ing water (~3 mg/day given for 10 wk), inclusions are not observed by light microscopy in the renal tubular cells. The Pb content of kidneys from such rats is only 2-3 mg/g of wet weight, while in this experiment (intake of 150 mg/day) the kidney was 30-70 µg/g of wet weight. Whether there is intranuclear complexing of Pb by proteins at a lesser dosage of Pb than that producing observable inclusions may be important with regard to the cellular metabolism of environmental Pb or the chronic body burden of Pb endured by the present population. (26 references)

630. Hatch, R.C., and Funnell, H.S. (Univ. Guelph, Ontario, Canada): LEAD LEVELS IN TISSUES AND STOMACH CONTENTS OF POISONED CATTLE: A FIFTEEN-YEAR SURVEY. Canadian Veterinary Journal 10:258-62 (Oct.), 1969.

Following a review of reported values of Pb in tissues of cattle poisoned through various sources of Pb, the authors describe their study designed to reassess the diagnostic significance of tissue Pb concentrations and to determine the need of testing rumen contents.

During the period 1954-1969, random samples of ingesta, liver and kidney from 175 cattle in Ontario whose death was most likely due to Pb poisoning were analyzed for Pb content. A modification of the method described by Sandell (1944) was used. Diagnosis was based on reported clinical and postmortem findings: Diarrhea, colic, central nervous system signs, motor abnormalities, blindness, congestion or hemorrhages in the gastrointestinal tract, kidney, heart, brain, lungs or omentum, and "pulpy" kidneys, spleen or liver. No grouping of the cattle as to age, sex, breed or duration of Pb exposure was possible. For this reason, the data of this survey were based on random samples from the referrals. Among the 175 referrals strongly supporting Pb poisoning, 158 kidney samples (cortex + medulla) averaged 137 ppm Pb (2-2355); in 13.9%, levels ≤25 ppm found in the cortex were regarded as being of diagnostic significance. Liver (170 samples) averaged 43 ppm (0-1300). Ingesta of 133 showed wide variation: av 3427 ppm (0(in 6)-146,200). As tabulated, kidneys of 80% of the dead cattle contained 1-200 ppm, 80% showed 0-50 ppm in liver, and no characteristic range of Pb levels could be associated with the ingesta samples. The authors conclude that the survey supports the opinion that Pb accumulates predominently in the kidneys of Pb-poisoned cattle. Liver and other tissue may be free of Pb despite fatal poisoning. Therefore, the mere presence of Pb in the kidney (or liver) and ingesta should lead to a presumptive diagnosis of Pb poisoning in cattle which die with signs, lesions, and histories characteristic of Pb poisoning. Diagnosis may be confirmed by proof of access to, or ingestion of, a source of Pb.

631. Hopkins, A. (Inst. Neurology, Queen Sq., London, England): EXPERIMENTAL LEAD POISONING IN THE BABOON. British Journal of Industrial Medicine 27:130-40 (Apr.), 1970.

This study was undertaken because the nature of Pb palsy remains obscure in spite of much animal experimentation. The reason for this is the differing response of different species to Pb. The author therefore chose the baboon as representative of a species closer phylogenetically to man. Twelve baboons (7.2-13.6 kg weight), 9 females (judged to be >4 yr) and 3 males (on basis of weight, not full grown); and 3 infant females (2.8-3.3 kg) were

