to show increase in titre after 4 months of further treatment. Discarded and replaced by Horse No. 1204.

Horse No. 1204—Serum showed an increasing rise in neutralization titre, reaching maximum of 1:40 after 6 months. Subsequent subcutaneous and intramuscular injections failed to increase potency of its serum.

Horse No. 1247—Serum reached maximum neutralization titre of 1:60 after 6 months of treatment. Subsequent intramuscular and subcutaneous inoculations raised the potency of its serum to a titre of 1:100. The concentrated pseudoglobulin of this serum has a neutralizing power of 1:1200.‡

The serum and concentrate is not toxic for monkeys even when given in doses as large as 90 cc.

Preliminary experiments on passive immunization, with the serum concentrate, indicate that it may be of value, since monkeys have been protected against intracerebral doses of highly infective virus for several days.

Two new sets of horses are now being immunized by different methods with the hope of obtaining even more potent products.

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Modification of Vagus Inhibition of the Heart by Quinidine.

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Quinidine acts directly upon the myocardium and is a powerful cardiac depressant. The drug depresses auriculo-ventricular conduction and retards the rate of the sinus node in dogs.[1] Auricular irritability is definitely diminished in the terrapin's heart.[2] However, when applied to clinical cases of hyperactivity of the sinus node as in sinus tachycardia, quinidine does not consistently exhibit its depressor effect. The rate of the sinus rhythm is frequently increased rather than retarded.

‡ This serum is 3 to 4 times as potent, and the concentrate about 40 times as potent as human convalescent serum. The concentrate is at least 10 times as potent as the previous one prepared in this laboratory.[5]

[1] Lewis, T., Drury, A. N., Iliescu, C. C., and Wedd, A. M., *Heart*, 1921, **9**, 55.

[2] Hirschfelder, A. D., and Cervenka, C., *J. Pharm. and Exp. Therap.*, 1925, **26**, 19.

Lewis and his associates[1] have demonstrated in dogs that in addition to its direct cardiac action, quinidine also modifies the response of the heart to vagus stimulation. The prolongation of auriculoventricular conduction time on vagus stimulation was markedly lessened under quinidine. In some instances vagus stimulation actually shortened the conduction period. The reaction of the sinus node to vagus stimulation was only slightly affected. In the cat, however, Dale[3] showed that the vagus effect on the sinus node was not only eliminated by quinidine, but a reversal of vagus action could be obtained with an acceleration of the sinus rate. In man it is possible to study the effect of vagus stimulation on the sinus node by application of the carotid sinus reflex. In some subjects an intense reflex stimulation of the vagus nerve is obtained[4] with temporary inactivity of the sinus node and cardiac standstill. This reaction can be abolished by atropine. Six subjects were selected in whom a prolonged cardiac standstill could be consistently induced by pressure on the right carotid sinus. These subjects were repeatedly tested to determine the consistency of the response. In each instance a uniform reaction was obtained under repeated application of the reflex. Following a control electrocardiogram recording the effect of right carotid sinus pressure, quinidine sulphate was administered orally for a period of 4 or 5 days in increasing doses. On the final morning of the experiment 1.8 to 2.2 gm. was given in divided doses. One hour after the last dose, an electrocardiogram was made, again recording the effect of carotid sinus pressure. In each case the prolonged standstill (intense vagus effect) was replaced by a slight slowing of the sinus rate (mild vagus effect). Figures 1 and 2.

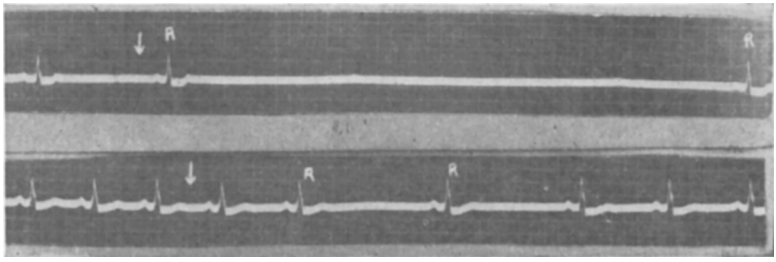

FIG. 1.

Subject H. B. Upper strip shows cardiac standstill (R — R = 9.1 seconds) after pressure on right carotid sinus (arrow). The lower strip after administration of quinidine sulphate 2 gm., maximum R — R = 2.2 seconds.

[3] Dale, H. H., *Heart*, 1921, **9**, 87.

[4] Nathanson, M. H., PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 1037.

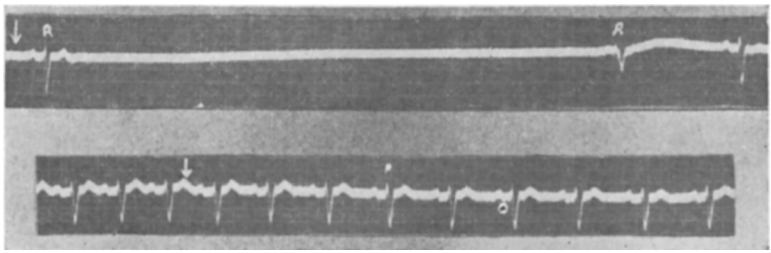

FIG. 2.

Subject J. Q. Upper strip shows cardiac standstill (R — R = 11 seconds) after pressure on right carotid sinus (arrow). Lower strip after administration of quinidine sulphate 2.2 gm. Carotid sinus pressure produces slight slowing of heart rate from 80 to 58 per minute.

These observations indicate that the action of the vagus nerve on the sinus node in the human heart is definitely modified by quinidine. This effect must influence the general reaction of the heart to the drug and may explain the variable results which follow its administration in clinical cases.