tor. No inhibitory effect was observed in these systems.

The substance formed in the reaction described above would thus, on the basis of these tests, appear to have a specific antagonistic effect to vitamin B_{12}, since it is counteracted by the vitamin and has no inhibitory effect where the vitamin is not an essential factor. The chemical structure is not known, although the fact that the solution was decolorized during the reaction would indicate that the cyanide-cobalt complex was attacked. That this complex could be broken up by permanganate oxidation was reported by Brink *et al.* (*2*). These authors, however, identified hydrocyanic acid as a reaction product and considered that they had converted vitamin B_{12} into vitamin B_{12a}. This is apparently not the case with the peroxide oxidation reported here, since free cyanide could not be found with the $FeSO_4$ test (*3*), and the reaction product has an antivitamin rather than a vitamin activity.

Further chemical and biological work on this material is in progress.

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Functional Activity of the Sweat Glands in the Hairy Skin of the Dog

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The presence of the sweat glands in the dog not only in the foot pads but also over the body surface covered with hairs was described first by Gurlt in 1835 (*1*). His findings were confirmed by a number of investigators, and the literature was fully reviewed by Claushen (*2*). Nevertheless, we have found in several textbooks, monographs of physiology, and scientific encyclopedias a misleading description that in the dog sweat glands are found only in the foot pads. On the other hand, the lack of convincing evidence concerning the functional activity of the sweat glands in the hairy skin of the dog has hitherto led us to believe that this animal does not sweat over the general body surface.

The present paper is concerned with a demonstration of the sweating response in the hairy skin of the dog to some sudorific drugs and to local heating of the skin. For visualization of sweat we have used the iodine-starch method of Wada and Takagaki (*3, 4*), which proved to be suitable for this purpose. More than 30 dogs, mongrels and fox terriers, between the ages of 1 and 8 years were studied. Unanesthetized dogs were fastened to animal boards in either the supine or the prone position. The hairs of the regions to be tested were cut as short as possible, and the skin was painted first with iodine-alcohol solution and then with a starch–castor oil mixture. The sweating was designated by the appearance of black spots at each orifice of the hair follicle (Fig. 1). In the skin with black hairs, it was somewhat difficult to find the sweat spots when there was little sweating. The front aspect of thorax and abdomen and ventral surface of the thigh were chosen as the most suitable regions for observation. In most of the animals no spontaneous sweating was observed on the hairy skin during the whole time of the experiment, even during violent struggling.

The first tests of the functional activity of the sweat glands were made with intradermal injections of pilocarpine, acetylcholine, or adrenalin. Pilocarpine hydrochloride (JSP), acetylcholine (Roche), and adrenalin hydrochloride (Sankyo Co.) solutions were diluted with 0.9% NaCl to appropriate concentrations. One tenth or 0.2 ml of each solution was injected intradermally. With concentrations of $1:10^3$ to $1:10^5$ each of these three drugs was effective in producing visible sweating around the site of injection. The sweating by adrenalin was not inhibited by atropine, unlike the sweating by pilocarpine or acetylcholine.

The excitability of the sweat glands was measured by determining the minimal effective concentration of adrenalin for sweating, as tried previously with human sweat glands (*3*); it was found to be of almost the same order as that of the sweat glands in the trunk and extremities of healthy young men and women. The minimal effective concentrations of adrenalin ranged from $1:10^6$ to $1:10^8$, and those of acetylcholine from $1:10^8$ to $1:10^{10}$.

Another evidence of the functional activity of the sweat glands in the hairy regions was the fact that the sweating response was easily elicited by a local application of heat. The upper or lower portion of the trunk was introduced into a wooden cabinet ($50 \times 80 \times 60$ cm) and subjected to the radiant heat supplied by four 100-w electric bulbs. The response was observed through glass windows in the top and in the side walls of the cabinet. When the temperature inside the heating cabinet, which was measured at some distance above the skin surface, reached 30°–35° C, sweating was found to have been induced. In some dogs it occurred at a temperature below 30° C. Usually sweating was localized in the heated regions, and areas of skin outside the cabinet showed for the most part no sweating, in spite of the fact that the heat was so excessive as to cause severe panting and a considerable rise in rectal temperature. In a few dogs, however, spontaneous sweating was observed to occur slightly in some restricted areas—e.g., around the umbilicus and in the median part of the hypogastric region—when the upper portion of the body was intensively heated.

The local sweating induced by application of radiant heat was through the peripheral mechanism, since it was produced even in skin areas in which the nerve supply had been removed by sympathectomy either

with or without excision of the ventral and dorsal roots, including their ganglia, of the corresponding spinal nerves. Such sweating could also readily be brought about in summer by direct exposure of the skin to excessive heat of the sun.

