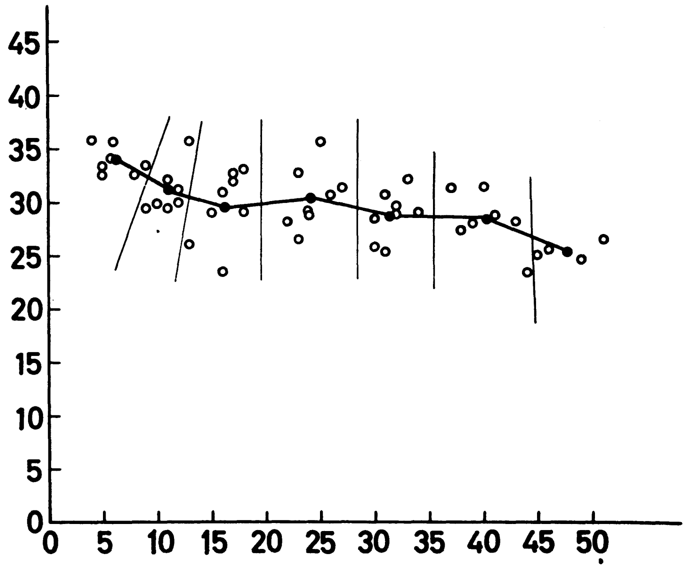

Fig. 1. EFS as a percentage of body-weight (vertical axis) of 8 suckling pigs. The age in days (horisontal axis). The straight lines intersecting the curve separate different examination intervals, each mostly comprising the whole litter.

C_{20}-values were situated within the $\pm$ 2 standard-error limits of these lines.

Equilibration time in those cases in which the renal vessels had been ligated seemed to be somewhat longer than 20 minutes. It did not exceed 30 minutes, however.

EFS. The results of the 49 single determinations of the EFS measured as the volume of distribution of TS, are set out in Table 1 and Fig. 1. The division into groups in the figure was made according to the following principles. An examination interval is the time required to examine the whole litter once, usually about a week. Thus, in the nth examination interval, or group, each pig is examined the nth time. With a few exceptions, the

Table 1. EFS and disappearance rate (k) in 49 experiments including 8 pigs whose ages ranged from 4 to 50 days.

Piglet no.	Age days	Body-weight kg.	EFS		
			litre	% of body-weight	k-value
1	9	2.01	0.67	33.5	0.96
	13	2.24	0.80	35.8	0.96
	18	2.86	0.84	29.2	1.36
	27	4.35	1.37	31.4	0.80
	33	5.43	1.75	32.2	1.45
	41	7.57	2.18	28.9	1.89
2	8	1.74	0.57	32.6	1.09
	12	2.32	0.70	30.0	1.30
	18	3.10	1.03	33.2	1.25
	26	4.06	1.25	30.7	1.21
	32	5.02	1.49	29.7	1.62
	40	6.95	2.19	31.5	1.37
	49	10.56	2.60	24.7	2.17
3	5	1.88	0.61	32.6	1.20
	11	2.96	0.87	29.4	1.45
	16	3.79	0.89	23.5	1.86
	24	4.20	1.22	29.1	1.25
	34	6.61	1.93	29.1	2.16
	47	8.77	2.06	23.5	2.50
4	5	1.96	0.65	33.4	0.97
	10	2.90	0.87	29.9	1.05
	16	3.80	1.18	31.0	1.25
	23	4.83	1.28	26.6	1.35
	31	6.57	1.68	25.5	1.77
	38	8.80	2.42	27.4	2.02
	45	11.67	2.94	25.2	2.56
5	15	2.86	0.83	29.1	1.21
	23	4.04	1.33	32.8	1.48
	30	5.30	1.51	28.5	1.32
	37	6.91	2.17	31.4	1.39
	46	9.49	2.44	25.7	1.95
6	6	1.79	0.61	34.1	1.07
	12	2.52	0.79	31.3	1.26
	17	3.03	0.99	32.8	1.10
	25	3.88	1.38	35.7	0.82
	32	5.09	1.47	28.9	1.68
	43	8.54	2.42	28.3	1.90

Table 1 (continued).

