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Subnormal Temperatures from Poisoning in Relation to Toxicity Determination.

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It seems important, especially in connection with toxicity determination, to point out that toxic doses of many substances may produce fall of temperature before death or recovery. An old clinical direction calls for note of the body temperature in case of poisoning and special arrangements if needed to reduce heat loss. Incidentally, the statement, "quinine has no significant effect on the normal temperature in man or in animals",¹ appears to need revision, the statement, "in toxic doses the fall is proportional to the collapse",² being truer. Quinine has produced subnormal temperatures in man,³ and in the rabbit fall of 12°C.,⁴ and the related cinchonine fall of 14°C. in this animal.⁵

We were led to note rectal temperatures in guinea pigs, used for preliminary toxicity determinations on cinchona bases, by unwittingly repeating an old observation,⁶ finding live animals, sometimes quite active, cadaverously cold to the touch. The drugs were given subcutaneously in the flank, in doses mostly in the lethal range, which is for most of these bases 100-400 mg. per kg. Using an average of about 7 animals in each series, we found in the case of each of 22 cinchona bases at least one animal in each series showing fall of 6° C. or more before death or recovery. The phenomenon seems common to all members of the group, including quinine, and is not limited to the cinchona series, for we found it also with morphine and quinoline, and Louvier⁷ has noted it with phenobarbital.

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†This work has been aided by a grant from the Committee on Scientific Research of the American Medical Association.

¹ Pharmacology and Therapeutics, A. R. Cushny, 10th Ed., 1934, C. W. Edmunds and J. A. Gunn.

² Manual of Pharmacology, T. Sollman, 4th Ed., 1932.

³ Cordell, E. F., *Maryland M. J.*, 1880, **6**, 257. Roberts, A. E., *Lancet*, 1895, **1**, 644. Rosenberg, D. D., *Med. Rec.*, 1902, **62**, 151. Lavier, G., *Bull. soc. path. exot.*, 1931, **24**, 184.

⁴ Hoggies, A., *Arch. exp. Path. u. Pharm.*, 1881, **14**, 113.

⁵ Dupuis, L., *Thèse de Paris*, 1877. Dupuis, L., and Laborde, J. V., *Tribune Med.*, 1878, **10**, 147.

⁶ Grimaux, E., and Laborde, J. V., *Compt. rend. soc. de biol.*, 1892, **44**, 608.

⁷ Louvier, M., *Arch. di farmacol. sper.*, 1932, **54**, 68.

The fall is not necessarily premortal: thus, one of our animals recovered completely after fall of 9°C. from hydrocinchonine; Simpson⁸ reported recovery of a monkey after fall of 24.6°C. from ether anesthesia and chilling. Shivering is occasionally seen. Fall is not always immediately associated with collapse: a quinidine-injected animal with temperature 31.3°C. moved around at this time quite normally and drank water.

Partly as a result of these observations, one of us (W.T.D.) has since been led to accumulate data on determination of comparative toxicity, *e. g.*, the toxicity of a substance such as quinidine, capable of producing serious fall in temperature, is measured against that of a "standard" related substance, such as quinine, injected in doses toxicologically comparable, on the same day or days and as nearly as practicable just before or after, so that the heat loss conditions are substantially the same for the animals of both groups over the succeeding period during which death or recovery occurs.

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Nutritional Value of Human Milk, Cows' Milk and Goats' Milk.

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Prolonged feeding with pure milk leads to a series of anemic conditions which generally are classified under the term of nutritional anemia of infancy (MacKay¹). Different reactions of the organism to various kinds of milk have been observed clinically and experimentally, and attempts have been made to separate the types of goat milk anemia and cow's milk anemia from the simple anemias of breast-fed infants (Baar²). But the formerly believed identity between the anemic conditions caused by goats' milk and cows' milk has been disputed lately by various authors (Brouwer³), and the experimental work of Rominger and coworkers⁴ seems to justify a doubt in the identity of both forms of nutritional anemias. In our

⁸ Simpson, S., *J. Physiol.*, 1902, **28**; *Proc. Phys. Soc.*, xxxvii.

¹ MacKay, H. M. M., *Nutritional Anæmia in Infancy*, London, 1931, p. 9.

² Baar, H., *Beih. Jahrb. f. Kinderheilk.*, 1927, **16**, 1.

³ Brouwer, E., *Jahrb. f. Kinderheilk.*, 1923, **102**, 257.

⁴ Rominger, E., Meyer, H., and Bomskov, C., *Z. f. d.*, 1933, **89**, 786.