

cytes, which sets in immediately after injection and lasts for about three days.

After the process has run its course the animal resists a second inoculation.

In affected rats the agent has been found in the lymph nodes, which readily transmit the disease, rarely in the spleen, and not yet in the heart's blood.

The testis is especially vulnerable, for the introduction of 0.2 cc of a 1:10,000 dilution of the original 10 per cent extract into this organ has resulted in its total destruction by suppuration.

Intraperitoneal injection causes an occasional abscess in the abdominal cavity, as, for example, in the gastrosplenic omentum, but no generalized peritonitis or noticeable disturbance of health.

After intravenous inoculation the results are more serious. Within three days the feet often become edematous and reddened and in such an event abscesses are prone to develop there a few days later. By then the rats are obviously ill and lose weight rapidly, though how much of their emaciation is due to the disease itself and how much to the starvation entailed by their difficulty in obtaining food has not yet been determined.

In addition to this predilection for the feet this agent has the curious property, after introduction into the blood-stream or the testis, of frequently eliciting an abscess in the suprascapular region on one side or both. Such a localization is difficult to explain, for no lymph node occupies this site in the rat.

The agent has now undergone eight passages in the subcutaneous tissue of the rat with no diminution in virulence, and was transmitted for six in the mouse brain, though with some loss of infectivity for the rat at the end of the series. Mice that have been intracerebrally inoculated almost invariably die after from three to eight days with edema of the skin overlying the head and a mild degree of meningitis.

The rabbit is partially refractory and the guinea-pig almost completely so.

The agent is now in its sixth passage in the chorio-allantoic membrane of the chick. After the third it was tested in the mouse brain and the subcutaneous tissue of the rat, and found to display its customary activity.

Having found in the literature no account of this disease or of any resembling it we submit this brief report, which will be followed in due course by a more complete description.

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THE INHIBITORY EFFECT OF OXIDIZED ADRENALIN

In a recent paper from this laboratory (Lissak and Morison, in press) evidence is presented that 933F (piperidino-methyl-3-benzodioxane) increases the rate of oxidation of adrenalin *in vitro* and *in vivo*. In the course of this experiment it was observed that if oxygen or air was bubbled through an adrenal in solution (1:100,000) after one to two days it lost its positive effect on the frog heart and had a negative, inhibitory effect. In order to test further this negative inhibitory effect of oxidized adrenalin, different dilutions of adrenalin (Parke, Davis) were made with standard Ringer's solution. Through these adrenalin solutions oxygen was bubbled at room temperature one to four days. The evaporation of water from the solutions was compensated for by adding distilled water to restore the original volume. When tested on isolated hearts of winter frogs, according to the method of Straub, the adrenalin solution (1:100,000), treated as described above for 72 hours, has a negative inotropic and sometimes a negative chronotropic effect. The negative effect was not completely inhibited by atropine (1:50,000).

During the course of my experiments papers were published by Heirman¹ and by Baeq.² They have shown that oxidizing adrenalin with phenolase (tyrosinase, catecholoxidase) a substance "adrenoxine" appears, which has a negative, inhibitory effect on the frog heart and blood pressure of the cat and the rabbit, *i.e.*, the same effect as described above.

Furthermore, Baeq concluded that the non-pregnant uterus of the cat contains a catecholoxidase, which after 45 to 90 minutes transforms adrenalin into inhibitory "adrenoxine," and that the presence of this phenolase "undoubtedly" determines the inhibitory reaction of the non-pregnant uterus to adrenalin. Since Baeq did not report control experiments it seemed desirable to repeat his procedures with properly controlled tests. On doing so, using exactly his method, I found no evidence that extracts of either the pregnant or the non-pregnant uterus of the cat contain a ferment which destroys or transforms adrenalin, but that actually such extracts check adrenalin destruction. Apparently this is because the tissues contain an inhibitor which is very efficient in protecting adrenalin from auto-oxidation.^{3, 4, 5, 6} Adrenalin, when mixed with extracts of the feline non-pregnant uterus, will produce, even after 3 to 4 days, typical reactions:

¹ P. Heirman, *Compt. rend. Soc. de Biol.*, 124: 1250, 1937a; *ibid.*, 126: 1264, 1937b; *ibid.*, 127: 343, 1938.

² Z. M. Baeq, *Compt. rend. Soc. de Biol.*, 127: 341, 1938.

³ R. D. H. Heard and A. DeM. Welch, *Biochem. Jour.*, 29: 998, 1935.

⁴ A. Láng, *Ber. ges. Physiol.*, 101: 675, 1937.

⁵ A. DeM. Welch, *Am. Jour. Physiol.*, 108: 360, 1934.

