animals (80, 82), and questionably a third (81) showed definite circulatory signs of shock. In 5 experiments (76, 78, 79, 84, 85), mean arterial pressure never fell below 80 mm for 3 to 7 hr after discontinuance of the adrenalin infusion.

Necropsies were made on all animals and the most conspicuous changes are recorded in Table I. This serves to indicate that extensive hemorrhagic lesions occurred fairly generally in all animals regardless of the course. Their distribution was far more general than has ever been observed in hemorrhagic shock. Involvement of the endocardium, epicardium, and sometimes the liver was far more common. Small pericardial and pleural effusions were frequently present. However, the duodenal mucosa which showed such characteristic changes in hemorrhagic shock was negative in 3 dogs (76, 79, 85), moderately congested in 3 animals (78, 82, 84) and intensely congested or hemorrhagic in only 2 dogs (80, 81). These observations, correlated with the dynamic course, indicate that prolonged vasoconstriction by adrenalin *can cause* damage to smaller vessels, but its action is by no means as selective as appears to be the case in hemorrhagic shock. Even if we add together the animals which showed *either* a progressive downward trend of blood pressure *and/or* significant intestinal changes (78, 80, 81, 82, 84), prolonged administration of adrenalin gave dynamic or pathological evidence of an impending irreversible state in only half of our animals (total 10 dogs).

Conclusion. In about 50% of our experiments prolonged administration of adrenalin (.00694 to .0398 mg kilo/min.) caused 2-7 hr after cessation of infusion either dynamic evidence of irreversibility or postmortem changes in the upper intestine which resembled those of hemorrhagic hypotension. Adrenalin constriction can lead to shock, but does not unfailingly do so. Our experiments have no bearing on the problems, whether equally intensive generalized constriction occurs in other types of clinical or experimental shock or whether lesser degrees of vasoconstriction can cause similar consequences.

13988 P

Reactions of Monkeys to Experimental Respiratory Infections. VI. Spontaneous and Experimental Infections in Nutritional Deficiency States.*

S. SASLAW, J. L. SCHWAB, O. C. WOOLPERT, AND H. E. WILSON. (Introduced by C. A. Doan.)

From the Departments of Bacteriology and Medicine, Ohio State University, Columbus, Ohio.

Clinical observations have indicated that patients affected with certain deficiency diseases are prone to develop infections. Experimental data in support of the apparent relationship of B-avitaminosis to susceptibility to infection in monkeys have been accumulating in recent years.[1-6]

With increased knowledge of the components of the vitamin B complex, experimental diets more accurately known and controlled with respect to vitamin fractions than those previously used, are now available. Our interest has been not only to study spon-

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taneous infections as they developed under these conditions, but also to follow the measurable resistance to selected infectious agents when experimentally introduced.

The experiments previously reported[7] from these laboratories were conducted simultaneously with monkeys from the same stock but maintained on a complete diet, and furnish a basis for comparison.

Methods. The diets used and the hematologic changes noted have been described in the preceding paper.[8] The monkeys (*Macaca mulatta*) were isolated in individual cages for 2 to 3 weeks preceding the experiments and throughout the course of the studies. Daily clinical observations and periodic stool cultures were made. Serologic and bacteriologic examinations were conducted when indicated.

Results. Eleven monkeys developed spontaneous infections while in a poor nutritional state and died between the 23rd and 180th diet day. Monkey No. 119, receiving the basic diet with only ascorbic acid as supplement, died in 23 days with dysentery. Monkeys No. 4 and 11 on diet 1 and monkeys No. 33, 42, 66, 136 and 146 on diet 2 succumbed with dysentery on the 107th, 85th, 122nd, 120th, 180th, 154th and 95th days respectively. *Shigella dysenteriae* (Flexner) was isolated from the stools during life from monkeys No. 33, 66, 136 and 146 and was cultured from the scrapings of the ulcerated mucosa of the colon at necropsy in all cases. No dysentery occurred in any animals on normal diets.

Monkey No. 8 on diet 600 exhibited marked ulcerations of the gingiva and buccal and labial mucosa, as well as anorexia, diarrhea and general malaise. During the last few hours of life, the animal's condition changed precipitously from a state of fair activity in the morning to one of complete prostration in the late afternoon. Postmortem findings included the recovery of hemolytic *Staphylococcus aureus* from the spleen, kidney, liver, blood and peritoneal fluid. The primary focus of infection was probably the markedly ulcerated upper lip which yielded *Staphylococcus aureus* on previous culture. All monkeys on the 600 diet developed lesions of the oral mucous membranes which often became infected with streptococci, staphylococci or the flora of Vincent's angina. In monkeys on normal diets, no such lesions appeared spontaneously, and when accidental trauma of gingival or buccal mucosa occurred, no secondary infections were observed.