Piglet no.	Age days	Body-weight kg.	EFS		
			litre	% of body-weight	k-value
7	4	1.95	0.70	35.9	0.88
	9	3.01	0.89	29.5	1.20
	13	3.53	0.92	26.1	1.34
	22	5.38	1.52	28.2	1.06
	30	7.40	1.91	25.9	1.38
	39	10.41	2.93	28.1	1.77
8	6	1.91	0.68	35.7	0.92
	11	2.92	0.94	32.2	1.41
	17	4.11	1.32	32.1	1.12
	27	5.71	1.65	28.9	1.44
	31	6.94	2.15	30.9	1.49
	50	13.60	3.61	26.6	2.30

order of examination of the individual pigs was the same within each examination interval. Because of interfering circumstances of different kinds, the complete examination interval did not always include the whole litter, however. The exact number will be seen from Fig. 1 and Table 3.

Reproducibility.

The reproducibility of the method was tested in 11 cases by duplicate determinations (Table 2). As mentioned above, they included 4 piglets whose renal vessels had been ligated before the second examination. The deviations of the EFS between the first and the second determinations are probable in 10 cases. In 1 case, however, the volume would have increased by 0.4 litres during the experiment, which is definitely improbable.

The reproducibility can also be seen in Table 1, where individual pigs are followed through the experimental time of more than 6 weeks.

Disappearance rate.

The slope (k) of the disappearance curve, which is depending on both renal and extrarenal elimination of TS, increases with age, (Table 3). The duplicate determinations, where the renal

Table 2. EFS and disappearance rate (k) in 11 duplicate experiments and differences in body-weight and EFS between the first and second determinations.

Piglet no.	Age days	Body-weight kg.	Difference kg.	EFS litre	EFS difference litre	EFS % of body-weight	EFS difference % of body-weight	k-value
a. Two experiments of the same kind with 4 hours' interval.								
1	33	5.43		1.75		32.2		1.45
			—0.01		—0.18		—3.3	
	„	5.42		1.57		28.9		1.62
2	40	6.95		2.19		31.5		1.37
			—0.07		—0.07		—0.6	
	„	6.88		2.12		30.9		1.29
3	34	6.61		1.93		29.1		2.16
			—0.01		—0.08		—1.0	
	„	6.60		1.85		28.1		2.28
4	38	8.80		2.42		27.4		2.02
			—0.20		+0.40		+5.3	
	„	8.60		2.82		32.7		1.79
4	45	11.67		2.94		25.2		2.56
			—0.15		—0.18		—1.3	
	„	11.52		2.76		23.9		2.91
5	37	6.91		2.17		31.4		1.39
			—0.12		—0.20		—2.4	
	„	6.79		1.97		29.0		1.92
8	50	13.60		3.61		26.6		2.30
			—0.30		+0.07		+1.1	
	„	13.30		3.68		27.7		2.41
b. The second experiment with ligated renal vessels.								
1	41	7.57		2.18		28.9		1.89
			—0.15		—0.12		—1.1	
	„	7.42		2.06		27.8		0.30
2	49	10.56		2.60		24.7		2.17
			—0.28		—0.19		—1.2	
	„	10.28		2.41		23.5		0.67
5	46	9.49		2.44		25.7		1.95
			—0.27		—0.22		—1.6	
	„	9.22		2.22		24.1		0.57
7	39	10.41		2.93		28.1		1.77
			—0.31		—0.20		—1.0	
	„	10.10		2.73		27.1		0.37

