possible to expand frozen sections in lead and have them placed against a photographic plate within a few minutes after their removal from the animal. A technique for expanding frozen sections should also be very useful as a means for binding in place the volatile and diffusible radioactive substances ordinarily lost or displaced during tissue processing procedures.

On occasion it has been desirable to cut out a small portion of a lead square and the expanded tissue embedded in it in order that further expansion of the selected portion of tissue might be carried out more easily. With a tracing of the radioautograph as a guide such cutting can be done with a high degree of accuracy, and feats of microdissection which would originally have been exceedingly difficult may be reduced by the tissue expansion to a level of difficulty approximating that involved in the cutting out of paper dolls. Although radioautographic procedures have been used for some time to localize radioactive *elements* on a relatively fine scale, studies of the biochemical transformations which a radioactive element or compound undergoes have for the most part been limited to whole organs or macroscopic tissue structures. With experiments of the type in which the use of high concentrations of radioactivity is allowable, this simplified microdissection technique, combined with very sensitive analytical procedures such as paper chromatography of radioactive compounds (*10*), may aid in extending our knowledge of intermediary metabolism by facilitating a more accurate localization of the sites at which various biochemical processes take place.

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Technical Papers

The Influence of Skin Temperature upon the Pain Threshold as Evoked by Thermal Radiation[1]

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That reduced skin temperature can result in cutaneous analgesia is well known, and skin temperatures near 0° C cause local anesthesia (*1*). Also, Schumacher (*2*) and Graham, Goodell, and Wolff (*3*) have reported that vasodilation of the superficial vessels of the skin lowers the cutaneous pain threshold. However, a systematic investigation into the effect of the level of skin temperature upon the pain threshold for pricking pain evoked by thermal radiation has not been reported. To investigate this matter quantitatively the following experiments were performed.

The pain threshold on the blackened skin of the forehead and the back of the hand of 4 subjects was measured by the Hardy-Wolff-Goodell (*4*) method, in a room at 26° C. Skin temperatures were measured with a radiometer (*5*) prior to each test of pain threshold. The subjects then moved into a room at 8° C, and the skin temperature and pain thresholds on the forehead and back of the hand were measured at 5- to 10-min intervals over a period of 1 hr. The subjects returned to the room at 26° C, and the measurements were continued for 2 additional hr as the skin temperature returned to control levels.

The results of these observations are shown in Fig. 1 by the solid line drawn through the averaged readings plotted for the forehead and the hand. The same relationship of pain threshold to the level of skin temperature was observed for both areas. Cooling of the skin 10° C resulted in an elevation in pain threshold of roughly 200 millicalories/sec/cm².

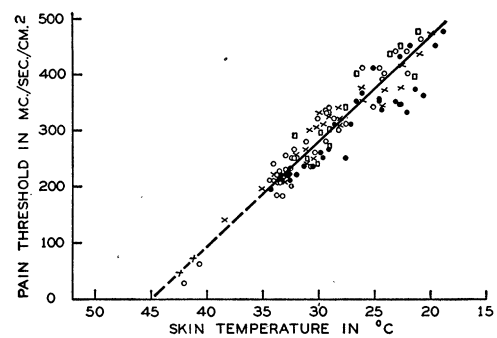

FIG. 1. Relationship between pricking pain threshold and skin temperature.

In a second experiment, the blackened skin of the forehead of 2 subjects was irradiated with intensities of thermal radiation which caused elevation of skin

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temperature. During this heating there was no visible sweat on the forehead even though the skin temperature was maintained at levels between 38° C and 43° C. When a constant skin temperature had been attained, the warm skin was exposed for 3 sec to a second source of radiation, the intensity of which was adjusted to give a threshold pricking pain at the end of the exposure. The pain threshold was ascertained by measuring the intensity of the radiation incident upon the skin from the second source. Skin temperatures were measured with a bare wire thermocouple laid on the forehead after the method described by Stoll and Hardy (*6*). The dashed portion of the line in Fig. 1 is drawn through the averages of the results of this series of measurements. Heating the skin of the forehead 10° C caused a lowering of the pain threshold of approximately 200 mcal/sec/cm².