observed for at least 3 mo before Pb intoxication by intratracheal injection of a suspension of Pb carbonate, to assure the most complete absorption of Pb (suggested by Minot, 1924). The usual dosage was 1 g/ml, equivalent to 50-135 mg/kg initial weight; the infants received smaller amounts, but dose/kg was the same; 1 baboon received a single dose of 105 mg/kg; in repeated dosage, 1 injection was given every 3 wk, although modified as required according to condition of animal or blood Pb. The procedures and methods used are described in detail; Pb was determined in hemolyzed whole blood by Delves and Vinter's method (1966). Ten animals were studied until death (39-265 days after 1st injection), mean survival was 120 days; 2 were killed after 336 and 362 days. Blood Pb, determined before Pb treatment on these and 12 other healthy baboons used in other studies, gave a mean of 11.7 μg/100 ml (3-27, SD 5.5); 87% were <16 μg. In the baboon that received a single dose, blood Pb rose to a peak of 310 μg/100 ml by the 4th day; it remained at this level for 7 days, then declined exponentially, remaining >100 μg/100 ml for at least 24 days. The most striking finding in all animals receiving repeated injections was the loss of weight in spite of normal appetite (5 lost 40%, 1 lost 46%, and 5, 25%). Pb line was seen in none. Eight baboons had 1 or more fits (34 in all), and others may have occurred in the observers' absence. The 13 fits seen by the author were of grand mal type; 2 began with focal seizure. The latter occurred in 1 baboon 149 days after beginning of poisoning. Paresis of limbs occurred in 3, associated with fits or other signs of encephalopathy, and thus were believed to be of central origin. Fits were particularly frequent 4-11 days after an injection of Pb, when the blood Pb reached its peak. All 5 baboons which began convulsing in this period died during 1 of a number of immediately following seizures; in the 3 survivals, convulsions occurred 23-29 days after injection, while blood Pb was falling. There was no clear relationship between blood Pb, which rose as high as 4550 μg/100 ml, and other signs of poisoning, ie, weight loss, hemoglobin levels (Hb); as to the latter, results of 136 analyses of blood Pb, grouped into 100 μg/100 ml up to 1000, 1000-1499, 1500-1999 and >2000, plotted against Hb levels showed that there was no significant decrease in Hb with increasing blood Pb. As determined by nerve conduction velocity (16 times) in the median and anterior tibial nerves of 6 baboons 35-346 days after 1st injection, electromyography, and preliminary histologic examination showed no abnormality of the peripheral nerves.

In the 3 infant baboons, loss of weight occurred in all. They became progressively more wasted and timid. No fits were observed. Hb decreased to 66 and 79% in 2; 1, still gaining weight, died in 5 wk. No Pb line or stippled cells were observed. The tolerance for high blood Pb levels observed in the adults did not apply to the infants: 2 that died on days 75 and 117 had highest blood Pb of 560 and 140 μg/100 ml; 1, sacrificed on day 150 with no signs save weight loss, showed 230 μg/100 ml.

In discussing the results, the author reviews extensively the literature, pointing out the species differences; these are illustrated in a table, listing man, guinea pig, rabbit, rat, baboon, dog, cat, and their response to Pb in anemia and stippled cells, encephalopathy, palsy, changes in anterior horn cell, Wallerian-type degeneration, and segmental demyelination. In conclusion, he states that the findings in various species do not throw any light on the metabolic lesions produced by Pb in the red cell

precursors and in the neurone or Schwann cell. Even animals with clear histologic lesions in the nervous system exhibit obvious species differences, eg, guinea pig and rabbit that develop a mild paresis in spite of extensive lesions in the peripheral nerves, and humans in whom sudden severe palsy may occur with relatively slight changes in the peripheral nerves. (43 references)

632. Lucas, H.F., Jr., and Markun, F. (Argonne Natl. Lab., Ill.): THOROTRAST: AN INTRAPERITONEAL INJECTION. In Radiological Physics Division Annual Report July 1967-June 1968. US Atomic Energy Commission Document No. ANL-7489, pp. 30-3.

Thorotrast was injected ip into a male rat in a comparatively large dose (4 ml) to determine whether this technique would offer opportunity to study the translocation of radionuclides in vivo. The animal was sacrificed 280 days after injection (1085 days of age). Results are presented in tables for urine and feces samples collected throughout the period, for ^{228}Ra and ^{228}Th excretion rates, whole-body content, and ^{212}Bi, ^{212}Pb, ^{228}Ra, and ^{228}Th in blood, bone, lung, muscle. ^{212}Pb results in pCi/g were: bone, -; muscle, 0.6; lung, 2.0; blood, 41. The authors concluded that the experiment was successful and that even larger doses would permit accurate evaluation of the complicated metabolism of Thorotrast daughters accurately. It appeared that ^{228}Th produced in vivo is excreted at a higher rate than following an iv injection.