Monkey No. 131 after 31 days on diet 1 succumbed to pneumonia due to *Klebsiella pneumoniae.* This organism was found occasionally in throat cultures of our stock monkeys. Monkey 41, kept on diet 2 for 124 days, died with an intestinal infestation with *Trichomonas intestinalis* and pneumonia due to *Streptococcus hemolyticus,* Group C. In addition, it exhibited facial edema.

Of 6 monkeys in a deficient state and inoculated intranasally, under light ether anesthesia, with *Streptococcus hemolyticus,* Group C, 5 (No. 23 on diet 1, Nos. 51, 54, and 55 on diet 2, and No. 14 on diet 600), developed specific infections ending fatally 7 to 13 days after inoculation. Monkey No. 23 (Fig. 1) was inoculated on the 154th diet day at the time of a nutritionally induced leukopenia (W.B.C. 3000, neutrophils 800). A typical but abortive leukocytic response to infection (W.B.C. 10,000, neutrophils 8800) was promptly followed by exhaustion of marrow reserves (terminal W.B.C. 1600, neutrophils 880). (Contrast with Fig. 1, Ref. 7, p. 562). Of the 5 monkeys dying of streptococcus septicemia, 3 had facial erysipelas that yielded the same organism. Precipitin, antistreptolysin and complement titers, as well as opsonocytophagic activity, were similar to those found in monkeys on adequate diets[7] similarly treated.

Of 7 monkeys inoculated intranasally, under light ether anesthesia, with the PR-8 strain of influenza virus A, 5 (No. 27 on diet 1, Nos. 53, 56, 69 on diet 2, and No. 24 on diet 600) died 2, 8, 11, 7 and 3 days, respectively, after inoculation. Small peribronchial areas of consolidation were observed at necropsy, and virus was recovered from fil-

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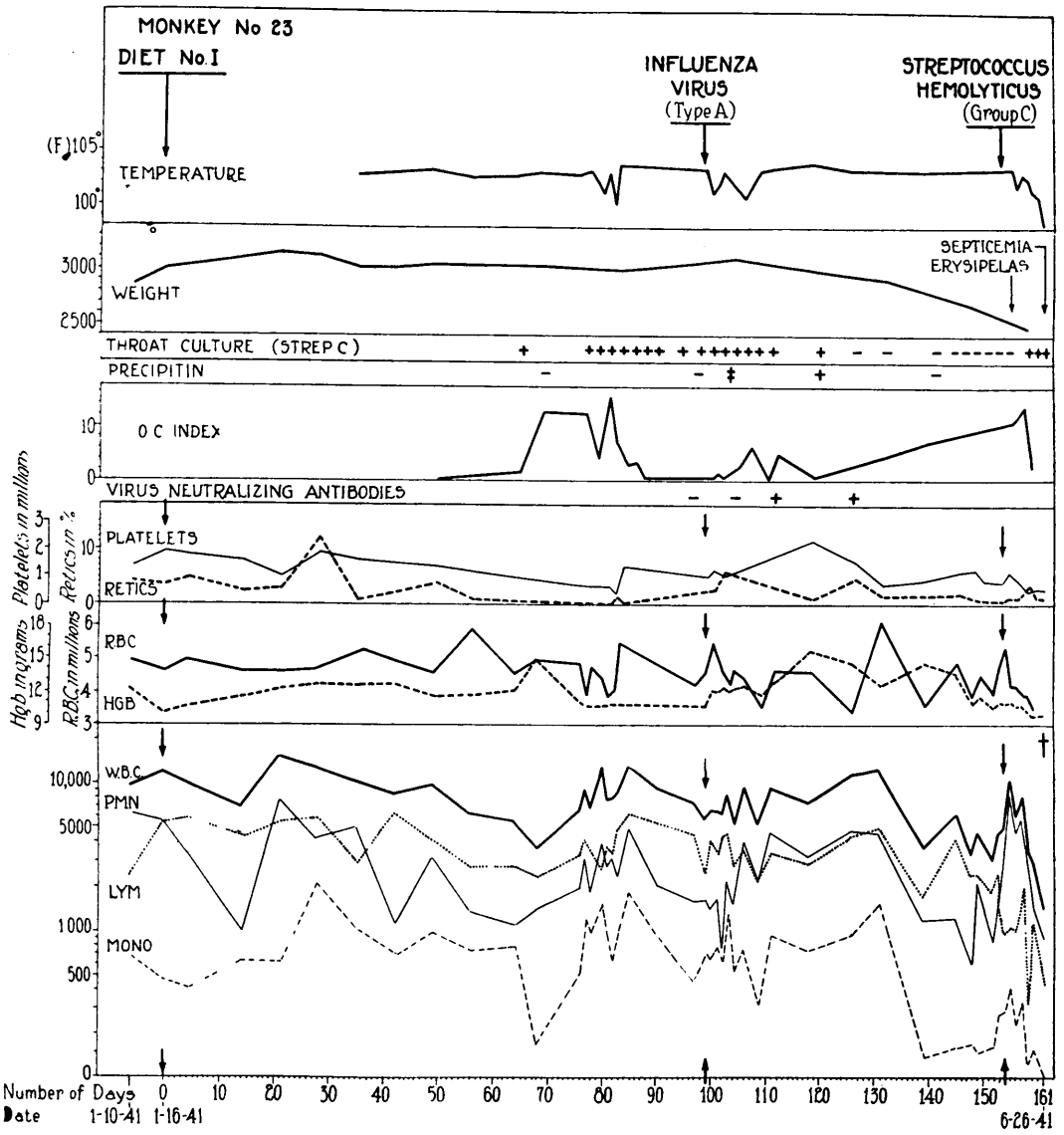