Further, such sweating could be demonstrated in skin strips excised from the body (Fig. 1), for a certain length of time after removal from the body.

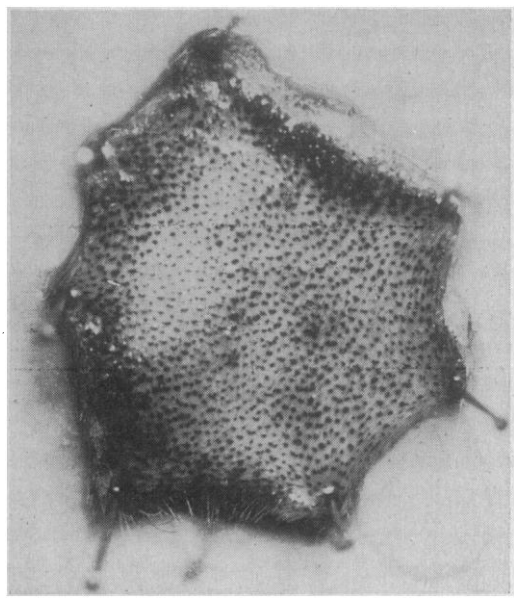

FIG. 1. Sweating response to radiant heat in dog's skin removed from front aspect of the thorax 5 min before heating. Sweating was rendered visible by black spots formed at the openings of hair follicles. Photographed after heating 10 min. (× 2.)

The fact that local sweating induced by radiant heat in the dog was not inhibited by atropine agrees with observation made by Randall (*5*) upon human skin. Yet the threshold skin temperature at which the sweating began to occur was 38.4° to 38.7° C in three of our dogs, in contrast to 38.4° to 45.5° C measured by Randall in cases of human skin.

Our findings suggest that the sweat glands in the hairy skin of the dog do not participate actively in the central thermoregulatory mechanism, but that they subserve chiefly the protection of the skin from an excessive rise of temperature.

Additional evidence of the secretory activity of the sweat glands in the dog's hairy skin under the influence of the sudorific drugs and radiant heat has been obtained by histological studies.

Recently, Coon and Rothman (*6*) discovered that in the human skin nicotine applied intradermally causes local sweating through the axon-reflex carried by the post-ganglionic sympathetic nerve fibers. Some of their experiments were repeated by one of us (W.) and our colleagues with similar results. In contrast, the hairy skin in most of the dogs showed no sweating response to a local application of nicotine in concentrations of $1:10^3$–$1:10^4$, except in the restricted skin areas of some dogs, where spontaneous sweating, probably reflex in mechanism, was produced. This suggests the possibility that functional integrity of the sudomotor fibers may be judged by the response of the sweat glands to nicotine.

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The Quantitative Relationship between pH and the Activity of Weak Acids and Bases in Biological Experiments

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The influence of pH on the bactericidal and fungicidal effects of weak acids and bases has been recognized for some time, but the implications of this effect for metabolic studies have frequently escaped attention. Such studies on living cells and tissues often involve the use of weak acids and bases as substrates, inhibitors, or stimulants, and the pH at which they are applied may have an important bearing on their activity. Thus many acids of biochemical importance with pK values of about 4 or 5 are routinely used in solutions in which they are partially dissociated, and their activity can be shown to be influenced in a regular manner by changes in the pH of the medium.

Fig. 1, in which the concentrations of weak acid required to produce a standard response are plotted, shows the magnitude of this influence of pH. It is based on a study of graphs from 90 pH experiments

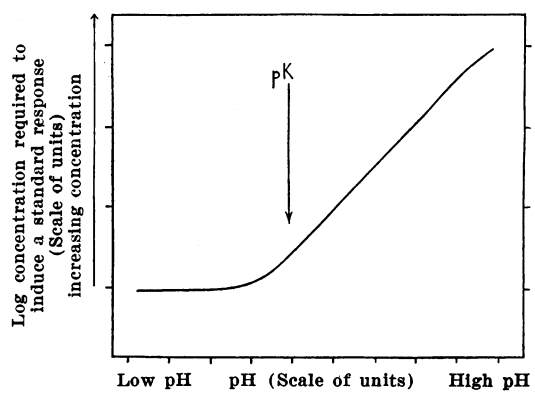

FIG. 1. The effect of pH on the concentrations of a weak acid that are required to give a standard response from the test organism. The corresponding graph for a weak base is obtained by reversing the pH scale. The curve is derived from a study of graphs from 90 pH experiments (*1*).