633. Matone, S., Conterno, G., Ramello, A., and Pich, P.G. (Univ. Turin, Italy): Effetto della penicillamina sull'escrezione urinaria del piombo nell'intossicazione sperimentale. (EFFECT OF PENICILLAMINE ON URINARY LEAD EXCRETION IN EXPERIMENTAL POISONING.) Gazzetta Medica Italiana 128, No. 12:673-8, 1969.

After a discussion of the work of other authors in which D-penicillamine was used as a chelate in the treatment of Wilson's disease and occupational Pb poisoning, the authors report their own investigations in which they used 8 rabbits (3-4 kg) poisoned by im administration of 20 mg of a Pb acetate solution, injected every other day up to a total of 200 mg. Penicillamine was given in 1 dose of 60 mg in 5 ml of a physiologic solution, iv, repeated after 24 hr. Urine samples were collected before and after penicillamine. After 10 days, during which interval the animals were left untreated, a 3rd dose of 60 mg penicillamine was given and urine samples were collected before and 24, 48 and 72 hr after the last injection.

The urinary Pb excretion before Pb intoxication was 9 µg/24 hr. After the Pb intoxication, the average daily urinary Pb excretion was 85 µg. After the 1st injection of penicillamine, excretion was 855 and 805 µg/24 hr, and after the 2nd injection, 216 µg/24 hr (10 days later). The 3rd produced urinary Pb excretion rates of 801, 426 and 279 µg after 24, 48 and 72 hr, respectively.

From these data it is concluded that in Pb-intoxicated rabbits the administration of penicillamine causes a significant increase in the urinary Pb excretion. (30 references)

634. Nilova, N.A., and Mambeeva, A.A. (Inst. Norm. Pathol. Physiol., Acad. Med. Sci. USSR, Moscow): Porazhenie slizistoi obolochki zheludochno-kishechnogo trakta pri svintsovoi intoksikatsii v eks-

corresponding figures were: 0.99, 5.94 and 0, thus showing a difference between the 2 groups of 105.71 and 1.85 μg/g in red cells and white muscle, respectively. The average urinary CP and ALA excretion in the treated animals was 2.75 mg/l and 2.60 mg/100 ml, respectively. Presence of ALA dehydratase activity was observed in the red muscles (supplied with myoglobin) but it was absent in the white muscles (without myoglobin); there was also marked inhibition of ALA-D activity in the erythrocytes in Pb poisoned animals while the muscular ALA-D showed no significant change even after prolonged administration of Pb.

The authors explain the different behavior of the enzyme in erythrocyte and muscle by suggesting that ALA dehydratase is present in both in the form of 2 different iso-enzymes or, that in muscular tissue, substances exist which are capable of protecting the enzyme from the action of Pb. (12 references)

636. Sauer, R.M., Zook, B.C., and Garner, F.M. (Natl. Zoological Park, Washington, D.C.): DEMYELINATING ENCEPHALOMYELOPATHY ASSOCIATED WITH LEAD POISONING IN NONHUMAN PRIMATES. Science 169:1091-3 (Sept. 11), 1970.

The cases of accidental Pb poisoning here described were: I, a female Barbary ape (Macaca sylvanus) born and housed in an outdoor all-season cage until found dead at the age of 22-1/2 mo after having suffered intermittent convulsions for 18 mo; II, an adult red-faced macaque (Macaca speciosa) that had lived in an outdoor cage for 11-1/2 mo until death following 2 days of convulsions; III, a juvenile male red-faced macaque was placed in an indoor cage after a 6-wk quarantine in a galvanized cage. He developed a convulsion 8 wk later and was taken to the hospital; he appeared blind and had frequent intermittent convulsions for 6 days. Euthanasia was performed after a 2-day coma. Case IV, an adult lesser spot-nosed guenon (Cercopithecus nictitans), housed in an indoor cage during the winter and an adjoining outdoor cage during the summer for 2 yr, suddenly became paraplegic. A prolapsed intervertebral disk (T_{12}-L_1) was diagnosed and euthanasia performed 2 wk after the 1st clinical signs.