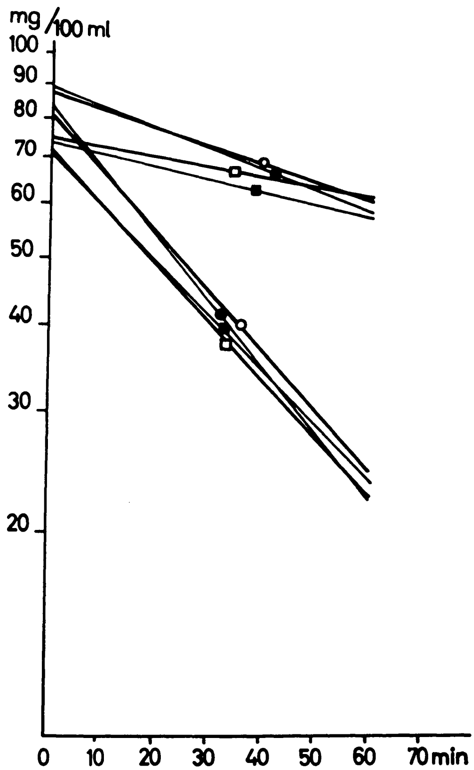

Fig. 2. Disappearance of TS from plasma in 4 duplicate determinations of EFS. The steep lines show the disappearance lines in the first determinations, the virtually horizontal lines the disappearance lines in the second determinations, after ligation of renal vessels. Corresponding lines have the same signs. The TS dose per kg. bodyweight was 1.23 ± 0.63 % larger in the second than in the first determination.

vessels were ligated (Fig. 2, Table 2 b), show the order of importance of different elimination routes. The ratio of k after and before ligation is 0.24.

Influence of "Mebumal" anaesthesia.

The influence of deep "Mebumal" anaesthesia on the disappearance curve was examined in 5 piglets. The usual procedure was followed for at least 35 minutes after the injection of the TS. The additional dose sufficient to keep the pig in light sleep was then doubled or even trebled, resulting in a deep level of

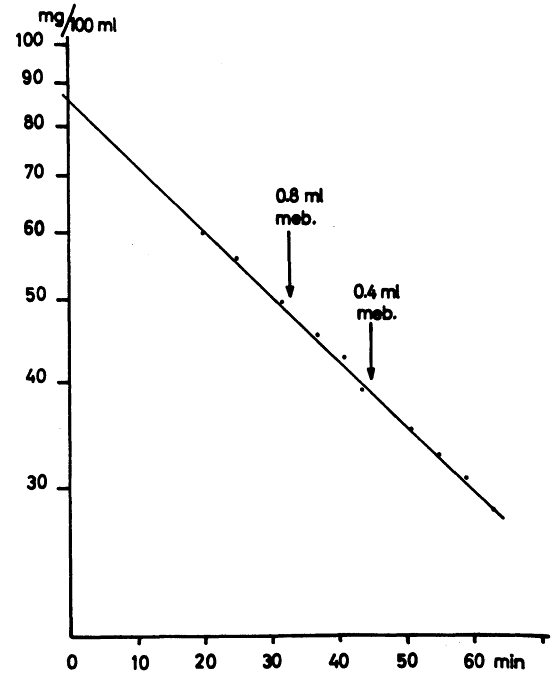

Fig. 3. Disappearance of TS from plasma in a 31 days old pig weighing 6.6 kg. The arrows indicate when exceptionally large doses of "Mebumal" were given intravenously.

Table 3. EFS and disappearance rate (k) in 7 age-groups, k is calculated from the slope of the disappearance curve, expressed as per cent per minute.

Age-group	Number of obser-vations	Mean age days	Mean EFS % of body-weight	Mean k	Range
I	7	6	34.0	1.01	0.88—1.20
II	7	11	31.2	1.23	0.96—1.45
III	8	16	29.6	1.31	1.10—1.86
IV	8	24	30.4	1.27	0.82—1.48
V	8	32	28.8	1.61	1.32—2.16
VI	7	40	28.4	1.83	1.37—2.50
VII	4	47	25.6	2.25	1.95—2.56

anaesthesia with abolished toe reflexes. In no case did this produce any deviation from straight linearity on semiligarithmic paper (Fig. 3.).

DISCUSSION

It is obvious that there are great variations of the EFS between different pigs of about the same age, and in the individual pig from time to time.

The variations within the age-groups are shown in Fig. 1. The degree of variation can be conveniently expressed as coefficient of variation. The coefficients of variations for the groups in Fig. 1 are 4.0, 7.3, 11.3, 9.5, 8.0 and 9.5 % (The last group is not included because of the few values).

The variation from time to time for the individual pig can be seen in Table 1. Although the mean values of the age-groups can be connected by a fairly continuously descending curve (Fig. 1), it is apparent that if the same is done for the individual pigs the tendency to decline is obscured by a considerable variation. Thus, the correlation of the EFS with age, although obvious from Fig. 1, is not close and the relative size of the EFS is not characteristic of the individual pig.

