

tion of the motor nerves of the abdominal musculature in pregnancy is not more effective in causing alterations of the pressure curve than in the non-pregnant cat. The function appears to be part and parcel of the musculature itself rather than of the extrinsic nerves, although some slight nervous regulation and coördination does undoubtedly exist.

79 (1539)

Coli fever and blood volume in dogs.

By **H. G. BARBOUR** and **A. J. HOWARD.**

[From the Pharmacological Laboratory of the Yale University School of Medicine.]

For the continuation of work on the mechanism of fever reduction by drugs we have been seeking a satisfactory method of producing fever in dogs. In these animals a predictable curve of neurogenic fever is very difficult if not impossible to obtain. A few injections of peptone have given us a maximum rise of less than 1° C. with a rapid return to normal within two or three hours (maximum dose employed: 7 c.c. per kilo of 67 per cent. "bactopeptone.")

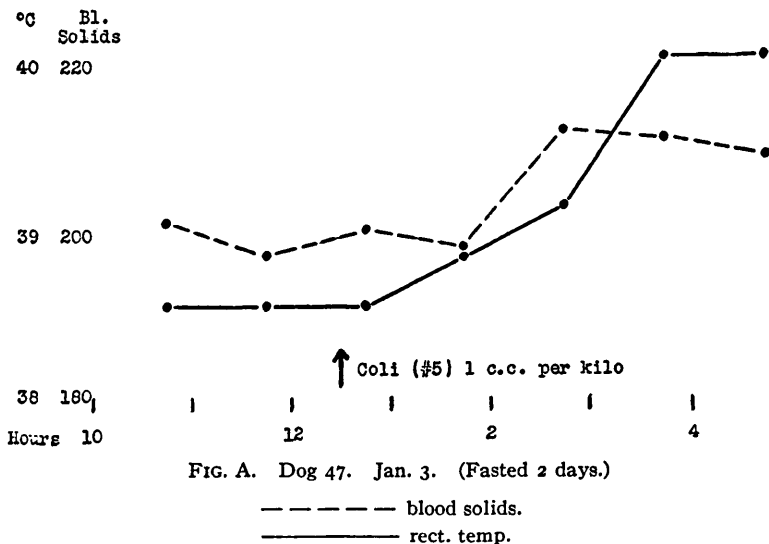
Turning to injections of killed cultures of colon bacilli we made nineteen experiments with subcutaneous injections of a vaccine containing 325,000 million bacilli per c.c. and in fourteen of these obtained a temperature the following morning (that is, after 15 hours), varying from 0.4° to 1.7° C. above normal. In the other five, no elevation of temperature was seen.

The next procedure was to inject in the morning, following the curve throughout the day. For this purpose a more concentrated vaccine was selected, containing 1,625,000 million bacilli per c.c. In five uncomplicated experiments in which this vaccine was used, maximum temperature increases of 2.4° to 1.5° C. (with hourly readings) were obtained with doses of 1 c.c. per kilo. With ½ c.c. per kilo the maximum increase was 2.4°. A smaller dose (0.2 c.c. per kilo) gave, however, an increase of only

0.6° C. A third strength of vaccine used contained one million bacilli per c.c.; doses of $\frac{1}{2}$ and 1 c.c. per kilo, gave maximum increases of 1.0° and 1.2° C. respectively. In all of the experiments with the last two vaccines the maximum temperature was attained by either the second or the third hour after the subcutaneous injection. At the end of the day (6–8 hours after injection) the temperature elevation was usually reduced by about one half.

The last two strengths of vaccine mentioned were therefore considered suitable for further studies. On the second day the temperature was usually found somewhat elevated, but thereafter not at all. The dogs could not as a rule be used for more than one injection each as repetition of the same or larger doses after four days gave a less pronounced effect, indicating that some degree of immunity had been produced.

In all experiments the injections gave sterile abscesses developing to a considerable size and breaking down several days after the injection. About half of our dogs were fasted for two days before being injected, the others being kept on a constant adequate diet of meat, lard, and bread; water ad libitum was always allowed. No essential differences were noted between fed and fasted animals.



Changes in the blood volume of coli fever dogs were followed by means of hourly determinations of hemoglobin and blood solids. In uncomplicated experiments the blood solids showed constantly an increase running parallel with the increase of body temperature. This increase varied at the maximum point from 3.3 to 7.6 per cent. in five different animals. It is illustrated in the accompanying figure (A) as well as in Figures 2 and 3 of the following paper on dextrose plethora. Similar hemoglobin changes were quite definite in some cases.

The increase in the percentage of the blood solids is interpreted as a diminution in the volume owing to loss of water. We are not yet prepared to discuss the fate of this water, but have noted no significant increases in the amount of urine. The loss of water from the circulation is probably the chief factor in the decreased heat dissipation which accompanies the initial rise of temperature in infectious fevers.

80 (1540)

Dextrose plethora and its antipyretic effect in coli fever.¹

By **H. G. BARBOUR** and **A. J. HOWARD**.

[*From the Pharmacological Laboratory of the Yale University School of Medicine.*]

The antipyretic action of dextrose was pointed out by one of us in the PROCEEDINGS of this Society about one year ago in connection with observations upon rabbits with peptone fever, and febrile human individuals to whom the sugar had been administered by mouth.² In view of the experiments reported some

¹ The assistance of an appropriation from the Bache Fund of the National Academy of Sciences in support of the researches reported in this and in the preceding paper is gratefully acknowledged.

The authors desire to thank Dr. George H. Smith, of the department of bacteriology, for valuable assistance in the preparation of the greater part of the coli vaccines used in this work.

² "The Antipyretic Action of Dextrose," *PROC. SOC. EXP. BIOL. AND MED.*, 1919, XVI, 136.

In connection with the demonstration that antipyretic drugs increase the blood sugar this has been interpreted as a potent factor in their action. See Barbour and Herrmann, "On the Mechanism of Fever Reduction by Drugs," *Proc. Nat'l. Acad. of Sci.*, 1920, VI, 136.