killing chick embryos more rapidly and reaching higher titers than any of the other strains tested; and strain ASGH consistently kills chick embryos one day earlier than strain BOUR for all doses inoculated(2). Reeve and Taverne(4) suggested that the greater virulence of some TRIC strains for the chick embryo could be due to the greater toxicity of these strains: The results presented here suggest that all strains were equally lethal for mice, and thus toxicity tested in mice cannot explain these differences in virulence. Since all strains, including TE 55, appeared equally toxic, the ability to produce disease in primates may not depend on this factor; with strains pathogenic for the conjunctiva toxicity appears unrelated to the severity of disease induced in experimentally inoculated primates.

Summary. Yolk-sac suspensions of 3 strains of trachoma and 3 strains of inclusion conjunctivitis virus isolated and grown in this laboratory, and the TE 55 strain of trachoma, were tested for toxicity for mice following intravenous injection. All suspensions were equally toxic for mice, requiring between 3.3 $\times$ 10^5 and 8.4 $\times$ 10^6 ELD 50 per MLD 50, and all contained similar numbers of virus particles, an average of 6 $\times$ 10^9/g of yolk sac. The egg-lethal titers of TE 55 virus suspensions were 10-fold higher than those of the other strains tested, but this strain was no more toxic for mice and possessed the same total number of particles per g of yolk sac. Biological differences of the strains, such as virulence for chick embryos and pathogenicity for the conjunctiva, do not appear to depend on the relative mouse toxicity of the strains.

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Distribution of Cesium^{137} After Chronic Exposure in Dogs and Mice.* (29252)

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The distribution of cesium in mammalian tissues resembles that of potassium, in that the higher concentrations are found in muscle and other soft tissues(1-3). Reports from Japan(4) and from the United States(5) indicate that the concentration of fallout Cs^{137} is at least as high in bone as in muscle. Exposure to fallout products usually is a chronic exposure to a varying daily dose, and equilibrium conditions (output equals intake) can only be temporary or fortuitous. Body burdens vary with time and intake(6,7) and can be distributed among tissues in different proportions from those that follow acute exposure. The distribution of Cs^{137} in 3 dogs and 6 mice, after more than 400 days of continuous exposure to a constant daily dose, is reported here.

Methods. The three 7-year-old male beagles weighed between 14.4 and 15.1 kg each at the beginning of exposure. Each dog was

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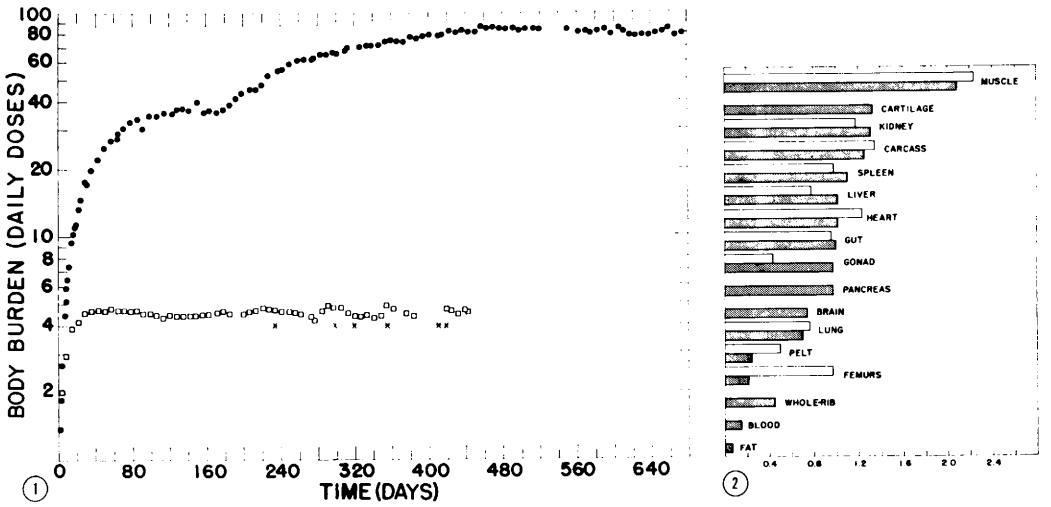

FIG. 1. Whole-body activity in dogs (circles) and in mice (squares) chronically exposed to Cs^{137}. Asterisks indicate death among the 12 mice started.

