TABLE 1

Estrogen used	Number of animals*	Absorbed per day µgr	Uterine weight Average† gr	Uterine weight Range gr
		Intrasplenic		
Estriol	10	115	1.6	0.6–2.7
Equilenin	12	80	0.9	0.5–2.8
α-dihydro-equilenin ...	10	97	1.1	0.3–4.4
β-dihydro-equilenin ...	10	137	0.8	0.4–2.2
		Subcutaneous		
Estriol	15	111	5.4	3.7t.§–15.0t.
Equilenin	15	97	6.8	3.8 –15.5t
α-dihydro-equilenin ...	12	111	7.5	3.6t. –15.1t.
β-dihydro-equilenin ...	12	136	5.9	3.4 –10.5t.

* Animals with adhesions of the spleen to the abdominal wall were discarded; see circles with dot in the center in the figure.

† 0.3 to 0.5 gr is the uterine weight of a castrated guinea pig; 1 gr is the approximate uterine weight of an adult virginal female.

§ Uterine weight including subserous or mesometric tumors.

in the present series also an estrogenic action on the vaginal mucosa in about two thirds of the animals, though a weak one in most cases.

Our experiments leave no doubt about the statement that the liver is able to inactivate great quantities of estriol and equilenin. Though these urinary estrogenic metahormones derive from the intrahepatic conversion of ovarian estrogens, they are not the end-products.[7] On the other hand, the question remains open about the special changes the metahormones undergo in the liver.

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THE FIRST STAGE OF ANTIGEN-ANTIBODY REACTION IN INFECTIOUS MONONUCLEOSIS

ONE of the problems posed following the description of the pathogenesis of erythroblastosis fetalis was the failure to demonstrate anti-Rh agglutinins in about 50 per cent. of the Rh – mothers of erythroblastotic infants.[1] It was assumed that in these individuals the antibodies are fixed to the tissue cells of the reticulo endothelial system.[1, 2] This view is no longer tenable because Race[3] and Wiener[4] independently described antibodies which unite with Rh + blood but fail to cause visible agglutination.[5] Presumably the Rh + cells are specifically coated with the antibody so that they are no longer susceptible to the agglutinins in anti-Rh sera. These immune substances are referred to as blocking or incomplete antibodies. These significant observations were amply confirmed by the writers.

TABLE 1

THE SERUM USED IN THESE TESTS WAS DERIVED FROM A PATIENT SUFFERING FROM INFECTIOUS MONONUCLEOSIS

Blood	Agglutination titer	Hemolysis with complement*	Absorption for sheep blood†	Absorption for goat, type 3†	Blocking antibody‡
Goat, type 1	1:20	1:400	almost complete	none	strong
Goat, type 2	1:100	1:400	complete	complete	very strong
Goat, type 3	1:4000	1:400	complete	complete	
Sheep	1:2000	1:400	complete	none	

* Fresh guinea pig serum 1:10 was added. The values given indicate complete hemolysis.

† The agglutinating serum was diluted 1:20 and absorbed with one-half volume washed sediment of each of the four bloods. The absorbed fluids were tested with sheep blood and goat blood, type 3.

‡ Sheep blood was added after the initial readings were made.

It is known that the vast majority of the sera of patients suffering from infectious mononucleosis agglutinate sheep blood (Paul-Bunnel reaction). Exceptionally, however, this diagnostic reaction can not be demonstrated in otherwise typical cases.[6] Apparently, this state of affairs is quite analogous to that existing in erythroblastosis fetalis.

Accordingly, a search was made of sera of patients in whom a diagnosis of infectious mononucleosis was established. A number of sera containing potent agglutinins for sheep blood were collected and one serum was found with almost complete lack of action on sheep red blood cells.[7] This serum, however, contained antibodies which coated the surface of sheep

[7] It has been shown in the meantime that also equilin is inactivated when injected into the spleen of the castrated rat. A. Segaloff, *Endocrinol.*, 33: 212, 1943.

[1] P. Levine, L. Burnham, E. M. Katzin and P. Vogel, *Am. Jour. Obst. and Gyn.*, 42: 925, 1941.

[2] A. S. Wiener, *Arch. Path.*, 32: 227, 1941.

[3] R. R. Race, *Nature*, 153: 771, 1944.

[4] A. S. Wiener, *Proc. Soc. Exp. Biol. and Med.*, 56: 173, 1944.

[5] A similar effect with bacterial anti-sera was observed by A. F. Coca and M. F. Kelley, *Jour. Immunol.*, 6: 87, 1921.

[6] N. Rosenthal and G. Wenkebach, *Klin. Woch.*, 12: 499, 1933.