The fact that the relationship between levels of skin temperature and pain threshold is characterized by a straight line passing through zero stimulus at a skin temperature of 44.9° C suggests that the skin in the areas tested must be raised to this temperature to be noxiously stimulated, regardless of the initial level of skin temperature. Thus it is the actual skin temperature level that is critical as regards noxious stimulation of the skin, and not the rate of skin temperature rise nor the amount of skin temperature elevation (*4, 7*).

From these observations it follows that to obtain the most accurate measurement of pain threshold by the thermal radiation method it is necessary to correct for the temperature of the skin being tested. This can be done for the forehead and back of the hand from the curve in Fig. 1 or by the following formula:

$$\text{Pain threshold} = 220 + 20\ (34^\circ\text{ C} - T_s')\ \text{mcal/sec/cm}^2,$$

where T_s' = skin temperature in °C at the time of observation.

Originally the forehead was the only skin area used for pain threshold tests because of the constancy of its skin temperature (34° C ± 0.5° C) under laboratory conditions. However, errors will be introduced into measurements of pain threshold even on the forehead if the room temperature is lower than 20° C. In warm rooms (30°–35° C) the forehead temperature will not increase greatly, but sweating will occur and thus interfere to some extent with the measurement of pain threshold. It is desirable to keep the laboratory temperature between 20° C and 30° C when making pain threshold measurements on the forehead. When other parts of the body are being studied their skin temperature should be ascertained and corrections applied to the pain threshold measurement. The average skin temperature on other parts of the body, in the comfort zone of environmental temperature, is roughly 33° C. It should not be inferred that the pain threshold on all parts of the body when corrected for skin temperature will be the same as that obtained on the forehead or the back of the hand. For example, it has been found that the pain threshold on the lips and on the lumbar region of the back ranges from 80 to 150 mcal/sec/cm², even with skin temperatures between 33° C and 34° C (*8*). This difference in pain threshold must be attributed to differences in skin thickness, sensitivity of nerve endings, or both.

Pain evoked by thermal radiation stands in contrast to the sensations of warmth and cold as regards the effects of altered skin temperature upon the threshold (Fig. 2). Warmth shows no change in

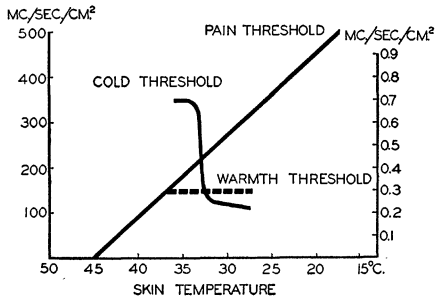

FIG. 2. Influence of skin temperature upon the thresholds of warmth, cold, and pain. Pain thresholds are referred to ordinate at left; warmth and cold thresholds, to ordinate at right of diagram.

threshold between skin temperatures of 27° C and 36° C, although there is an *elevation* in the cold threshold for an *increase* in skin temperature from 32° C to 34° C (*9*). From this it can be deduced that the effects of the thermal stimulus on the skin in producing noxious stimulation are entirely different from those evoking thermal sensation, and that the cutaneous receptive mechanism subserving pain is distinct from that for warmth and cold.

Buettner (*10*) and Henriques and Moritz (*11*) have shown that reversible tissue damage in the skin of the forearm and upper leg of humans is produced at the critical temperatures of 44° C to 45° C. In the above experiments threshold pain has been elicited when the skin temperature has been raised to roughly this same level, irrespective of the initial level of skin temperature. From these two independent observations the close relation between tissue damage and noxious stimulation can be inferred, thus significantly supporting the concept that the adequate stimulus for pain is tissue injury.

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