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DISTRIBUTION OF SE^{75}-TAGGED SODIUM SELENITE IN PIGS

By

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In recent years it has been found that the use of selenium as selenite is an effective prophylactic and therapeutic measure against muscular degeneration in pigs (*Lannek et al.*, 1960, 1961). Selenite is also effective in preventing the development of toxic liver dystrophy in pigs (*Eggert, Patterson & Stokstad,* 1957; *Grant & Thafvelin,* 1958).

The use of selenium as selenite in veterinary medicine necessitates a full knowledge of its metabolism in swine, since selenium and selenium compounds may be toxic to man and farm animals. In certain seleniferous areas manifestations of poisoning like "blind staggers" and "alkali disease" have been reported in farm animals (vide *Goodman & Gilman,* 1946; *Underwood,* 1956).

The metabolism of sodium selenite tagged with radioselenium (Se^{75}) has therefore been studied in pigs after oral, subcutaneous and intramuscular administration in single doses with and without the addition of stable selenite.

MATERIAL AND METHODS

Sodium selenite tagged with Se^{75} was obtained from Amersham with a specific activity of 2 mC per g of selenium. The radioactive dose administered was between 116 and 130 μC. Seven healthy pigs of the Swedish Land Breed, females and castrated males, whose weights ranged from 30 to 36 kg received doses of Se^{75} with or without stable Se (sodium selenite) as specified in Table I. Subcutaneous injections were given behind the ear and

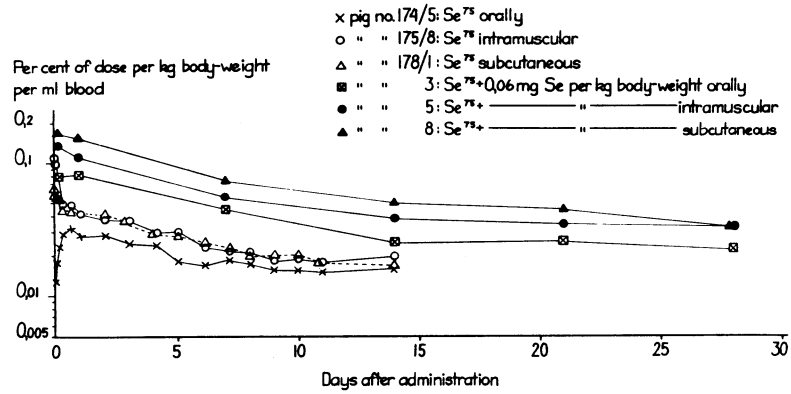


Fig. 1. Per cent of dose (sodium-Se^{75}-selenite) per kg body-weight per ml of blood after respectively oral, intramuscular and subcutaneous administration with and without extra carrier. No blood samples were taken from pig 34/9.

intramuscular injections in the neck. The oral doses were given after 12 hours' fasting, mixed in about 100 g of feed. Blood samples were drawn from the anterior vena cava of the pigs at intervals as shown in Fig. 1. Heparin was always added to the blood samples. At slaughter, which occurred after 7, 14, and 28 days, respectively, the organs, as shown in Table I, were examined for radioactivity. The organs chiefly used for human food were chosen.

The radioactivity measurements were performed in a well crystal (NaCl, Tl) manufactured by Frieseke & Hoepfner). The volume of the samples was always 2.0 ml. Measurements were made during at least 1 minute, or at least 1000 counts were recorded. Samples of organs were wet-ashed and 2.0 ml of a dissolution in nitric acid counted in the crystal.

As a standard 0.00116, 0.00123 and 0.00130 μC, respectively, of sodium-selenite-Se^{75} in 2.0 ml of distilled water served throughout the measurements. The standard was prepared simultaneously with the samples injected.

The results of the radioactivity determinations were generally expressed as the percentage of the dose admistered per kg body-weight that was found in 1 kg of organ examined. Radioactivity in blood samples was expressed as the percentage of original dose per kg body-weight that was found in 1 ml of blood. This

value was corrected for total body-weight of the pig at the time of blood sampling, because of the increase in body-weight during the experiments.

RESULTS

Biological half-life of Se^{75}: The results of radioactivity determinations in blood samples from the pigs are shown in Fig. 1. After a rapid initial fall in concentration, the blood content decreases with a half-life of about a week.

From the determinations in organs (Table I) it will be seen that the concentrations vary considerably from organ to organ with time and that with a few exceptions they decrease with time.

Radioselenium in organs at slaughter: In Table I the content of Se^{75} in the tissues examined are expressed as the percentage of original dose per kg body-weight found in 1 kg of organ examined.

Effects of sodium selenite as carrier: Sodium selenite was in some cases administered simultaneously with the radioselenium as carrier. Details are given in Table I. The results of the blood determinations (Fig. 1) show that the addition of carrier resulted in higher relative radioactivity values in the blood. The slope of the blood-curves seems, however, to coincide with those from animals which did not receive extra carrier.