[7] For this specimen, I am indebted to Dr. J. H. Scherer, of the Medical College of Virginia.

blood, rendering these cells resistant to the action of active agglutinins. The blocking effect was distinct but not very potent.

However, strong support for the specificity of the reaction was derived from an unexpected source. In view of the close serological relationship of goat and sheep blood, an attempt was made to elicit the Paul-Bunnel reaction with goat instead of sheep blood. The first results with six different goat bloods apparently met with failure. But on extending the series to include an additional eight goats, three sorts of reactions were observed as indicated by the results summarized in Table 1.

With goat bloods of types 1 and 2 a strong blocking effect was obtained which is quite analogous to that observed in Rh – mothers of erythroblastotic infants. That specific union occurred is evident from the uniform results obtained in the hemolytic tests and the absorption effect on sheep blood.

It is of interest that sheep blood did not remove much of the agglutinin for goat blood, types 2 and 3. This suggests that for the serological diagnosis of infectious mononucleosis, selected goat blood may be preferable to sheep blood. It is still to be determined whether or not individual differences of sheep blood can be demonstrated with sera of patients suffering from infectious mononucleosis.[7a]

A close analogy to the blocking effect obtained with goat blood or with Rh + blood is the specific absorption of phage by resistant strains of S. Stanley of the paratyphosus B group as observed by Levine and Frisch.[8] In other words, the first stage of the reaction—specific union—occurs in the absence of the visible effect of lysis.

The observations in erythroblastosis fetalis and infectious mononucleosis emphasize the practical and diagnostic importance of the first and far more fundamental reaction of antigen and antibody, *i.e.*, specific union. At the same time, another source for the study of serological components of red blood cells is now available. Thus, one can no longer refer to agglutinable properties demonstrable by direct reactions as the only serological components of red blood cells.

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[7a] Since this paper was submitted, Levine and Waller found individual differences in the agglutinability of sheep blood. However, selected goat bloods of the Nubian breed gave the highest titers.

[8] P. Levine and A. W. Frisch, *Jour. Immunol.*, 30: 63, 1936.

ALTERATIONS IN THE ANTIDROMIC POTENTIAL OF MOTOR NEURONS FOLLOWING CHROMATOLYSIS[1]

As a result of injury or virus invasion, neurons exhibit a wide range of pathological reactions. The best known of these and the one which is most easily controlled experimentally is retrograde chromatolysis. This may be produced in the spinal motor nuclei by cutting a peripheral nerve. Previous papers have shown that neurons so treated will not respond to the proprioceptive reflex[2] and that the motor neuron itself, rather than "presynaptic" elements, is the site of the deficiency.[3] However, a gap still exists in the demonstration that the activity of the whole cell is changed by the chromatolysis, for it is possible that the phenomena depend upon alteration of parts of the cell in contiguity with the *boutons termineaux* of the primary afferent neurons. The data described below were derived from a series of eight experiments which rule out the participation of such local mechanisms in the development of the deficiencies of the chromatolysed cell.

Cats were prepared by cutting the right tibial nerve in the popliteal fossa and allowing the retrograde degeneration to reach its height. The technic of firing the motor neurons antidromically[4] has been used in these experiments. The potentials of the cells, discharged without the mediation of other nervous elements, were recorded with a cathode-ray oscillograph. Systematic probing of the affected segments with micro-electrodes yielded data by which maps were made showing the distribution of the potential fields[5] of both the degenerated tibial nucleus and its normal control on the other side of the spinal cord.

The normal antidromic potential (Fig. 1a) consists of two phases, a positive deviation which represents the approach of the conducted impulse to the cells[6] and a second wave, of positive or negative sign depending on the spatial relations of the micro-electrode to the cells,[7] which represents the discharge of the neuron. The early component is unaffected by degeneration, but the second or cellular component is greatly decreased in amplitude in the chromatolysed nucleus (Fig. 1b). As conditioning curves of the affected nuclei (plotting height of response to a second shock to the interval between two stimuli) show

[1] From the Department of Anatomy, University of Minnesota Medical School. Aided by a grant from the National Foundation for Infantile Paralysis.

[2] B. Campbell, SCIENCE, 98: 114–115, 1943.

[3] *Idem, Anat. Rec.*, 88: 25–33, 1944.

[4] J. C. Eccles, *Proc. Roy. Soc.*, B107: 557–585, 1931.

[5] B. Campbell, *Anat. Rec.*, 91: 77–88, 1945.

[6] R. Lorente de Nó, *Jour. Neurophysiol.*, 2: 402–464, 1939.

[7] Descriptions of the potential fields will be published elsewhere.