Upon necropsy, gross findings were unremarkable in cases I and II; in III, swelling of the cerebral cortices were evident, and in IV, prolapsed intervertebral disk was confirmed, with no obvious compression of the spinal cord. In I, II, and III, in which the clinical signs were primarily amaurosis and epilepsy, the histologic findings in the brain were characterized by proliferative and degenerative vascular changes, edema, laminar necrosis, and demyelination. In Case IV, where sudden paraplegia rather than epilepsy was present, vascular lesions were minimum but bilateral symmetrical demyelination was much more extensive. These were similar to those found in idiopathic leukoencephalomyelosis of nonhuman primates occurring concurrently with amaurotic epilepsy. In the other organs, acid-fast intranuclear inclusion bodies were found in hepatocytes and renal proximal tubular epithelial cells in all 4 cases. The Pb content in liver and kidney of cases I and II was 110 and 65 and 120 and 90 ppm wet tissue, respectively; in III, 360 ppm in dehydrated, paraffin-embedded liver; in IV, 10 ppm in wet liver (spectrographic).

The authors concluded that the findings suggest a new animal model for the study of demyelination and strengthen the supposition that Pb may be a factor in some idiopathic demyelinating diseases. They also note that a de-

tailed study of a larger number of similar cases is being prepared for publication. (11 references)

637. Schroeder, H.A., Mitchener, M., and Nason, A.P. (Dartmouth Med. School, Hanover, N.H.): ZIRCONIUM, NIOBIUM, ANTIMONY, VANADIUM AND LEAD IN RATS: LIFE TERM STUDIES. Journal of Nutrition 100: 59-68 (Jan.), 1970.

To evaluate innate effects of the trace elements Zr, Nb, Sb, and V, and to reevaluate those of Pb, 603 rats of the Long-Evans strain were fed a diet containing relatively small amounts of these elements in an environment reasonably free of trace contaminants. Groups of 100 or more, divided as to sex, were given 5 ppm (as metal) of the 1st 4 ions, and 25 ppm Pb (males only) in drinking water from the time of weaning until natural death, and compared with an equal number of controls. Cr, 1 ppm, was in the water. These doses were tolerable for growth which was enhanced in the male Nb group. Innate toxicity in terms of life span and longevity occurred in the Sb groups. In these rats, nonfasting serum glucose levels were lower than fasting levels. Serum cholesterol was abnormal in the Sb and V groups. Sb and Pb accumulated in soft tissues, the former with age. Considering the dose used, the accumulation of Pb in soft tissues was surprisingly small. Mean values were, in µg/g: Kidney, 2.65; liver, 2.06; heart, 1.28; lung, 1.04; spleen, 1.04; total mean accumulation, 1.71 µg/g of tissue, wet weight.

Glycosuria was found in 23% of 90 controls, 43% of 23 in the Sb group, 52% of 56 in the Zr group, 63% of 16 in the Pb group, and in 71% of 24 in the V group. No significant differences in proteinuria were found between the several groups.

None of these 5 metals was tumorigenic. There were more than twice as many tumors in females as in males. No metal significantly suppressed the incidence of tumors. Blanching of incisor teeth, which has occurred in a number of older rats, was found in the various groups with the following frequencies: Zr 7, Nb 5, Sb 5, Pb 9, V 9 and controls 12. It was somewhat more prevalent in females than in males.

There were no significant differences from controls in Zr, Nb, Pb and V groups for survival and longevity. Pb-fed males lost weight from 24-30 mo of age and their coats were poor, the only signs of toxicity. A previous series of Cr-deficient rats given the same dose of Pb showed early mortality, shortened life span and decreased longevity. In the Cr-supplemented rats of this study, Pb was not toxic to males in terms of growth and survival (median age of 52 males, 883 days). As mentioned above, there was a remarkable resistance to accumulation of Pb in the soft tissue of these rats. Although bone was not analyzed, this tissue probably stored Pb, as 91% of the Pb in the human body is in bone. Whether the Cr-deficient rats of the 1st series of Pb-fed rats can be compared with the present series of Cr-supplemented rats is problematical; however, the diets and regimens were identical, the rats were of the same type and other criteria were the same. If the profound differences in mortality between the 2 series can be accepted, it appears that Cr protects against innate Pb toxicity.

If any of the 5 trace elements in this study are essential for rats and mice, they are required at concentrations less than those present in our diet. There is no evidence, however, that Sb and Pb are essential elements. (16 references)