Radioactivity present at the site of injection at death: The sites where radioselenium had been administered subcutaneously or intramuscularly were examined separately. The results, expressed as the percentage of total original dose found in 1 kg of tissue, are shown in Table I.

DISCUSSION

The curative dose in muscular degeneration was by *Lannek et al.* (1961) found to be 0.02 mg of Se per kg body-weight given parenterally for 3 days. Accordingly, a total of 0.06 mg of Se per kg body-weight would be administered in such cases.

In the present investigation the animals were slaughtered at 7, 14 and 28 days, respectively, after administration of selenium. The highest contents were found at the sites of injection in the kidneys and the liver, whereas low values were found in the muscles.

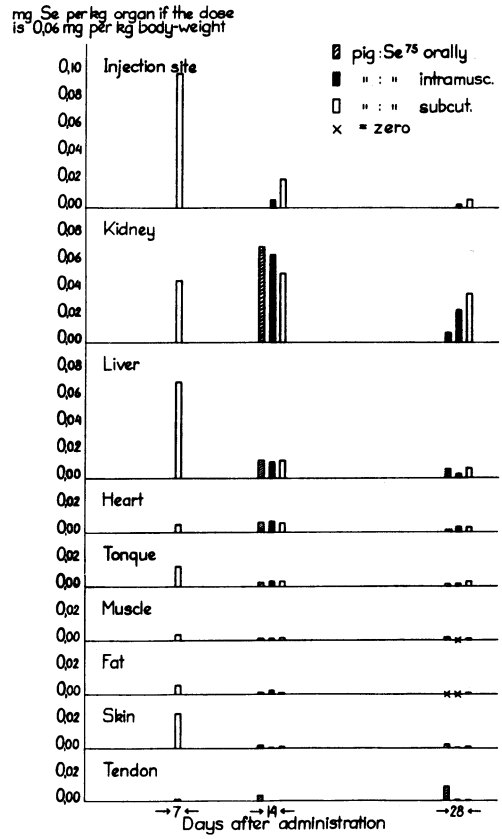
From the data given above and in Table 1 calculations have been made and expressed in Fig. 2 in order to obtain an approxi-

Table I.

Dose of selenium, route of administration and percentage of dose per kg body-weight present per kg organ at slaughter.

Pig no.	μC of Se-75	Carrier-Se	Route	Weight kg	Killed days after administration	Percentage of original dose per kg body-weight per kg of organ								
						Site of injection	Kidney	Liver	Heart	Tongue	Muscle	Fat	Skin	Tendons
34/9	130	0.2	subcutaneous	36	7	164.6	77.0	119.2	10.0	25.5	7.15	12.4[1])	43.0[1])	3.67
174/5	116	—	oral	30	14	—	117.3	21.3	11.9	5.18	2.67	1.37	3.14	6.95
175/8	116	—	intramuscular	34	14	9.43	108.6	19.5	12.8	6.10	2.71	4.23	0.71	not measured
178/1	116	—	subcutaneous	31	14	34.9	86.3	21.3	11.2	6.41	3.16	1.14	1.50	not measured
3	123	0.06	oral	31	28	—	11.5	10.4	2.84	2.09	3.13	0	4.17	17.8
8	123	0.06	intramuscular	33	28	4.03	39.4	4.78	7.21	3.63	0	0	0.97	1.51
5	123	0.06	subcutaneous	33	28	9.20	56.1	11.2	6.49	5.60	1.47	0.86	2.22	0.93

[1]) These extraordinary high values cannot be explained at present. The difficulties in estimating radioactivity in wet ashed fat should be pointed out, however.



F i g. 2. Graphical demonstration of theoretically deduced values for Se (as mg per kg of organ) in various organs after administration of a single dose of 0.06 mg Se as sodium-selenite per kg body-weight.

mate value for the amount of selenium that will be present in the organs after oral and parenteral administration of a single dose of 0.06 mg Se per kg body-weight as selenite.

A total parenteral dose of 0.06 mg per kg would give 0.002 mg of selenium per kg flesh 14 days after the administration and 0.001 mg per kg flesh after 28 days. We wish to stress that these calculations are very rough and that they are made only in order to give an approximate value for the selenium retention to enable evaluation of the possible risk of the therapeutic use of selenium from the viewpoint of food hygiene.

The kidneys and the liver show considerable retention of selenium. For the kidneys a similar calculation gives values of

0.07 mg 14 days after parenteral administration of the doses mentioned above, and for the liver 0.07 mg 7 days after parenteral administration. All these figures represent mg of selenium in 1 kg of organ.

At the site of injection 0.1 mg per kg is deposited 7 days after injection and 0.006 mg 28 days after injection.