The reason for these variations are probably several. Errors introduced after the infusion of the TS become apparent through the somewhat scattered values of TS-plasma concentrations along a straight line on the semilogarithmic paper. These errors, the error of extrapolation included, amount to $\pm$ 3.34 %. For an EFS equal to 33.3 % of the body-weight, this corresponds to $\pm$ 1.11 % of the body-weight.

Varying speed of the TS infusion will probably influence the volume of distribution. If the infusion is rapid, a relatively larger quantity of TS will be eliminated through the kidneys at an early stage, *i. e.* during and shortly after the infusion. The measurements after the equilibration time will then show low TS concentrations and consequently an erroneously large volume of distribution.

Although efforts were made to keep the infusion time constant, it did in fact vary. The possible effect of this variation was examined as follows. The infusion time for each experiment is known. The EFS-values were grouped into those being higher and those being lower than the mean of the respective age-group. The mean infusion time was calculated for these two groups. It turned out to be 203 seconds for the group of higher values and 207 seconds for the group of lower values. Thus it seems to be none correlation between time of infusion and the EFS.

All the piglets appeared to be in good health, except on one occasion, when 2 piglets had diarrhoea for 2 or 3 days. No experiment was done on these piglets during that time. At 42 days of age the mean body-weight of the pigs was 9.24 kg. (range 7.75—11.90). The low mean and great range of body-weight depend on the following factors. The mother was a gilt. Gilts generally give smaller amounts of milk than do older sows. The piglets must be quite awake before being returned to the sow after the experiment. At each experiment they were therefore separated from the sow for 10 to 20 hours. When taken back, the piglets had to struggle to get her teat again, which, especially for the smaller ones, could be quite a task. Thus, the variation in size of piglets may explain part of the variation of the EFS within the same age-group.

The piglets were taken to the experiments without previous starvation. The object was to shorten the time of their separation from the sow as much as possible, and thus the time of starvation. Their stomachs must therefore have changed with regard to quantity of food contents. Over the first 4 weeks the food of piglets consists almost entirely of the sow's milk. During this period the contents of the intestines are fairly constant and small in relation to the contents of the stomach. The piglets suckled on an average every 2 hours in the day. As a rule the experiments were made at 11 a.m. and 2 p.m. Weighing some of the pigs at the age of 3 weeks (body-weights about 4½ kg.) showed that they ate approximately 60 ml. per meal. The variation of body-weights, brought about the fact that the pig might on one occasion have been taken for experiment shortly before and on another shortly after a meal, was roughly $\pm$ 1.2 %. A corresponding calculation for other ages shows a relative influence of similar order of magnitude.

When the pigs began to eat creep feed it could be expected that the contents of their stomachs would not vary so much from time to time. Accordingly, the error introduced by variation of body-weights ought to be less during the last 2 weeks.

On the other hand, it is conceivable that the contents especially of the large intestine, increased as the pigs started eating creep feed. This may have increased their body-weights so that the calculated relative EFS became too low. The intestinal content was weighed after the second experiment with 3 nephrectomized pigs and expressed as a percentage of the whole body-weight. The body-weights were 9.33, 7.51, and 10.21 kg. and the percentages 3.21, 3.72, and 4.21, respectively, with a mean of 3.71. When they were killed, these pigs had been starved for 5—6 hours, which may have had some influence on the ratio of the intestinal content weights to the body-weights. Yet, the figures give a rough estimation of the error introduced by a varying intestinal content in pigs of this size. The mean EFS as a percentage of the whole body-weight is 26.3. When the intestinal-content weight is subtracted, the percentage is 27.5. The difference is 1.2 %. The ranges of the EFS within the different age-groups, the last one excluded, are 3.3, 6.4, 9.7, 9.1, 6.7, and 8.0 %. It is therefore probable that varying filling of the digestive tract contributes but little to the variation of the relative EFS within the age-groups of pigs.

Ikkos et al. (10), in man, compared the TS method with the inulin method (8), which is considered to be the most reliable method for EFS determination. Although the mean values obtained with the two methods were nearly equal, the discrepancies between apparent volumes were fairly great. These discrepancies could in part be accounted for by the variation of the rate of disappearance of TS from plasma. By introducing a corrected formula for calculation of k they were able to produce a closer agreement between the inulin and TS methods.