FIG. 2. Relative activity of tissues in dogs (hatched) and in mice (open). Relative activity is the ratio of concentration in an organ or tissue to whole-body concentration.

handfed daily with a food pellet contaminated with aproximately 16 nanocuries of carrier-free $Cs^{137}Cl_2$. The dogs were maintained on Kasco dog food and water *ad libitum*. Whole-body activity was measured periodically in the Los Alamos human counter(8).

The 12 RF_1 female mice, 215 days old at beginning of exposure, were maintained with free access to Purina Lab Chow and water, and the water was contaminated with approximately 13 nanocuries of carrier-free $Cs^{137}Cl_2$ per ml. Whole-body activity was assayed periodically in the Los Alamos small animal counter(9).

The dogs were killed by bleeding under nembutal anesthesia 674 days after the beginning of exposure. At 442 days after exposure, half of the 12 mice had died, presumably from natural causes. The remaining 6 were killed by ether anesthesia. From each animal the following tissues and organs were assayed for Cs^{137} activity: kidneys, spleen, liver, heart, gut with contents from esophagus to rectum, gonads (testes of the dogs; ovaries, accessory sex organs, and mesenteric fat of the mice), lungs, pelt and adherent tissues, and both femurs. The following tissues were assayed from the dogs only: brain, rib bone and costal cartilage, pancreas, blood, and fat. The carcass, chiefly muscle, bone, and fat, was assayed separately after removal of the other tissues. The proximal and distal heads of the dog femurs were removed and the heads and shafts assayed separately. Then the marrow was scrubbed from the shaft with tap water and cotton swabs, and the activity of the empty femur shaft was measured. The marrow was removed from the ribs by scraping, and the ribs were assayed both with and without marrow.

A group of 10 RF_1 female mice, approximately 90 days old, was exposed to a constant dose of Cs^{137} for 50 days and then killed. Both femurs were removed from each mouse, cleaned with scalpels, and the 20 whole femurs assayed as a group. Both heads were removed from each femur and all the femur heads assayed together. The Cs^{137} activity in the grouped shafts was assayed before and after the marrow was removed from the shafts by flushing with tap water and swabbing with tissue paper.

Results. Average whole-body activity for both species is shown in Fig. 1. The X axis represents days, and the Y axis represents whole-body activity in units of daily doses. Mouse deaths are indicated by asterisks. The distribution of Cs^{137} is given in Table I as the average per cent of body burden per gram. Fig. 2 shows the average "relative

TABLE I. Cesium^{137} Distribution in Dogs and Mice After Chronic Ingestion.

Organ	% of body burden per g	
	Mice	Dogs
Whole body	3.72	.00620
Carcass	5.05	.00781
Pelt	1.84	.00156
Gut	3.58	.00622
Liver	2.91	.00636
Lungs	2.83	.00434
Heart	4.60	.00632
Kidneys	4.40	.00824
Spleen	3.66	.00690
Gonads	1.63	.00603
Muscle	8.34	.01294
Pancreas	—	.00602
Blood	—	.00082
Fat	—	.00041
Brain	—	.00451
Femurs	3.60	.00127
Whole rib	—	.00279
Rib bone	—	.00168
Rib marrow	—	.00480
Cartilage	—	.00830

activity" for the two species. The "relative activity" is the ratio of tissue concentration to whole-body concentration and affords a basis for comparisons among species.

When the marrow was removed, the femur shafts of both dogs and mice lost about two-thirds of their activity, while the ribs lost a little more than half their activity.

Discussion. The source of the increased whole-body activity among the dogs at 190 days is uncertain. Tentatively, a move from unheated quarters to heated dog runs during severely cold weather was implicated, but absence of further seasonal fluctuations in whole-body activity eliminates temperature as the cause. Whole-body activity in both species had become constant when the animals were killed to determine isotope distribution.

