must conclude that the fragile enamel seen in hypothyroid patients is a result of disturbed metabolism, not a developmental anomaly.

[1] Swingle, W. W., *Am. J. Physiol.*, 1924, lxx, 70.
[2] Hoskins, M. M., *J. Exp. Zool.*, 1927, iv, 48.

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Pressor Effect of Guanidine Salts on the Non-anesthetized Rabbit.

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A possible relationship between guanidine intoxication and essential hypertension has been suggested.[1] It was of interest to study the question in non-anesthetized animals. This report contains the results of daily examinations for blood pressure and pulse rate in 12 experiments performed on 5 rabbits provided with a good carotid loop (Van Leersum). The salts used (Eastman Kodak Co.) were methylguanidine nitrate (9 experiments), methylguanidine sulphate (2 experiments), and guanidine nitrate (1 experiment). All the rabbits received 0.1 gm. per kilo of body weight but in different concentrations, 1:10 and 1:20 in distilled water, and 1:20, 1:30 and 1:50 in salt solution (4 and 8 per 1000). The total volume of fluid injected was from 3.7 to 8.2 cc. of distilled water and from 6 to 18 cc. of saline. The weights of the rabbits varied from 2.945 to

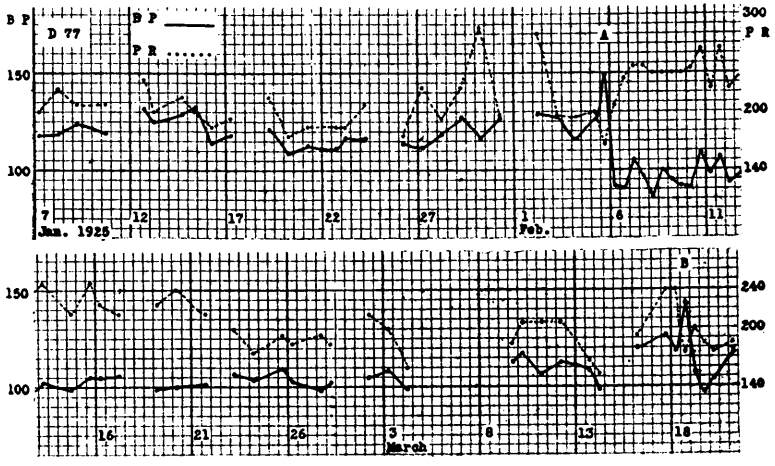

Figure 1.

4.125 kg. After several weeks of observation, the animals received one of the guanidine salts, injected slowly intravenously (marginal vein of the ear). Blood pressure, pulse rate and general reactions were carefully observed immediately after the injection and daily thereafter.

The behavior of blood pressure and pulse rate, in one of the animals, is shown in Fig. 1. Blood pressure is expressed in mm. Hg. (scale to the left); pulse rate in beats per minute (scale to the right). The space between two vertical lines corresponds to one half day. Blood pressure values are the mean of 10 consecutive readings. After the first injection, A, the blood pressure fell and the pulse rate increased, in marked contrast to their behavior before the injection. This condition lasted 18 days after the injection. At B, another injection of same amount of same salt (8.4 cc. of 1:20 in 4:1000 saline) had a similar effect immediately following the injection, but practically no after effect. The graph after this point is similar to the portion before the injections, and has been omitted. The graph under B is a good example of most of the experiments. In a few instances the dip of the pulse rate is more pronounced, reaching 128 per minute, in a few others the peak of the blood pressure is higher.

In one animal the effect after injection was more pronounced than shown in A. The blood pressure oscillated about 80, the pulse rate about 300. The animal died on the fifth day. At autopsy a marked dilatation of the heart was found, hydrothorax (bilateral) and ascites. There is little doubt that methylguanidine produced in this rabbit a severe injury of the myocardium.

The observations may be summarized thus:

1. In no instance did blood pressure reach 170 mm. Hg., *i. e.*, within normal limits.[2, 3] The highest reading was 165 mm. The highest averages were: 150-159 mm. Hg, 2 instances; 140-149, 7; 130-139, 0; 120-129, 3. The last three are negative as far as blood pressure is concerned. Two of these negative results (in the same animal) show that with this dose the pressor effect of methylguanidine may be absent. The other occurred with guanidine nitrate. De Waele and Bulcke have already said that: "Chez le lapin, même à hautes doses, la guanidine reste sans effet sur la pression sanguine et sur le vague."[4]

2. The pulse was slowed in all cases even when the blood pressure was not greatly altered. Slowing of the pulse rate is, in these experiments, more conspicuous than in Alles's report.[5] My results with methylguanidine salts are comparable to his, and, in a few instances more pronounced than the effect he obtained with ethylguanidine.

