

have also been noted by other observers after excluding the pancreatic juice from the gut.

None of our dogs showed polyuria; 580 c.c. was the largest recorded daily output. Acetone was seen only exceptionally.

All of the dogs showed an initially rapid and then slowly progressive loss of weight. Thus No. 5 lost 3.25 kilos in 12 days, but during the next 90 days lost only a little more than one kilo.

The experiments are being continued.

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Does a fatigue toxin exist?

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In 1904 Weichardt claimed to have found a specific substance, a fatigue toxin, as the chief agent in the production of fatigue. When present it was capable of forming in the tissues its own antidote, an antitoxin. A substance identical with fatigue toxin, named "kenotoxin," was obtained *in vitro* by treating proteins in various ways. However obtained, the substance, when injected into animals in small quantity, resulted in the production of antitoxin; when in larger quantity, it caused a great reduction in bodily temperature, slowing of respiration, sleep, and ultimately death.

In the present experiments animals, such as rabbits or cats, were fatigued by running in a revolving wheel. After fatigue was pronounced the animals were killed by decapitation, and the muscles of the hind legs were stimulated directly by the faradic current until they ceased to contract. Soon after death, in some cases within six to eight minutes, marked rigor was observed in the skeletal musculature. Immediately after the cessation of response to faradic stimulation the muscles of the hind legs were removed, cut to pieces and ground thoroughly with sand, and the muscle juice was squeezed out by a powerful press, all procedures being carried on with aseptic precautions. The juice was found markedly acid to litmus. When this juice was injected into the

peritoneal cavity of guinea pigs, usually in quantities as large as 10 c.c., either at the temperature of the room or after being warmed to bodily temperature, the animal became quiet; there was no constant effect on respiration, which sometimes increased in rate and sometimes decreased; and the bodily temperature began to fall at once. The fall continued during 30 minutes to 1 hour, the maximum so far observed being 1.6° C., after which there was a slower return toward the original temperature. These are the only immediate effects that have been observed. Occasionally the animal died on the following day. Precisely the same effects, including occasionally death on the next day, were obtained when the muscle juice of non-fatigued animals was used.

The working power of excised gastrocnemius muscles of the frog, when suspended in a bath of muscle juice prepared from fatigued and non-fatigued cats respectively, was studied. With the juice from fatigued muscles the duration of the working period of the gastrocnemii and the total amount of work performed were each diminished by about one half when compared with normal muscles not treated with juice. Practically the same quantitative effect was observed when the gastrocnemii were treated with non-fatigued juice.

There can be no doubt that by the methods employed above, the muscles were thoroughly fatigued. The conclusion seems justified that no acutely toxic fatigue substance was produced. Weichardt's assumption of the existence of a specific fatigue toxin is therefore not sustained. It seems probable that Weichardt's animals, which were actually killed by his extreme methods of inducing fatigue, were put into a profoundly pathological condition in which the toxic component of the protein molecule was split off. There is no reason to believe that this occurs in the normal course of fatigue.