total loss, "net loss" and feces were between 4,000 and 8,000 ft.; for urine below 4,000 ft.

The curves for per cent increase in total weight loss and "net loss" for the 2 groups of rats are fairly consistent with each other and together indicate increases proportionate to the altitude. The rats of Group 4 did not display as intense a polyuria in response to anoxia as those of Group 1, but they, nevertheless, had an increase in urine secretion which was proportionate to the altitude. The rats of Group 4 had a greater increase in fecal excretion at all altitudes than those of Group 1. These differences between the 2 groups were most probably due to the character of the diet; that for Group 1 being inferior. The eventual decline of the fecal excretion curves with altitude was probably due to a reduced intake of the diet, since loss of appetite is a well known symptom of anoxia.[1] The increased fecal excretion confirms the impression gained in this laboratory that in dogs, also, defecation is frequently one of the responses seen at 28,000 ft. It is of interest that colonic motility as registered by an enterograph in barbitalized dogs is usually greatly reduced by anoxia.[4]

Swann and Collings,[2] who subjected their rats under different conditions to 18,000 ft. for periods of time between 6 and 23 hours, found much greater increases in the rate of insensible water loss than reported here. This may explain in part their failure to find a diuresis at high altitude. Time may be a factor also, because their results for an exposure of 23 hours were less than those at shorter exposures and practically no different than the controls. Their finding an increase in the rate of fecal loss during the 6-hour exposure only, is to be expected in fasting rats.

The increases, here reported, in urine secretion are even greater than those found by Silvette.[5] The few experiments in which cocaine was administered did not reveal increased urine secretion above that seen without this epinephrine-potentiating agent, nor did they reveal a reduced secretion. This result was obtained in spite of the fact that cocaine caused in the control experiments, an increase of over 200% in urine secretion. Such results are not favorable to the view that anoxia-induced changes in urine secretion are a result alone of epinephrine and/or augmented sympathetic impulses to the kidneys. Such an explanation is more in accord with the results found in anesthetized animals[6] where oliguria is frequently found as well as polyuria in response to anoxia. Furthermore, 32,000 ft. proved lethal to all but one of the rats, but in spite of this severe stimulation of the autonomic nervous system, they continued to respond with polyuria.

Summary. The body weight loss in rats is proportional to the altitude up to 28,000 ft. The thresholds for increased total body weight loss, "net loss" (insensible water loss) and fecal excretion lie between 4,000 and 8,000 ft.; that for urine, below 4,000 ft. The administration of cocaine did not change the urinary response to anoxia (28,000 ft.)

[4] Van Liere, E. J., Northup, D. W., Stickney, J. C., and Emerson, G. A., *Am. J. Physiol.*, 1943, **140**, 119.

[5] Silvette, H., *Am. J. Physiol.*, 1943, **140**, 374.

[6] Toth, L. A., *Am. J. Physiol.*, 1940, **129**, 532.

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Neural Effects of DDT Poisoning in Cats.

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The literature of the last few years contains several reports[1,2] of nervous disorders produced in laboratory animals by DDT poisoning. Our aim was to investigate whether DDT has, to any extent, a selective action

[1] Lillie, R. D., and Smith, M. I., *Pub. Health Rep.*, 1944, **59**, 979.

[2] Nelson, A. A., Draize, J. H., Woodard, G., Fitzhugh, O. G., Smith, R. B., Jr., and Calvery, H. O., *Pub. Health Rep.*, 1944, **59**, 1009.

TABLE I.

Animal No.	Wt, kg	Total amt DDT in mg/kg	Days injections given	Onset and duration of symptoms
263	2.1	370	1, 8, 11, 18, 28	Onset: 30th day Death: 33rd "
264	1.6	665	1, 8, 18, 28, 33, 39, 78, 85, 92	Onset: 232nd " Death: 235th "
287	1.5	200	1, 8	Onset: 13th " Death: 16th "
288	2.4	275	1, 31, 38, 45	Onset: 114th " Death 116th "
289	2.0	100	1	Died 3rd day without neurological signs
291	4.0	135	1, 13, 23	Onset: 42nd day Death: 45th "
292	2.2	225	1, 13, 23	Onset: 29th " Death: 29th "

on definite portions of the nervous system, such as other drugs possess.