The difference may be accounted for by the urethane anesthesia and the smaller doses of methylguanidine used by him. Practically all workers agree that this circulatory effect of guanidine salts is independent of the vagus.[1, 4, 5]

3. The time relation of blood pressure and pulse rate effects cannot be made as precise with the method I have used as with a continuously recording device. I find that the highest blood pressure and the lowest pulse rate coincided in 8 out of 12 experiments and that in the remaining 4 experiments the pulse rate effect preceded the rise in blood pressure. The slowest pulse rate was recorded as early as 5 minutes and as late as 49 minutes after the injection. The rise in blood pressure was recorded as early as 8 minutes and as late as 2 hours and 10 minutes after the injection. The blood pressure curves had a single peak in 7 experiments, and a plateau in 5; this plateau was observed to extend for from 35 to 272 minutes. The pulse rate curve had an inverted peak in 8 experiments; and a low flat part in 4, the latter extending in an interval of time varying from 26 to 95 minutes. The blood pressure rise lasted more than the slowing of the pulse in 5 instances, about the same in 4, and less in 3.

4. The other signs of intoxication occurred as follows: salivation (11 instances out of 12 experiments), jerks of the extensors of neck (8 instances), diarrhea—soft feces (7), clonic spasms of legs (6), dyspnea, occasionally violent (4), tremor of lips (3). Of these signs, salivation was first to appear and diarrhea the last to disappear.

5. In a subsequent experiment, part of the graph being reproduced, the injection was repeated when the blood pressure rise of the first injection was beginning to subside. Immediately after the second injection the animal became very weak, the blood pressure rose again (maximum 165 mm. Hg.) without any slowing of the pulse rate, and the respiratory movements became very frequent. Half an hour later the blood pressure was 132 mm. Hg., pulse rate 284 per minute, and dyspnea violent. Eighty minutes after the second injection the animal went abruptly into collapse. The pulse was imperceptible, respiratory movements progressively weaker. The animal died 5 minutes later.

6. The circulatory effect of the methylguanidine salts used is inconspicuous when compared with the general picture of the intoxication.

7. One animal died with all the signs of circulatory embarrassment due to myocardial weakness, as shown at the autopsy by dilatation of the heart, hydrothorax and ascites.

8. A toxic theory of essential hypertension would be more plausible if a substance were found which causes, in normal animals, persistent elevation of blood pressure above normal limits, without obvious signs of general intoxication.

[1] Major, R. H., and Stephenson, W., *Bull. Johns Hopkins Hospital*, 1924, xxxv, 186, 140.

[2] Dominguez, R., *J. Met. Res.*, 1924, vi, 123.

[3] Dominguez, R., *J. Exp. Med.*, 1927, xlvi, 443.

[4] De Waele, H., and Bulcke, G., *Arch. int. Physiol.*, 1925, xxv, 74.

[5] Alles, G. A., *J. Pharmacol. Exp. Therap.*, 1926, xxviii, 251.

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An Improved Arrangement for Bacteria-Retaining Filters.

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Attention has lately been redirected to the importance of *adsorption* in filtration through bacterial filters[1]; however, if filtration is prolonged, the adsorbing surface may become saturated and substances at first retained may appear in the filtrate. The range of particle size from the smaller filterable viruses to the ordinary bacteria, on the other hand, is a critical zone in which *mechanical retention* plays an increasingly important and finally a determinative rôle.[2] Certain ultramicroscopic viruses may pass the more porous filters in almost undiminished concentration, others in greatly reduced concentration. The visible microorganisms pass the filters only in sufficient numbers to inoculate the filtrate, and only pass at all when certain attributes of the microorganism (*e. g.*, small size, motility, flexibility), or the circumstances of the filtration are especially favorable.

It does not suffice, then, to report that a certain virus is or is not filterable through certain filters.[3] The circumstances must also be known. Incomplete recording of the details of procedure, together with diversity of filtration methods and lack of exact experimental control of the filtration technique, have often introduced needless confusion into the literature on filterable viruses.

The arrangement shown in the accompanying figure offers advantages in point of control over the filtration process, as well as in convenience of operation. The reduced filtration pressure is shown by the manometer. The filtrate is received into a graduated vessel.