bisacetamidocarbanilide involves a reduction of DNC to the soluble diaminocarbanilide, which is readily excreted by dogs but is converted to an insoluble acetylated derivative in rats and calves. The *in vitro* demonstration of the reduction and acetylation of DNC to a compound identical with that found in the kidney tubules further supports the probability of this method for the metabolic degradation of nicarbazin in the bovine.

Summary. The feeding of large doses of nicarbazin to calves produced moderate nephrotoxicity associated with precipitation of crystalline deposits in the renal tubules. These crystals were identified as 4, 4′-bisacetamidocarbanilide. Additional evidence is presented that, after absorption, nicarbazin splits into its components, dinitrocarbanilide and hydroxydimethylpyrimidine, which are metabolized separately. The dinitrocarbanilide is first reduced to soluble diaminocarbanilide and then acetylated to insoluble 4,4′-bisacetamidocarbanilide. The renal tissue reaction and the metabolic degradation of 4,4′-dinitrocarbanilide resembles that known for the sulfonamides.

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Demonstration of Central Nervous Mediation of Acute Pulmonary Edema Produced by Intravenously Administered Epinephrine. (22722)

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Experiments have been previously reported (1) on the phenomena associated with production of acute pulmonary edema in mice and rats. The most straightforward interpretation of the observations was obtained on the assumption that the genesis of the acute pulmonary edema either produced by air blast or by massive doses of epinephrine was mediated via the central nervous system. As other interpretations were not entirely ruled out, it was considered important to obtain a more rigorous proof of the central nervous mediation, especially when produced by epinephrine. Usually the physiological effects of intravenously administered epinephrine are interpreted in terms of its well-known peripheral effects. However, it can be easily demonstrated that massive and even lethal doses of epinephrine can be administered intravenously to cats without any evidence of acute pulmonary edema production, while the typical acute edema can often be produced by injection of epinephrine into the hypothalamic regions of the brain of the cat. A natural interpretation of these observations is that the cat has a blood-brain barrier more impervious to epinephrine than that of rodents.

To prove conclusively the central nervous mediation of the acute edema in rats, the experiment was performed of severing the spinal cords of a group of rats at a position between the second and third vertebrae. The respiration was maintained with a mechanical respir-

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TABLE I. Spinal Severance.

Lung wt in g	
Total body weights from 288 to 452 g (avg 351 g)	
1.923	
1.227	
2.295	(respirator blocked)
1.781	
2.570	(respirator blocked)
1.421	
2.665	(some jerking of hind legs)
1.705	
1.312	
1.417	
1.166	
2.683	(some jerking of hind legs)
1.665	
2.166	(some jerking of hind legs)
1.470	
Avg 1.831	
No Spinal Severance (But on Respirator).	
Total body weights from 331 to 435 g (avg 383 g)	
4.384	(nasal frothing)
8.550	
4.219	
3.610	(nasal frothing)
7.063	(*Idem*)
4.896	(")
Avg 5.453	

ator. Massive doses of epinephrine, that in controls produced tremendously edematous lungs, were administered intravenously. Under these conditions it would be expected that if the mediation was central nervous, no acute edema would occur in the cord-severed animals, while if the mediation was peripheral, the edema would develop.

Procedure. Rats were anesthetized as required with 0.4 ml to 1.0 ml of a one-gram 10 ml solution of Evipal Sodium administered intraperitoneally. They were laid on their backs and tied to a board by their feet. A tracheal incision was made and a cannula connected with a respirator was inserted and fastened, following well-established methods. The rats were turned over and refastened to the board. An incision was made in the back of the neck and a drill used to sever the cord between the second and third vertebrae. The animal showed a typical reaction to the severance by becoming momentarily rigid and then limp. Rats which withdrew their limbs on pinching were not considered to have their spinal cords completely severed and were not used. The rats were again turned over on their backs and freshly prepared adrenalin, 2 mg/kg, was injected into their femoral veins.