Seven normal adult cats were given intramuscular injections of DDT solution in olive oil. This way was chosen with the belief that it afforded, as compared to the oral route, a better control of dosage and a prolonged absorption time. By slower absorption, we hoped to produce less liver damage, and to be able to observe more easily the effects on the nervous system. It was hoped to obtain *chronic animals*, but, even though the dosage was far below the lethal amount, the animals either quickly developed steadily increasing signs of intoxication, ending in death, or, after transient illness, recovered completely.

The data gathered from our experiment are summarized in Table I. The occurrence of transient symptoms is not represented.

When using the same amount for each individual injection, and the same interval between injections, we observed in our animals a great variability of response. One animal died after only 135 mg per kg, in 3 injections, while another remained in good condition after having received a total dose of 665 mg/kg.

Very often, if not always, when the first signs of neurological disorder appeared, the animals exhibited signs resembling those of a cold: congestion and hypersecretion of the eyes and nose, without any rise in temperature. We could not decide whether these were autonomic effects of intoxication, the manifestation of a latent infection brought to light by the decreased resistance of the animals, or whether the occurrence of the neurological disorders was promoted by an occasional infection. This seems unlikely, since in our animals these symptoms resembling a cold and the neurological disorders always occurred simultaneously.

A few days (between 3 and 6) after the last injection, the animals began to show definite stiffness, especially in the hind limbs. Very soon afterward a fine tremor developed, first seen only in certain postures and movements, but rapidly becoming more coarse and permanent. If the animals recovered, after a few days (usually less than a week), the symptoms progressively disappeared and never went any further than this tremor.

In other cases, after 2 or 3 days, the tremor increased in amplitude and became constant, while the stiffness extended to the proximal muscles of the limbs and to the trunk. At that period the animal continued to eat well and was still able to walk. The only sensory change noticed was obvious hyperesthesia. After that the clinical picture changed very rapidly. Muscular twitching appeared, first in the face, and soon became generalized. The animal could not walk, but retained consciousness. Within one day, the twitching became grosser, with resultant clonic movements of the entire limb. Finally the condition resembled status epilepticus, and the animal died. Injections of barbiturates may prevent the clonic movements for a short

time.

Pathology. The lesions were the same in all animals with progressive symptoms, whether they died spontaneously or were killed by exsanguination. They consisted in diffuse degeneration of the ganglion cells throughout the brain, without any visible difference between different areas. In Nissl sections, the ganglion cells showed either vacuolar degeneration, with swelling of the cell, disappearance of Nissl bodies and increased colorability of the dendrites, or pyknosis. Only occasional, normal cells were found. In Weigert-Pal sections, no definite changes could be found.

Clusters of unidentified cells were observed close to the ependymal lining. Such clusters have been described in various species. We are unable to decide whether these clusters have any pathological significance. No alterations were found in the liver, aside from moderate hyperemia of the capillaries. In none of our cases was there any fatty degeneration, such as has been described as one of the most constant features of DDT poisoning after ingestion of the drug.

No alterations were observed in other organs.

Conclusion. Progressive neurological symptoms were produced in cats by the intramuscular injection of DDT. The signs evolved in the sequence of stiffness, tremor, clonic movements, and death.

An animal with chronic neurological symptoms was not obtained, either because death supervened or because the animal returned toward normality.

Nissl sections revealed diffuse damage to the ganglion cells of the brain, characterized by vacuolar degeneration or pyknosis. No alterations, other than capillary dilatation, were recognized in the liver.

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Some Effects of Depletion and Repletion in Proteins on Body Fluids in Adult Dogs.*

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A decrease in plasma volume and a nutritional edema accompanies hypoproteinemia in dogs.[1-3] The fall in concentration of plasma proteins is associated also with an increase in the utilization of nitrogen, the nitrogen balance indexes of proteins being greater in protein-depleted than in normal animals.[4] An analysis of these data suggests that there are regular shifts in body fluids and in the utilization of nitrogen as the protein stores of the animal are altered. Experiments were organized, therefore, to study changes in plasma and "available fluid" volumes and in the excretion of various forms of nitrogen in adult dogs during control, depletion, and repletion periods.

Methods. Four dogs were depleted by feeding a protein-free diet; 3 days of plasmapheresis being used initially to speed up the process of depletion. The details of this method of

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