Cesium distribution in both species is uniform. Activity is highest in muscle, followed by carcass, kidneys, and cartilage, in each of which the concentration is greater than in the whole body. The carcass has a high concentration because it is largely muscle. The high concentration in the actively secreting kidney (urinary:fecal ratio for mice = approximately 7) is similar to the findings of others after both acute(1) and chronic(2) exposure. Nelson *et al*(3) report a high concentration in cartilage in mice after acute administration of Cs^{137} and suggest that cartilage acts as a cation exchanger. No mouse cartilage was measured in this experiment, but the cesium concentration in the costal cartilage of the dogs agrees with the findings of these investigators. The concentrations in other soft tissues, with the exception of the mouse gonad, pelt, blood, and fat, approximate the whole-body concentration. The low concentration in fat is similar to the low potassium concentration in fat(10). It is probable that the large amount of fat and the small amount of muscle account for the low concentration in the pelt and in the mouse gonad. Both the pelt and blood have low cesium concentrations after acute administration(1).

The concentration in bone differs in the two species (relative activity of mouse femur 0.97; of dog femur 0.21) and within the same species (relative activity of the dog rib 0.45). These results may be explained partly by the differences in activity and distribution of red and fatty bone marrow. The centrifugal distribution of fatty marrow in adult mammals has long been known(11). Hood and Comar(1) show that sternal marrow has a greater Cs^{137} concentration than femoral marrow. However, Jaffe(12) reports that the red marrow of the long bones of mice is not replaced by fatty, yellow marrow. The red marrow of the dog ribs and mouse femurs contributes to the activity of these bones, while the dog femur, with its fatty marrow, has only low activity. Other factors are involved, such as the ratio of marrow to bone which differs in rib and femur and probably is different in dog femur and mouse femur.

Anderson and Gustafson(5) confirm the finding of Yamagata and Yamagata(4) that the concentration in human ribs was a great as in soft tissue. The Yamagatas assumed the activity was in the marrow, while Anderson and Gustafson found the activity in ribs brushed free of marrow. The activity decreased between birth and the fifteenth year and increased as a power function thereafter. The early decrease in rib activity parallels pre-adolescent ossification at the expense of cartilage, according to the authors, who have

no explanation for the increasing activity after the fifteenth year.

Summary. The tissue distribution of Cs^{137} after chronic administration is markedly similar in mice and dogs. The highest concentration is found in muscle, while fat, blood, skin, and bone have lower concentrations. Other tissues tend to conform to the concentration in the whole body, which is less than in muscle and more than in fat. Differences in whole bone concentration are due in part to the state (red or fatty) and quantity of marrow; for example, dog ribs have a higher concentration than dog femurs.

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Urinary Excretion of THAM Citrate Orally Administered.* (29253)

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Tris(hydroxymethyl)aminomethane (THAM), a weak organic base of low toxicity, has been widely used both experimentally and clinically in an intravenous solution to correct respiratory and metabolic acidosis (1,2,3). Although the intravenous infusion of THAM must be performed with caution, it is the most effective mode of administration for rapid and stochiometric titration of fixed acid *in vivo.* Indeed, when administered orally, some systemic alkalinization is produced, but it is accompanied by marked diarrhea(4). In addition, THAM is very unpalatable, and in the few cases reported of oral administration, a gastric tube had to be used. Administration of THAM crystals in gastric coated capsules is also accompanied in animals and man by diarrhea(5).

It has also been observed that THAM, titrated with acid to a less alkaline pH, is not as irritating to the tissues at the site of infusion(6). To increase gastric and intestinal tolerance to THAM administration, therefore, tests were made on THAM salts of a number of weak acids. THAM citrate was selected because it is stable and very soluble in water. A mixture was made containing 20% of THAM, 4.2% of citric acid, a cherry-flavored syrup and 2% alcohol. The pH of the mixture is 8.50 at 37°C and it retains 70% of its titrating activity. Each ml contains 1.3 mM of un-ionized THAM, an amount of base which compares well with standard bicarbonate solutions used for treatment of renal acidosis(7). The purpose of the present study was to determine the effect and mode of action of THAM citrate administered orally.

Method. Three series of experiments were performed on 4 normal mongrel dogs. The animals were given a meat diet and water *ad libitum.* In the first series of experiments 3

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