were made on serum cannot be used to establish the relationship and, for the short experimental periods which we used, no transport of fat was observed. It is apparent that further work, using analysis of whole blood, is necessary. It may be noted, however, that even the shift of fat from red blood cells to plasma may have some significance as regards fat transport, since it represents a higher concentration of fat in that portion of the blood which is immediately concerned with the transfer of food stuffs to the tissue cells.

Conclusions. 1. A reciprocal relationship has been shown to exist between the carbon dioxide combining power of the blood and the concentration of total fat in the blood serum. 2. Changes in serum fat content produced by altering the acid-base balance are not accompanied by changes in the fat content of the whole blood, within the duration of our acute experiments. 3. The changes in serum fat are therefore the result of a shift of fat between the red blood cells and the blood plasma. 4. The significance of serum and whole blood lipemias as regards fat transport, is discussed.

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Effect of Certain Yohimbine Derivatives upon Arterial Strips.

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Previous work by F. Meyer,[1] Hamet,[2, 3] Weger[4] and others indicates that the yohimbine radicle exhibits a rather marked antisympathicomimetic action in various organs. Some investigators have studied various isomers of yohimbine with similar results but our present work deals with several newly formed HCl salts of the yohimbine radicle in the form of ethyl, allylamine, butyl, diethylaminoethyl, phenyl and allyl derivatives.* Essentially, these derivatives behave similarly to yohimbine HCl but ethyl yohimbine

[1] Meyer, F., *Arch. f. d. ges. Physiol.*, 1912, 223.

[2] Hamet, M., *Comp. rend. Acad. d. sc.*, 1925, **180**, 2074.

[3] Hamet, M., *Comp. rend. Soc. de Biol.*, 1931, **108**, 963.

[4] Weger, P., *Comp. rend. Soc. de Biol.*, 1927, **96**, 801.

* The yohimbine derivatives used in this research were made by Professor David Worral of Tufts College, Medford, Mass.

HCl seems to be the most promising for future studies since it is least toxic.[5]

Attempts at quantitatively determining the effects of the yohimbine derivatives were made by using the method of O. B. Meyer[6] for studying isolated arterial tissue *in vitro* with modifications of Lewis and Koessler,[7] using suspended beef carotid arterial spirals of uniform lengths in the standard Locke oxygenating bath at 37.5°C.

Results and Conclusions. This investigation embraces about 60 experiments as represented by a typical tracing (Fig. 1). Epinephrine was effectively constrictor in dosages ranging from 1-200,000,000 and up, but 1-1,000,000 concentration was commonly employed throughout as the standard dosage. The yohimbine derivatives added to the bath after an effective constricting dose of epinephrine exerted no visible response other than nullifying the usual constrictor effect of a second application of epinephrine (Fig. 1B), or the response was in the direction of accelerated relaxation (Fig. 1A). However, after an *exaggerated* constrictor effect of epinephrine as induced by preliminary cocaine application, yohimbine derivatives brought on an accelerated relaxation of the pronounced arterial contraction. This cocaine sensitization of epinephrine activity confirms the well-established work of Froehlich and Loewi[8] and further suggests that epinephrine produces a normal, although diminished, adrenergic response *after* cocaine and yohimbine, because the arterial strip, with its neural components, is *still sensitized* to epinephrine. That is, yohimbine derivatives in the concentrations employed, 1-50,000, do not obliterate cocaine sensitization to epinephrine.

Ephedrine was less responsive as an arterial strip constrictor but its effect also was neutralized by the yohimbine derivatives.

To preclude the probability that "epinephrine reversal" might be due to profound muscular depression by yohimbine derivatives, histamine and barium chloride were added to the bath after yohimbine radicles and their customary constrictor effects observed. Also, sodium nitrite was found to be capable of markedly relaxing strips which had been exposed to the yohimbine derivatives.

Thus the conclusion seems warranted that the yohimbine derivatives, in the concentrations employed in these studies, exhibited no direct muscular effects, and hence that "epinephrine reversals" were due to depression of adrenergic neural components.

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5 Young, A. G., *J. Pharm. and Exp. Therap.*, 1935, **54**, 164.

6 Meyer, O. B., *Z. f. Biol.*, 1906, **48**, 352.

7 Koessler, K. K., and Lewis, J. H., *Arch. Int. Med.*, 1927, **39**, 182.

8 Froehlich, F., and Loewi, O., *Arch. Exp. Path. Pharm.*, 1910, **62**, 159.

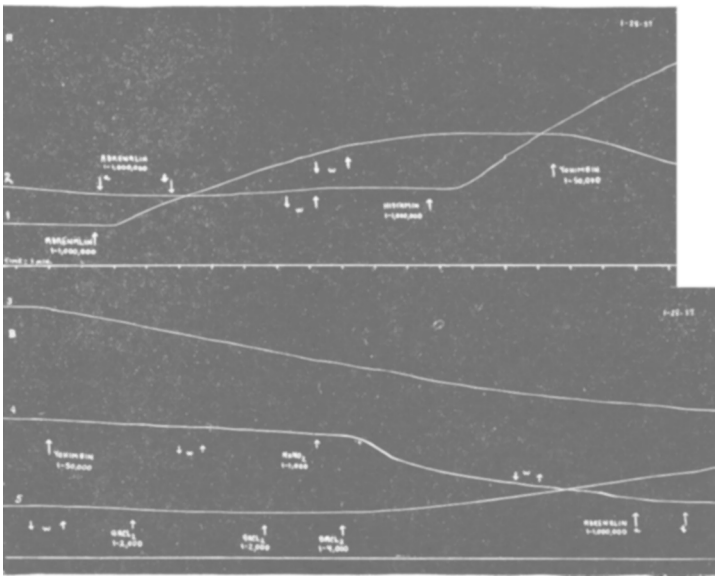

FIG. 1.

Time = 1 minute.

A—No. 1, Adrenalin, 1-1,000,000
Yohimbine, 1-50,000
No. 2, Adrenalin, 1-1,000,000
Histamine, 1-1,000,000
w = washing

B—No. 4, Yohimbine, 1-50,000
Sodium nitrite, 1-1,000
Adrenalin, 1-1,000,000
No. 5, Barium chloride, 1-2,000
" " 1-4,000

Summary. 1. The hydrochloride salts of yohimbine derivatives (ethyl, allyl-amine, allyl, butyl, phenyl and diethylaminoethyl) in the dosage used, 1-500,000 to 1-50,000, do not seem to directly affect the arterial muscle strip whether it is in a contracted or relaxed state. 2. A predetermined, consistently constricting dose of epinephrine HCl, 1-1,000,000, or ephedrine, 1-25,000, administered after yohimbine derivatives is inhibited in its action. 3. This inhibitory action of the yohimbine radicle on epinephrine can be obviated by previously sensitizing the arterial strip to epinephrine by addition of cocaine. 4. Musculo-tropic agents such as histamine, 1-1,000,000, barium chloride, 1-1,000, and sodium nitrite, 1-1,000, are not modified in their actions by yohimbine derivatives. 5. These new yohimbine derivatives are antisympatheticomimetic agents.