In the seleniferous parts of the world no clear human disease has ever been found to be attributable to the selenium content of the food locally produced (*cit. Underwood,* 1956). It might be interesting to compare our calculated values with those reported in food from seleniferous parts of the world. The levels in such meat are reported to vary from 1.17 to 8.0 mg per kg (*Underwood,* 1956). Judging from our results, therapeutic use of sodium selenite in the doses mentioned here would never give selenium concentrations of such an order if the pigs are slaughtered one week or later after receiving the last dose. At present it is not possible to state whether earlier slaughter would be safe.

It is our opinion, however, that solutions of sodium selenite used parenterally for curative purposes in pigs should be stained with, *e. g.,* Sudan red, so that the site of injection could easily be avoided for human food.

In the blood a maximal amount of 0.17 per cent of the original dose per kg body-weight per ml was found. This peak occurred 3 hours after parenteral administration. This would give roughly 0.1 mg of selenium per kg of blood at 3 hours and 0.05 mg per kg of blood at a week after administration, which would not seem dangerous to man, judging by the figures from seleniferous districts.

According to *Smith et al.* (1940) people in a seleniferous district (South Dakota, USA) consume about 0.2 mg of selenium per kg body-weight and day, as judged by the urinary excretion of selenium. This is further evidence showing that the selenium content in organs and flesh from pigs given therapeutic sodium selenite in the dose here discussed should not be harmful to human consumers.

The excretion curves in the blood (Fig. 1) show that there must be several ways of elimination simultaneously involved. The first rapid fall is probably due to urinary and faecal excretion as well as to some elimination through the lungs (*McConnell,* 1941, 1942). Later on the curves are not straight, probably owing to the fact that selenium enters several metabolic pathways,

for instance replace sulphur (*Underwood,* 1956) and, furthermore, is accumulated in erythrocytes (*McConnell,* 1941) and combines with proteins (*McConnell & Wabnitz,* 1957). Experiments with the animals in a state of equilibrium will probably throw further light on these mechanisms.

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SUMMARY

Pigs were given sodium-selenite-Se^{75} orally, subcutaneously and intramuscularly without and with extra carrier. After 7, 14 and 28 days, respectively, the animals were slaughtered and the organs removed and examined for radioactivity. Blood samples were drawn regularly between the injection and the slaughter. There was an accumulation of selenium at the site of injection, in the kidneys and the liver. A calculation reveals that therapeutic use of sodium selenite in doses recommended in the literature will not cause selenium concentrations in flesh and organs of a magnitude harmful to man, as judged by the amounts of selenium reported in food from seleniferous districts.

ZUSAMMENFASSUNG

Verteilung von Se^{75}-gekennzeichnetem Natriumselenit bei Ferkeln.

Natriumselenit-Se^{75} wurde Ferkeln oral, subkutan und intramuskulär gegeben sowohl mit als auch obne Vehikel verabfolgt. Nach 7, 14 bzw. 28 Tagen wurden die Tiere geschlachtet und der Radioselengehalt in verschiedenen Organen bestimmt. Ebenso wurde der Radioselengehalt in Blutproben festgestellt, die regelmässig während der Versuchsperiode entnommen wurden.

Selen häufte sich in den Nieren sowie der Leber an und blieb lange an der Injektionsstelle zurück. Mit Hilfe der erhaltenen Werte für Radioselen in den Organen wurden die Selengehalte berechnet, die sich vermutlich bei Ferkeln nach der Verabreichung der in der Literatur empfohlenen Dosen aufspeichern können. Es zeigte sich, dass die Selengehalte nicht diejenigen Mengen übersteigen dürften, welche im Futter aus selenhaltigen Landwirtschaftsdistrikten in USA berichtet wurden, und deshalb sollte eine Selentherapie und Selenprophylaxe für die Konsumenten unschädlich sein.

SAMMANFATTNING

Fördelning av Se^{75}-märkt natriumselenit hos grisar.

Natriumselenit-Se^{75} administrerades till grisar oralt, subkutant och intramuskulärt såväl med som utan extra carrier. Efter respektive 7, 14 och 28 dagar slaktades djuren och radioselenhalten i olika organ bestämdes. Likaså bestämdes radioselenhalten i blodprov som togs regelbundet under försöksperioden.

Selen ackumulerades i njurarna och levern samt stannade länge kvar på injektionsplatsen. Med tillhjälp av de erhållna värdena för radioselen i organen beräknades de selenhalter som kan tänkas uppkomma hos grisar som erhåller natriumselenit i de doser som rekommenderas i litteraturen. Det visade sig att selenhalterna icke kommer att överstiga de som rapporterats i föda från selenhaltiga jordbruksdistrikt i USA och därför torde selenterapi och selenprofylax vara oskadligt för konsumenterna.

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