

NOTE UPON ANTIPYRETIC STUDIES. By H. C. WOOD, M.D.

IN a recent number of Pflüger's *Archiv* Dr Hermann Arntz affirms that my assertion before the International Congress in 1881—that the theories then in vogue concerning the action of quinine upon the calorific functions—could have been based only on ignorance of the literature of the subject. An attempt to plummet the depths of my ignorance would probably interest no one, but it is a matter of importance that clear ideas should prevail in regard to what is needed to give us correct knowledge as to the action of pyretic and antipyretic remedies. It would seem very evident that the first studies should be directed towards investigating the action of such drugs upon the normal animal; i.e. to discover whether they affect the dissipation or production of heat, and, if so, whether such action is by an influence upon the nervous system or otherwise; and that, this having been settled, experiments should be made to determine the influence of the drugs upon the fevered state—the distinction between heat dissipation and heat production being always kept in view. I therefore desire to reaffirm that until we have more facts obtained by careful, calorimetric or chemical studies, all our theories concerning the action of drugs which lower temperature must remain mere speculations, guesses which may or may not be correct but which certainly are not proven to be true.

However ingenious they may be, and however valuable they may hereafter become, the researches of Prof. Binz and of Naunyn and Quincke, upon the effect of quinine on the rise of the temperature which, in dogs placed in very hot boxes, sometimes occurs after section of the spinal cord, are not available until by simpler experiments the fundamental portions of the problems are solved; for their researches were directed not towards the effect of the drug upon calorification in the normal animal, but to its action upon a highly artificial fever induced by several simultaneously acting causes (including external heating of the body and traumatic palsy of the thermogenetic nerves): a fever, presumably as complex in its nature as in its etiology, and therefore, so far as concerns its relations with antipyretics, of extremely

difficult interpretation. Further, the researches just alluded to appear to be not altogether consonant in their results.

Lewizky's experiments were performed by **wrapping** the animal in thick wadding and thereby attempting to control the heat dissipation. The crudity of this method it is **scarcely** necessary to remark upon. There must be great difficulty in **wrapping** up the animal exactly alike each time. Then there is **no** provision for the loss of heat by respiration, and when the **great** thickness of the rabbit's fur is borne in mind, it seems very **probable** that the cooling of the rabbit's body would scarcely be put **an** end to by wrapping it up. Moreover, it is well known that **binding** a rabbit down very sensibly affects its calorific functions, so that when the animal is not only bound but also swathed the conditions are highly unnatural, and a disturbing factor of unknown power is introduced into a problem which in its simplest form is one of the most difficult and recondite of physiology.

The recent direct thermometric experiments of Dr Arntz are of no more value than those of Lewizky, and what is still more strange the recorded results do not warrant the conclusions drawn from them by their performer. They were made upon men and animals. Those upon men were performed by wrapping the subject up and measuring the heat underneath the clothes: they were 4 in number, and as the mean temperature closely followed the maximum the results are embodied in the following table.

Experiment Number.	Dose.	Maximum Temperature under bed-clothes		Rectal Temperature	
		before.	after.	before.	after.
4	0.25	29.6	30	36.7	37.2
5	0.75	30.2	30.35	36.7	37
6	1	29.45	30	36.9	36.9
7	1	30.4	30.75	36.4	36.9
8	1.25	30.75	31.05	36.65	36.95

This table represents all of the experiments made upon man; of it Dr Arntz says that only a single time had quinine an increasing influence upon the giving out of the animal heat.

In the experiment in which quinine was not given the temperature under the clothes rose 0°.35C.: a rise which it will be seen was exceeded or equalled after the exhibition of quinine in Experiments 4, 6, 7. If Dr Arntz's experiments upon men prove anything it is

that the action of quinine is uncertain and variable; the alkaloid sometimes increasing, sometimes diminishing the dissipation of animal heat; but when it is remembered that the question becomes one of hundredths of a degree, that a minute variation in the perfection of the wrapping up of the patient would materially affect the result, and that no account is made either of the loss of heat by variations of perspiration or of respiration, it is plain that if science is to be encumbered by such experiments as these, those endeavouring to reach firm ground will have to spend much of their time in climbing over and pushing aside obstacles erected by others.

The first series of experiments made by Dr Arntz upon animals were similar to those of Lewizky, and are open to the same serious objections: in the second series of experiments the attempt was made to measure the effect upon heat dissipation of the respiratory exhalation by covering the rabbit's head by a sort of hood or bag. It is clear that the unnatural conditions were not by this made more natural.

Further these experiments do not bear out the theory that quinine has no effect upon heat dissipation. Thus in Experiment XIII., no quinine being used, the thermometer, underneath the covering, rose in one and a half hours $0^{\circ}4\text{C}$., whilst in Experiment XIV., quinine having been given, the temperature rose $7^{\circ}6\text{C}$. This immense difference is sufficient in itself to cast the gravest suspicion upon the method of experiment, especially when it is contrasted with the fact that with the same rabbit and about the same dose of quinine as in Experiment XIV. the temperature *fell* $0^{\circ}4\text{C}$. instead of *rising* at all.

In conclusion it may be allowable to state that this article has been written not because I have any theory as to the action of quinine, but as a protest against all theories that are not proven. One of the greatest difficulties in the way of clear pharmacological ideas is the tendency on the part of the profession to adopt any ingenious speculation—as witness the great mass of nonsense that has been written and *acted upon* as to the effect of chlorate of potassium upon blood oxygenation, and of the bromides upon the arterioles of the nerve centres.

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