FIG. 1.

trates of the lungs of 3 animals. Neutralizing antibodies were demonstrable in the antemortem serum of M. 56 (8th day) and M. 69 (11th day). In normal monkeys so treated the antibody was detected at about the same interval.

To date 2 monkeys of 32 maintained on an adequate diet and inoculated intranasally with hemolytic streptococci and influenza virus or with influenza virus alone have died from the experimentally induced infection. By contrast, 10 of 13 monkeys on the dietary regimes indicated have died following inoculation with the same agents.

None of the above spontaneous infections was observed over a period of 3 years in an average population of approximately 25 monkeys (total 100) maintained on a stock diet.

Summary. Monkeys on a vitamin B-free basic diet, supplemented by riboflavin, thiamine chloride, nicotinic acid amide, calcium pantothenate, pyridoxin hydrochloride, sodium paraminobenzoate, choline chloride, pimelic acid, glutamine and inositol, de-

veloped a striking granulopenic leucopenia, and manifested a markedly lowered clinical resistance to spontaneous infections with high mortality. The susceptibility to experimental infections with *Streptococcus hemolyticus*, Group C, and to influenza virus A, administered intranasally, was likewise increased in contrast with the controls on normal diet.

13989

Nutritive Value of Keratins. I. Powdered Swine Hoofs.*

JOSEPH R. WAGNER† AND C. A. ELVEHJEM.

From the Department of Biochemistry, College of Agriculture, University of Wisconsin, Madison.

Routh and Lewis[1] recently summarized the literature dealing with the indigestibility of keratins in their natural state. In the same paper they reported that wool which had been powdered in a steel ball mill was readily hydrolyzed *in vitro* by pepsin and trypsin. In subsequent studies Routh[2] found that rats were able to use powdered wool as a source of protein for growth when the material was supplemented with tryptophane, methionine, histidine, and lysine.

The results of these investigations on wool suggested the possibility of converting keratin waste such as horns, hoofs, hair, and feathers into animal feed. This report deals with studies on the nutritive value of powdered swine hoofs fed as a source of protein in the diet of rats and chicks.

Mixed hog hoofs collected at a packing house were ground to a fine, gray powder until all the material passed through a 60-mesh screen.‡ The nitrogen content of the material was 14.5% and it was compared on a weight basis with casein and cartilage without regard to differences in protein content.

Groups of male albino rats 21-22 days of age and weighing 40-50 g were fed the experimental diets given in Table I for 4 weeks. Water and feed were supplied *ad libitum* and body weights were recorded weekly. Typical gains obtained on the different diets are also given in Table I.

Powdered hoofs fed at a level of 18-20% in the diet of rats failed to produce rates of gain comparable to those obtained with equal weights of casein. However, when the level was increased to 30%, growth nearly equal to that of rats fed 18% casein was obtained. Some supplemental effect was obtained when the two proteins were fed together and it is of interest to note that better growth resulted when 15% powdered hoofs were fed with 5% casein than when 9% of powdered hoofs were fed with 9% casein.

The composition of the diets used for the chicks is given in Table II. Day-old White Leghorn chicks were fed the diets for a period of 4 weeks. At the end of 4 weeks the chicks were killed and the gizzards examined for possible lesions.

Powdered hoofs fed at the level of 24% in the diet of chicks produced a higher growth rate and a better development of feathers than an equal percentage of casein. Although the growth rate obtained when 18% casein was supplemented with 10% powdered hoofs was less than that obtained on the diet containing a 10% supplement of cartilage, it was appreciably more than the growth rate obtained with 24% casein. Examination of the gizzards revealed a distinctive condition of the lining in all of the groups fed powdered hoofs. The surface of the linings showed a widespread roughening and cracking. The majority of the fissures were parallel with the normal folds

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† Wilson and Company Fellow.

1 Routh, J. I., and Lewis, H. B., *J. Biol. Chem.*, 1938, **124**, 725.

2 Routh, J. I., *J. Nutrition*, 1942, **23**, 125.

‡ Prepared by Wilson and Company, Inc.