

### Possibility of Producing Arterial Hypertension by Intracisternal Injection of Kaolin.\*

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Experimental hypertension by means of intracisternal injection of kaolin was produced in dogs first by Dixon and Heller,<sup>1</sup> and Heller.<sup>2</sup> These authors observed a considerable elevation of blood pressure lasting many months. According to Heller, this type of hypertension is "central" in nature and due to increased intracranial pressure resulting from mechanical obstruction of the subarachnoid and ventricular spaces. Braun,<sup>3</sup> and Braun and Samet<sup>4, 5, 6</sup> showed that hypertension produced by injection of kaolin can be prevented or abolished by denervation of the kidneys. Bilateral adrenalectomy, on the other hand, does not prevent the development of this form of hypertension (Jeffers, Lindauer and Lukens<sup>7</sup>). Hoff<sup>8</sup> obtained a sustained increase of blood pressure of 90 mm Hg in 4 dogs. Since he could reduce the blood pressure by ventricular puncture, Hoff assumed that the elevation of blood pressure resulted from stimulation of the basal ganglia and mammillary bodies by increased intracranial pressure. Further successful results with the kaolin method were reported by Giordano and Galigani.<sup>9, 10</sup> Griffith and associates produced hypertension in a large number of rats by the same procedure,<sup>11-14</sup> but the high blood pressure was maintained for more than 2 months in only a few animals.

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<sup>1</sup> Dixon, W. E., and Heller, H., *Arch. exp. Path. u. Pharm.*, 1932, **106**, 265.

<sup>2</sup> Heller, H., *Wiener Klin. Wschr.*, 1934, **13**, 241.

<sup>3</sup> Braun, L., *Wiener Klin. Wschr.*, 1933, **46**, 225.

<sup>4</sup> Braun, L., and Samet, B., *Wiener Klin. Wschr.*, 1934, **47**, 65.

<sup>5</sup> Braun, L., and Samet, B., *Arch. exp. Path. u. Pharm.*, 1934, **177**, 662.

<sup>6</sup> Braun, L., and Samet, B., *Wiener Klin. Wschr.*, 1935, **48**, 940.

<sup>7</sup> Jeffers, W. A., Lindauer, M. A., and Lukens, F. D. W., *PROC. SOC. EXP. BIOL. AND MED.*, 1937, **37**, 260.

<sup>8</sup> Hoff, H., *Wiener Klin. Wschr.*, 1935, **48**, 545.

<sup>9</sup> Giordano, C., and Galigani, D., *Minerva Medica*, 1937, **2**, 395.

<sup>10</sup> Giordano, C., and Galigani, D., *Arch. It. di Med. Sperm.*, suppl. No. 5, 1939.

<sup>11</sup> Griffith, J. Q., Jeffers, W. A., and Lindauer, M. A., *Am. J. Physiol.*, 1935, **113**, 285.

In contrast to these successful results we were unable to obtain any significant increase in blood pressure in dogs after intracisternal kaolin injections.

Fourteen dogs were used in our experiments. The blood pressure was taken 6 to 9 times over a period of at least one month prior to the injection of kaolin. During the recording, the dogs, which were unanesthetized and trained to the procedure, remained perfectly calm and cooperative. After the average normal blood pressure had been thus established, kaolin was injected and then the blood pressure recorded at frequent intervals for a period of 32-61 days. One dog received a second injection of kaolin after 61 days of observation and the blood pressure was frequently recorded during a period of 56 more days.

Blood pressure was recorded directly by puncture of the femoral artery with a 21 gauge needle connected with a mercury manometer, the tubing of which contained a 5% solution of sodium citrate as anticoagulant.

The animals were anesthetized by intravenous administration of evipal or nembutal. Twenty mg per kg of kaolin were suspended in 3-5 cc of sterile physiological saline solution and injected into the cerebello-medullary cistern after withdrawal of an equal amount of spinal fluid.<sup>†</sup> After the injection, the dogs were kept on the operating table for 20 minutes with their heads lowered to facilitate the passage of kaolin into the ventricles and basilar cisterns.

The average blood pressure of 14 healthy dogs was found to vary between 102 and 155 mm Hg (average 120), but was fairly constant for the individual animal. Five of the dogs died within a few days following the cisternal puncture.

Of the remaining 9 dogs, 4 showed a moderate increase of blood pressure (30, 32, 38, and 39 mm Hg respectively) lasting for a period no longer than 20 days. Then, the blood pressure receded to its previous normal level. The remaining 5 dogs exhibited an increase in blood pressure of only 6, 10, 15, 19, and 19 mm Hg respectively, which is well within the normal range of physiologic fluctuations or within the possible range of error.

Autopsies, performed in 4 dogs, revealed considerable internal hydrocephalus of the lateral, third and fourth ventricles. Most of

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<sup>12</sup> Griffith, J. Q., and Roberts, E., *Am. J. Physiol.*, 1938, **124**, 86.

<sup>13</sup> Lindauer, M. A., Griffith, J. Q., and Jeffers, W. A., *PROC. SOC. EXP. BIOL. AND MED.*, 1938, **38**, 497.

<sup>14</sup> Freeman, N. E., and Jeffers, W. A., *Am. J. Phys.*, 1939-40, **128**, 662.

† In 6 dogs commercial kaolin USP was used; collosol kaolin was used in 8 dogs.

the kaolin injected was found in the basilar cisterns and subarachnoid spaces and only a minimal amount, if any, was noted in the fourth ventricle.

We are unable to explain why our results differ from those of other authors and why we failed to produce lasting arterial hypertension. We used the same kind and amount of kaolin as other investigators (no difference was found in the action of the two preparations of kaolin used); only our method of recording the blood pressure was different. Whereas, other authors used the indirect cuff method, we preferred the direct arterial puncture, the reliability of which has been proven by many recent investigators. We also checked the accuracy of our blood pressure readings by occasional use of larger cannulas (18 and 17 gauge).

*Summary.* A suspension of kaolin injected into the cerebello-medullary cistern of 9 dogs failed to produce a significant or sustained elevation of blood pressure, although considerable internal hydrocephalus was present in all autopsied dogs.

### 13011

#### **Production of Deciduomata in Ovariectomized Mice Receiving Progesterone.\***

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It has been recognized since the original experiments of Loeb<sup>1</sup> that the corpus luteum hormone is essential for the development of the maternal portion of the placenta. The belief has been quite general,<sup>2</sup> however, that this hormone must be supplemented by estrogen for the reaction to occur. Apparently the only instance of the induction of placentomata with progesterone alone is reported by Selye,<sup>3</sup> who traumatized the uterus of an ovariectomized rat receiving 15 mg of progesterone daily. In the experiments reported here much smaller amounts of progesterone were effective in eliciting

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<sup>1</sup> Loeb, L., *J. A. M. A.*, 1908, **50**, 1897.

<sup>2</sup> Allen, E., Hisaw, F. L., and Gardner, W. U., Chapter VIII in *Sex and Internal Secretions*, edited by Allen, E., Danforth, C. H., and Doisy, E. A., 1939.

<sup>3</sup> Selye, H., *Proc. Soc. Exp. Biol. and Med.*, 1940, **48**, 343.