All the rats cast litters, although in 3 instances the initial breeding proved unsuccessful. Number of young per litter varied from 2 to 13, with averages between 7.2 and 8.4 on the several diets. An average of 0.8 to 1.2 young per litter were born dead (omitting one litter on diet C which consisted of 9, all born dead). In all groups the young averaged 5 to 5½ g at birth and appeared grossly to be normal in all respects.

Lactation. At birth litters were reduced to 6 each. The young were nursed and weaned on all diets except E and F. On each of diets B, D and G, 3 mothers successfully nursed their young, which were weaned at 21 days of age at average weights of 36 to 41 g. Two litters on diet A were nursed, but only 5 of the 12 young survived until weaning (average weight at weaning, 22.8 g). The one litter weaned on diet C consisted of 3 survivors, average weight 24.6 g.

The findings indicate that the massive doses of inositol or *p*-aminobenzoic acid exerted no deleterious effects on growth or reproduction and that lactation may occur on diets containing 1% *p*-aminobenzoic acid or inositol. The cause of the poor lactation is unknown, but deficiency of folic acid was probably not a factor. To judge from the work of Maynard and Rasmussen,[6] failure of lactation may have been due in part to insufficiency of dietary fat.

Summary. No adverse effects on growth or reproduction were noted in female rats fed purified rations containing 1% *p*-aminobenzoic acid or inositol. Lactation was inadequate both in control and experimental rations, although some young were weaned on each of the above diets.

[6] Maynard, L. A., and Rasmussen, E., *J. Nutrition*, 1942, **23**, 385.

15644 P

Relief of Cardiac Pain by Local Block of Somatic Trigger Areas.

JANET TRAVELL AND SEYMOUR H. RINZLER.

From the Cardiac Service, Beth Israel Hospital, and the Department of Pharmacology, Cornell University Medical College, New York City.

Weiss and Davis[1] noted that referred pain from viscera could be abolished by procaine infiltration of tender areas in the somatic reference zone. Their observations became buried, however, in the controversy which developed over the mechanism of visceral pain reference and the role of afferent somatic impulses in this phenomenon. As a result, the therapeutic implications of their results have received little recognition. In agreement with their findings, our data indicate that under suitable conditions, cardiac pain may be abolished by local block of the noxious impulses which arise in trigger areas in the reference zone.

Procaine Infiltration. We became interested in this problem during studies on extracardiac sources of pain in the chest and arm, which in some respects simulates coronary artery pain.[2] By the technic of needling tender spots in the muscles in patients with various myalgic syndromes, we discovered the existence of a group of trigger areas, located chiefly along the sternal borders, mechanical stimulation of which uniformly induced a reference of pain perceived beneath the sternum and deep inside the chest; if located on the left side the referred pain was often described as "felt directly in the heart." Other trigger areas in the chest and shoulder regions induced a radiation of pain to the entire pectoral area, the interscapular region, neck and arm.

At that time we believed[2] that since local

[1] Weiss, S., and Davis, D., *Am. J. Med. Sci.*, 1928, **176**, 517.

[2] Travell, J., Rinzler, S., and Herman, M., *J. A. M. A.*, 1942, **120**, 417.

injection therapy afforded relief in such patients without organic heart disease, this procedure might serve as a therapeutic test to exclude a visceral etiology of pain. However, when we subsequently applied this technic for diagnostic purposes, we concluded that local infiltration of somatic trigger areas probably relieved the pain of both myalgias and effort angina. In 2 patients the angina of effort disappeared during the course of a series of such treatments. In one patient in an almost continuous anginal status, the nocturnal anginal attacks, which required repeated doses of glyceryl trinitrate, almost entirely disappeared after 2 treatments. The daytime attacks in this and in 2 other patients were apparently benefitted for only short periods of time after each treatment.

Because of the difficulties in evaluating results of therapy in chronic cardiac pain, we selected 4 patients with acute pain due to a recent myocardial infarct for a therapeutic trial. Three episodes of acute myocardial infarction (2 attacks in one patient 2 years apart) were treated by local procaine infiltration of the somatic trigger areas in the anterior chest wall, in about 7 hours, 13 hours and 21 days, respectively, after the onset of pain which was not completely relieved by morphine. In each instance this procedure afforded immediate, complete and permanent relief of chest pain and its associated radiation.

Ethyl Chloride Spray. The excellent results obtained by ethyl chloride spray in acute myalgias[3] and in sprains[4-7] indicate that this procedure, like procaine infiltration, blocks noxious impulses from somatic trigger areas following injury, provided the trigger areas are not deeply located beneath the body surface. We inferred, therefore, that ethyl chloride spray of trigger areas in the pectoral muscles, because fairly superficially located, might also abolish the pain of acute myocardial infarction. We found that when the major precordial trigger area was sprayed with ethyl chloride, the constant pain of a fresh myocardial infarct (23 hours old), unrelieved by demerol and papaverine, was in one case permanently abolished within 20 seconds after the start of spraying. It seems likely that relief afforded by ethyl chloride spray is at least in part due to refrigeration anesthesia of the myofascial structures, for in another patient our data suggest that if the trigger area is situated as much as one inch below the surface of the skin, it may be necessary to substitute injection with procaine for ethyl chloride spray.