⁶ M. O. P. Wiltshire, *Jour. Physiol.*, 72: 88, 1931.

increase of blood pressure of the cat, more rapid contractions of the isolated frog heart, relaxation of the isolated non-pregnant uterus and contraction of the pregnant uterus of the cat. Control tests showed that extracts of the feline uterus alone, not mixed with adrenalin, decrease the blood pressure.

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THE MOLECULAR WEIGHTS OF ANTIBODIES

It was shown by Heidelberger and Pedersen¹ that certain antibodies formed by the horse and the rabbit differed markedly in sedimentation constants and therefore probably also in size. It is of importance, therefore, to make accurate determinations of the molecular weights of these substances and also of the antibodies formed in other animal species.

Types I and III antipneumococcus sera from the horse, rabbit, pig, cow and monkey were used. The antibodies were purified by dissociation with 15 per cent. sodium chloride of the washed specific precipitate or agglutinate formed by adding type specific polysaccharide² or a heavy suspension of heat-killed pneumococci. Several of the antibody solutions used were prepared especially for this investigation by Dr. Michael Heidelberger, of the Presbyterian Hospital, New York. The 15 per cent. salt extracts were dialyzed against 0.9 per cent. NaCl and the sedimentation (*s*) and diffusion (*D*) constants determined.^{3,4} From these values the molecular weights were calculated according to the formula given by Svedberg:

$$M = \frac{RTs}{D(1-V\rho)}$$

Determinations of the partial specific volume for horse antibody gave $V = 0.715$, which was also assumed to be valid for bovine and pig antibody. The value for normal globulin $V = 0.745$, was used in calculating the molecular weights of rabbit and monkey antibody. Table I shows the average sedimentation constants, diffusion constants and molecular weights of the various antibodies. In the last column are given the ratios between the experimentally determined molar frictional constant and the molar frictional constant for a spherical particle of the same mass and density.

¹ M. Heidelberger and K. O. Pedersen, *Jour. Exp. Med.*, 65: 393, 1937.

² M. Heidelberger and F. E. Kendall, *Jour. Exp. Med.*, 64: 161, 1936; M. Heidelberger and E. A. Kabat, *Jour. Exp. Med.*, 67: 181, 1938.

³ For a review see The Svedberg, *Chem. Rev.*, 20: 81, 1937; *Nature*, 139: 1051, 1937.

⁴ O. Lamm and A. Polson, *Biochem. Jour.*, 30: 528, 1936.

TABLE I

Species	$s_{20} \times 10^{13}$	$D_{20} \times 10^7$	M	f/f_0
Pig	18.0	1.64	930 000	2.0
Cow	18.1	1.69	910 000	2.0
Horse	17.9	1.63	930 000	2.0
Rabbit	7.0	4.23	157 000	1.4
Monkey	6.7	4.06	157 000	1.5

The high value for the frictional ratio f/f_0 would indicate that the heavy antibody molecule is neither compact nor spherical, as $f/f_0 = 1$ is obtained only when the molecule is spherical and unhydrated.

The proportion of antibody N to total N in the solutions ranged from 40 to 100 per cent. In each case, however, it was possible to obtain solution showing only a single component with the sedimentation constant in the table. (A very small amount of a heavy component was found in the monkey antibody preparation).

The sedimentation constant was also measured in the 15 per cent. salt solution used for dissociation and found to be the same as after dialysis, indicating that the purification process had not altered the ultracentrifugal properties of the antibody.

In a horse antiserum and a pig antibody solution (each containing two components, $s = 6.7$ and 18.7×10^{-13}) it was possible to demonstrate that the heavy component was the bearer of the antibody activity by using the new analytical cell described in *Nature*.⁵ After centrifuging the heavy component into the lower compartment no antibody could be detected in the upper compartment. When the heavy component was centrifuged so that the boundary was only part of the way down, antibody still remained in the upper compartment.

The results indicate that there are two definite groups of animals, one usually producing antibody of the same size as the heavy component frequently observed in normal mammalian sera, and the other forming antibody of the same size as the principal globulin component of normal sera.

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VITAMIN L

THE specific dietary factor for lactation and vitamin B complex had long been confused, and it was not until 1934 that the two were clearly distinguished and the existence of the lactation factor established.¹ Since

⁵ A. Tiselius, K. O. Pedersen and The Svedberg, *Nature* 140: 848, 1937.

¹ W. Nakahara, F. Inukai and S. Kato, *Proc. Imp. Acad., Japan*, 10: 268, 1934; *Sci. Pap. Phys. Chem. Research*, Tokyo, 24: 155, 1934.