The inulin method is difficult to apply to piglets, because of the strain inflicted upon the animal.

The marked correlation between k and age (Table 3) makes it difficult to study a possible association between k and EFS.

The great variation of k and EFS in age-groups II, III, and IV (Table 3, Fig. 1) depends essentially on one experiment in each group. The values for EFS and k in these experiments and the respective means of the groups are shown below.

Pig. no.	age-group	EFS	k	mean EFS	mean k
1	II	35.8	0.96	31.2	1.27
3	III	23.5	1.86	29.6	1.31
6	IV	35.7	0.82	30.4	1.27

The two very low k-values seen above, *i.e.* a very slow elimination of TS from the blood, seem to give EFS-values that are much higher than those for the other pigs of the litter in the respective age-groups.

A low k-value can of course be a true expression for a larger

EFS, but in these cases the EFS seems to be improbably large. In the same way, the very high k-value seems to give an improbably small EFS.

Boling et al. (10) and *Chesley et al.* (14), by experimental alteration of k in different ways, without alteration of the EFS, were able to produce a significant change in the volume of TS distribution in dogs and in human subjects.

Reproducibility.

In the 7 duplicate determinations (Table 2a) the first one gave a mean EFS of 29.0 % of the body-weight. The mean decrease of the EFS in the second determination was — 0.31 ± 2.85 % of the body-weight. The standard error corresponds to 10.1 % of the mean EFS. The time between the 2 determinations was about 3 hours; during this interval the pigs were not given any food or water. If the mean decrease of body-weight is presumed to be due entirely to loss of extracellular water, the EFS would be expected to decrease by 1.4 % of the body-weight. It is difficult to decide, however, to what extent the weight-decrease depends on a decrease of the EFS. Absorption from the intestine influence the EFS, defaecation and urination influence the body-weight. Exchange between extracellular and intracellular water takes place, and water is produced by metabolic processes. Six of the duplicate determinations gave probable deviations, whereas one (piglet no. 4) resulted in an improbable deviation of + 5.3 % of the body-weight.

Therefore, it seems logical to make some calculations without this value. The mean decrease of the EFS in the second determination of the 6 other pigs is 1.25 ± 0.91 % of the body-weight. This standard error corresponds to 3.3 % of the mean EFS.

The results of the 4 duplicate determinations where the kidney function was interrupted before the second determinations are in good agreement with one another. The mean decrease of the EFS, 1.23 ± 0.25 % of the body-weight is probable. The disappearance rate (k) was reduced to about 24 % of the original value, but this way of altering k did not influence the EFS in an unlikely manner.

It is of interest to note that EFS-values obtained by the TS method in children between 1 month and 1 year of age (7) compare well with the values reported in this paper for piglets from 4 days to 1½ months old.

Engelhardt et al. (5), using the same method, found EFS-values of 29.1 % and 29.6 % in two 51 day old pigs. In the material presented here the corresponding group (VII, Fig. 1) at the age of 48 days showed a mean EFS value of 25.6 % of the body-weight. It is not possible to say whether the difference is due to inconsistencies in the application of the method or to real dissimilarities between the materials.