Mechanisms. A parallelism is apparent between mechanisms of pain following trauma to the somatic structures, as in sprains, and mechanisms involved in pain due to acute myocardial infarction, since pain following both types of injury can be relieved by local block of somatic trigger areas. The most reasonable explanation is that the initial insult, whether to visceral or somatic structures, sets in motion a chain of events perpetuated by a vicious cycle of nerve impulses which have no further dependence on afferent impulses from the heart and which are probably transmitted to and from the soma by virtue of sustained facilitation of the noxious impulses by the closed self-reexciting chains of internuncial neurons in the central nervous system.[8-10]

Certain similarities in the quality and behavior of referred somatic and referred visceral pain,[11-13] together with the results of local anesthesia of somatic structures, indicate that the physiologic mechanisms by which the body expresses pain are probably the same for visceral and somatic disease,

[3] Kraus, H., *J. A. M. A.*, 1941, **120**, 417.

[4] Cozen, L. N., and Hollombe, B. S., *Surgery*, 1940, **8**, 648.

[5] McIntosh, C. A., and Petrie, J. G., *Lancet*, 1942, **2**, 279.

[6] Henry, A. K., *Lancet*, 1942, **2**, 280.

[7] Bingham, R., *Mil. Surgeon*, 1945, **96**, 170.

[8] Lorente de Nó, R., *J. Neurophysiol.*, 1938, **1**, 207.

[9] Evans, J. A., *Surg., Gyn., and Obst.*, 1946, **82**, 36.

[10] Livingston, W. K., *Pain Mechanisms*, The Macmillan Company, 1943, p. 224, Chap. XV.

[11] Lewis, T., and Kellgren, J. H., *Clin. Sci.*, 1939, **4**, 47.

[12] Kellgren, J. H., *Clin. Sci.*, 1939, **4**, 35.

[13] Travell, J., and Bigelow, N. H., *Fed. Am. Soc. Exp. Biol. (Proc.)*, 1946, **5**, 106.

and as postulated by Weiss and Davis,[1] in both instances involve the soma as an integral part of the reference of pain. In this connection, it is important to recognize that disappearance of pain after blocking the somatic component does not exclude the diagnosis of visceral disease as the initiating cause of pain.[14] There is even some evidence that reflex coronary vasodilatation may follow the termination of the vicious cycle by precordial local anesthesia and that the visceral lesion is thus subject to influences from somatic trigger mechanisms.[15]

Conclusion. Data secured in 9 patients with effort angina and acute myocardial infarction indicate that local block of somatic trigger areas by procaine infiltration or ethyl chloride spray under suitable conditions may afford complete and prolonged relief of pain. Because of their simplicity and effectiveness, these procedures deserve extensive clinical trial.

[14] Gorrell, R. L., *Am. J. Surg.*, 1944, **63**, 102.

[15] Lindgren, I., *Nordisk Medicin*, 1946, **29**, 523; (Abs.) *J. A. M. A.*, 1946, **131**, 1536.

15645 P

Toxic Effects in Scorbutic Guinea Pigs Produced by Large Doses of Thiamin.*

DORIS M. HIGHET AND EDWARD S. WEST.

From the Department of Biochemistry, University of Oregon Medical School, Portland, Oregon.

During the study of the effects of administration of thiamin to scorbutic and non-scorbutic animals, it was observed that young scorbutic pigs fed large amounts of thiamin sometimes develop irreversible symptoms after the resumption of a normal diet. The strength of the jaw muscles decreases and the animals are unable to chew their food properly, although they appear hungry and persistently try to eat. There is also decreased control of jaw muscles and the animals often spend long periods with jaws constantly opening and closing in a rapid chewing motion. This condition sometimes becomes permanent until death. The lack of muscle control is also often manifested by a shivering movement of the face accompanied by chattering of the teeth. In some cases the mouth is distorted and the muscles involved are in spastic contraction, causing the animals to claw the face in attempts to relieve the spasm. These muscle dyscrasias are usually accompanied by increased salivation or loss of saliva which may be due to difficulty in swallowing.

The symptoms, once established, have been found irreversible and the animals inevitably die. Attempts to avert death by forced feeding, administration of large amounts of synthetic ascorbic acid or by offering green food have failed to keep the animals alive longer than one month.

Death is not primarily due to starvation, for if the food offered is well macerated these animals consume amounts normal for their size. At death the animals are extremely emaciated. (Pigs weighing 400 g initially, decreased to 270-300 g). At autopsy macroscopic hemorrhagic areas are found to vary inversely with the length of time the animals have lived after the onset of symptoms.

Several methods of producing the thiamin effect have been tried. The procedure giving the highest incidence was as follows:

Animals were fed a diet of Olympic rabbit pellets and water, until weight gain ceased and loss of appetite, joint stiffness and tender-

* Taken from a thesis submitted by Doris M. Highet in partial fulfillment of the requirements for the degree of Doctor of Philosophy. Aided by a grant from the General Research Council of the Oregon State System of Higher Education.