

follow its administration, and in rheumatism seems to accompany the diminution of pain, is probably due to relaxation of the cutaneous vessels, such as has been observed by Beyer (1) and others, and which naturally would feed and stimulate the cutaneous glands. It has been shown that the peripheral vessels dilate under the influence of antipyrin, the arteries dilating when large doses are administered. Whether this change of calibre is due to vaso motor influence or not is undecided, some claiming that the change is brought about by the direct action of the drug upon the vessels, since similar changes take place in isolated organs, (2) others claiming the reverse to be true. (3)

Antipyrin, when mixed with blood, does not cause a change of color or destruction of the corpuscles, as does kairin, thallin, resorcin, (4) and probably antifebrin.

Possibly its antipyretic properties are to be explained by the vascular changes which it produces, since they would contribute to increase the radiation of bodily heat. This is the explanation offered by Bettelheim, (5) Auseroff and Beyer. Arduin thinks the diminution in temperature is due to an influence exerted upon the thermogenic nerve-centres. During the last month P. J. Martin (7) has published the results of experiments which show that, almost uniformly, heat production is diminished by antipyrin, and heat dissipation is very much increased. It thus would seem to be an ideal antipyretic. In the small proportion of cases in which heat production was not diminished heat dissipation was so far in excess that the bodily temperature was lowered. Several observers have noted that under the influence of antipyrin the surface temperature rises while the internal temperature of the body falls. (8)

Its power of allaying pain in rheumatism is probably not dependent upon these vascular changes or the pyrexia produced by it, but upon a direct action on the nervous structure of the body. Antipyrin, though apparently most efficacious in rheumatic fever and least in muscular rheumatism; still, even in the latter, often acts beneficially. In many painful disorders purely neuralgic in character it gives the most prompt relief; for example, to the sharp neuralgic pains of locomotor ataxia. Ungar, (9) T. B. S. Robertson, (10) and

others, say it is efficacious in migraine. Germain Sée (11) has witnessed its power of relieving pain in other forms of neuralgic, and in gout, lumbago and sciatica.

The fact that there was in these diseases no common pathological effect except that of pain led the last writer to study particularly its action upon the nervous system. The results of his experiments he reported to the French Academy of Sciences on the 18th of April of last year. When injected subcutaneously in dogs three kinds of phenomena were observed: In the first place, a notable diminution of sensibility was observed, a true analgesia of the limb injected; sometimes, also, of the opposite one. In the second place, electric excitation of the sciatic nerve produced in the muscles of the opposite side only very feeble contractions, which points to diminished sensibility and reflex power in the spinal cord. In the third place, when antipyrin was introduced into the circulation of an animal except into one limb, the vessels of which were ligated, it was found that throughout the body the muscles contracted slowly and with difficulty, while those of the ligated limb contracted with their wonted vigor. It is evident, therefore, that antipyrin also affects the muscles; or more properly, perhaps, the nerve-endings in the muscles. Analgesic effects have been frequently noted by others. Large doses administered to animals cause convulsions, both clonic and tonic. Lessening of the reflexes, also, has been observed by others, as, for instance, by Arduin. (12) This last author, as well as Coppola, (13) thinks that the brain is influenced by the drug, since, when convulsions are produced by it, their severity is much diminished if the brain is separated from the cord.

Antipyrin does not affect the respiratory movements, although the frequency of respiration in fever diminishes as the temperature falls under its influence. As ordinarily administered, the rhythm and strength of the heart's action are not influenced. Beyer has shown by physiological experiments that when it exists in small amounts in the circulatory fluids, it causes an increase of work performed by the heart, while in large doses the contrary effect is produced. Some have also noted increased force in the heart's action, while others have observed a diminution in it. This discrepancy is probably due to the size of the dose administered.

The drug is eliminated by the urine, and can be found in it two hours after administration, and usually for thirty-six to forty eight hours afterwards. (14)

The following conclusions are, I think, justified by our present knowledge of antipyrin in the

1 "The Influence of Kairin, Thallin, Hydrochinon, Resorcin and Antipyrin on the Blood and Blood vessels." By H. G. Beyer, *Am. Journ. Men. Sci.*, April, 1886.

2 Quireilo and Coppola. See article by Beyer, *Am. Jour. Med. Sci.*

3 Auseroff, *Therapeutic Gazette* May, 15, 1886.

4 "De l'antipyrin contre la douleur." Par Germain Sée, *Le Bulletin Médical*, April 20, 1887.

5 Bettelheim, *Med. Jahr. K. K. Ges. d. Aerzt.*, ii, iii, 1886.

6 "Modern Antipyretics." By P. J. Martin, *Therapeutic Gazette*, May 16, 1887.

7 See Beyer, *Am. Journ. Med. Sci.*

8 Ungar. *Centralblatt f. d. Gesamte Therapie*, January, 1887.

9 "Antipyrin in Migraine, Pyrexia, etc." T. S. Robertson, *N. Y. Med. Record*, May 7, 1887.

11 Sée above, *Le Bulletin Médical*.

12 Arduin, *Therap. Gazette*, October 15, 1885.

13 Coppola, *Therapeutic Gazette*, October 15, 1885.

14 Marigliano Roberts. *Jahresbericht* p 313; *Therapeutic Gazette*, October 15, 1885.