REFERENCES

1. *Boling, E. A. and Wilson, G. M.:* The effect of changes in renal function on the apparent volume of distribution of sodium thiosulfate. Surgical Forum 1953, *4*, 572.
2. *Cardozo, R. H. and Edelman, I. S.:* The volume of distribution of sodium thiosulfate as a measure of the extracellular fluid space. J. Clin. Invest. 1952, *31*, 280.
3. *Chesley, L. C. and Lenobel, A.:* An evaluation of the single injection thiosulfate method for the measurement of extracellular water. J. Clin. Invest. 1957, *36*, 327.
4. *Dixon, W. J. and Massey, Jr., F. J.:* Introductions to statistical analysis. McGraw-Hill Book Company Inc. New York, 1957.
5. *Engelhardt, W. v. und Hörnicke, H.:* Untersuchungen über das extracelluläre Flüssigkeitsvolumen und die Thiosulfat-Total-clearance wachsender Schweine. Pflügers Arch. Physiol. 1958, *268*, 148.
6. *Frank, H. A. and Carr, M. H.:* A simplified method for estimation of the extracellular fluid space. J. Lab. & Clin. Med. 1955, *45*, 973.
7. *Friis-Hansen, B.:* The extracellular fluid volume in infants and children. Acta paediat. 1954, *43*, 444.
8. *Gaudino, M., Schwartz, I. L., and Levitt, M. F.:* Inulin volume of distribution as a measure of extracellular fluid in dog and man. Proc. Soc. Exper. Biol. Med. 1948, *68*, 507.
9. *Gilman, A., Philips, F. S. and Koelle, E. S.:* The renal clearance of thiosulfate with observations on its volume of distribution. Amer. J. Physiol. 1946, *146*, 348.
10. *Ikkos, D., Ljunggren, H., Luft, R., and Sjögren, B.:* Measurement of the extracellular fluid volume by thiosulfate II. Acta physiol. scandinav. 1956, *35*, 254.
11. *Mc Cance, R. A. and Widdowson, E. M.:* Hypertonic expansion of the extracellular fluids. Acta paediat. 1957, *46*, 337.
12. *Morril, C. C.:* Studies on baby pig mortality. X. Amer. J. vet. Res. 1952, *13*, 322.
13. *Nordbring, F. and Olsson, B.:* Influence of ingestion of colostrum on protein pattern and antibody titre in sera from suckling pigs and the changes throughout lactation. Acta Soc. Med. Upsal. 1957, *62*, 193.

14. *van Slyke, D. D., Hiller, A., Phillips, R. A., Hamilton, P. B., Dole, V. P., Archibald, R. M. and Eder, H. A.:* The estimation of plasma protein concentration from plasma specific gravity. J. Biol. Chem. 1950, *183,* 331.

SUMMARY

The extracellular fluid space (EFS) was determined using the thiosulphate method. One litter of piglets was used for the experiment, which comprised repeated determinations during the first 6 weeks of life. The mean EFS gradually fell from 34 % of the body-weight at the age of 6 days to about 28 % at the age of 41 days. The reproducibility of the method was tested by two determinations, one four hours after the other, on each of 11 piglets. Before 4 of the second determinations the renal vessels were ligated. The results were on the whole consistent. Large variations occurred in individual pigs from time to time and between pigs of the same age.

ZUSAMMENFASSUNG

Der Verteilungsvolumen des Natrium-Thiosulphat als Masstab für den extracellulären Flüssigkeitraum bei Säuglingsferkeln.

Der extracelluläre Flüssigkeitraum wurde mit der Thiosulphat-Methode bestimmt. Ein Wurf Ferkeln wurde während der sechs ersten Lebenswochen wiederholt untersucht. Der Flüssigkeitsraum betrug c:a 34 % des Körpergewichtes bei sechstägigen Ferkeln und verminderte sich bis 28 % bei 41 Tage alten Ferkeln. Zwei Bestimmungen mit einem Zeitunterschied von vier Stunden wurden bei elf Ferkeln vorgenommen. Vor den Bestimmungen aus der zweiter Reihe wurden bei vier die Nierengefässe unterbunden. Hauptsächlich zeigten die Ergebnisse eine gute Übereinstimmung. Grosse Variationen kamen vor bei einzelnen Ferkeln bei verschiedenen Untersuchungsgelegenheiten als auch zwischen den gleichältrigen Ferkeln.

SAMMANFATTNING

Distributionsvolymen av natriumtiosulfat som ett mått på extracellulära vätskerummet hos diande grisar.

Den extracellulära vätskevolymen bestämdes i enlighet med tiosulfatmetoden. En kull grisar följdes genom upprepade bestämningar under de 6 första levnadsveckorna. Vätskevolymen minskade från c:a 34 % av kroppsvikten vid 6 dagars ålder till omkring 28 % vid 41 dagars ålder. Metoden kontrollerades genom att två bestämningar med 4 timmars mellanrum utfördes på vardera av 11 grisar. Före 4 av andra-bestämningarna ligerades njurkärlen. Resultaten visade i stort sett god överenstämmelse. Stora variationer förefanns hos en och samma gris vid olika undersökningstillfällen liksom mellan lika gamla grisar.

(Received September 24. 1962).