Results. Table I gives the measured lung weights of the experimental animals and a group of controls kept on the respirator and administered the same dose level of adrenalin, but without cord severance. However, incisions were made on the back of the neck of the controls, similar to those on the experimental animals.

These results strikingly demonstrate without the necessity of a statistical analysis that cord severance prevents development of acute edema. The appearance of the lungs in the spinal severance group was not normal. Some had a peculiar spongy appearance but no edema fluid was apparent. The production of simultaneous peripheral effects by the epinephrine is in no way excluded as a possibility. Also, possible mechanical irritation could arise from abnormal inflation during the artificial respiration.

Discussion. Luisada(2) has claimed that pulmonary edema can be mediated via the central nervous system by controlling capillary permeability of the pulmonary capillaries. As there is no anatomical evidence of nervous control of capillary permeability, this hypothesis is not well supported. A hypothesis for a different mechanism of central nervous mediation has been presented by us(1) which seems to fit in well with all the observations to date. In this mechanism only the central nervous control of precapillary sphincters is assumed.

An animal with severed cord on a respirator can be killed with a massive dose of epinephrine, even though no pulmonary edema is generated. It is likely but unproved that the epinephrine produces many other central nervous misfunctions besides that presumably produced on the circulating lung resistance by loss of control of the pulmonary precapillary sphincter system.

Summary. Fifteen rats with severed spinal cords, kept alive on a respirator, were given massive doses of epinephrine, that on controls produced consistently an intense acute pul-

monary edema. None of these rats developed the usual acute edema, and in 10 cases the lungs had normal weight. This result is interpreted as a proof of the central nervous mediation of the acute pulmonary edema produced by administration of epinephrine.

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Passive Transfer with Circulating Leukocytes of Delayed Hypersensitivity to Cat Scratch Antigen.* (22723)

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The passive transfer of delayed type skin hypersensitivity in animals and in man has been demonstrated towards simple chemical compounds(1), to tuberculin(2), to whole streptococcal cells, to SK-SD, and to streptococcal M substance(3,4). Such transfer has been possible with the leukocytes from peritoneal exudates, from lymph nodes, from the spleen, and from the thoracic duct, and from certain fractions of disrupted leukocytes(5,6). Hitherto the passive transfer of skin hypersensitivity to virus diseases has not been reported. It is the purpose of this paper to report the successful passive transfer of the delayed type skin hypersensitivity to cat scratch disease by means of circulating leukocytes. Cat scratch disease is a benign, subacute, regional lymphadenitis that is characterized by reticuloendothelial hyperplasia with epithelioid cell granulomas having central necrosis. Patients with cat scratch disease develop a characteristic skin reaction to an antigen prepared from pus aspirated from other cases of cat scratch disease. In its temporal relationships and its morphological features the reaction to cat scratch antigen has features similar to the tuberculin reaction and is characteristic of delayed allergy in man. No causative agent has been isolated from the suppurating lymph nodes from patients with cat scratch disease despite cultures on all commonly used media, upon inoculation into laboratory animals including rabbits, cats, monkeys, guinea pigs, mice, rats, and chick embryos, or on inoculation of tissue culture of HeLa cells, kidney cells, liver cells, or corneal cells.§ No microorganisms are to be seen in sections of the involved lymph nodes although cytoplasmic basophilic inclusion bodies have been described in the cells of such nodes(7). Further evidence in support of a viral etiology for cat scratch disease is that patients with this disease have a distinctly higher incidence of low complement fixation titers against the lymphogranuloma-psittacosis group viruses than does the population at large(8).

Materials and methods. Obtaining white blood cells. The antecubital area is cleansed with tincture of iodine, alcohol and green soap. The skin is infiltrated with 1% procaine hydrochloride. The antecubital vein is punctured with a 15 gauge needle and the blood is withdrawn through silicone-coated tubing into a silicone coated vacuum bottle containing ACD as anticoagulant. (For volumes of blood less than 400 ml heparin, 5 mg/100 ml blood, is used as the anticoagulant). Twenty-five ml of 4.7% dextran is

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