With the shocking information that developed soon afterward of the teratogenic effects of thalidomide, my speculation seemed just a pale coincidence: the nervous system apparently was not directly involved, and the mechanism was totally different from anything anticipated. In a memorandum that I was asked to prepare for FDA Commissioner Larrick outlining events involving the application to market the drug, I even hesitated to include the matter. However, as I had reminded our medical officer to include it in our recorded notes of the May conference, and as allusions to it occurred in later transactions with the applicant, I did mention it briefly. (That memorandum later became public and underwent some rather distorted interpretations.)

Now, my earlier concern appears confirmed. In addition to an increased incidence of epilepsy,[1] recent articles in the *British Medical Journal*[2] and *Proceedings of the Royal Society of Medicine*[3] report belatedly recognized cranial nerve defects in thalidomide-damaged babies. Earlier reports had suggested that such effects were only secondary to musculoskeletal abnormalities. These neuropathies are evidently from central nervous system damage instead of peripheral, but it is clear that the reports from the early 1960s in adults involved central effects at least in part.[4] On the other hand, some evidence has emerged that the teratogenic effects of thalidomide may have been from damage to embryonic peripheral nerves.[5,6]

Whether this neurological damage to fetuses is entirely developmental—as opposed to toxicity for formed or partially formed structures—is not clear. It does, however, indicate that the actual effects of thalidomide are related much less remotely to my early theoretical speculation than seemed apparent several years ago. It also reemphasizes a general precaution in administering drugs to pregnant women: without good evidence to the contrary, a known but unpredictable reaction should at least be considered possible of manifesting itself unrecognized in a fetus, even though the mother is escaping.

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Carcinogenesis in Rats of Combined Ethylene Dibromide and Disulfiram

To the Editor.—A study of the toxicity of inhaled ethylene dibromide (EDB; 1,2-dibromoethane), a widely used industrial chemical, is currently being performed for the National Institute for Occupational Safety and Health by the Midwest Research Institute (MRI), Kansas City, Mo. Male and female Sprague-Dawley rats are being exposed to EDB at the current US Occupational Standard of 20 ppm or to filtered air (controls) for seven hours a day, five days a week.

There are four groups of animals in the study, each group containing 48 male and 48 female rats. The group designations are as follows: (1) control/control—filtered air exposed, standard rat diet; (2) control/disulfiram—filtered air exposed, diet containing 0.05% disulfiram by weight; (3) EDB/control—20 ppm EDB, standard rat diet; and (4) EDB/disulfiram—20 ppm EDB, diet containing 0.05% disulfiram by weight.

Disulfiram was chosen as a potential modifier of toxicity because of its known effect as an enzyme inhibitor and its use in humans in alcoholism-control programs. The MRI has now completed 11 months of exposure and has noted a substantial increase in morbidity and mortality of both male and female rats in the EDB/disulfiram group (deaths plus terminations because moribund or because of the presence of large tumor masses). In addition, the MRI has found a large number of tumors at various sites in both male and female rats in this group. Histopathologic examination of each of the animals in the EDB/disulfiram group is incomplete at this time. However, complete data are available on 13 males and 15 females with partial data on one additional animal of each sex. Potentially important findings include hemangiosarcoma of the liver (3/14 males, 6/15 females), hemangiosarcoma of the spleen (3/14 males, 4/16 females), hemangiosarcoma of the omentum (4/14 males, 5/16 females), hemangiosarcoma of the kidney (2/14 males, 1/16 females), and adenocarcinoma of the mammary gland (7/15 females); tubular atrophy of the testes (12/13 males) has also been noted.

The histopathologic changes reported have been noted only in the group exposed to both chemical agents. Corresponding obvious morbidity and mortality in groups exposed to EDB alone or disulfiram alone have not been noted.

These data strongly suggest the existence of an interaction between the drug and the industrial chemical in the rat. Whether this interaction is of clinical significance in man is not known. The data from this study, although incomplete, are being reported at this time because of the potential public health importance of these preliminary findings.

Those clinicians using disulfiram in alcoholism-control programs should be aware of this potential interaction and should determine whether or not their patients are occupationally-exposed to EDB. The advisability of continued disulfiram therapy for workers occupationally-exposed to EDB is uncertain, pending completion of the study.

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Needle in Heart

To the Editor.—In the LETTER TO THE EDITOR "Unusual Foreign Body Pathway to the Heart" (238:2016, 1977), correspondents McCormack and Knapper state that a review of the literature showed only one other case[1] of a sewing needle self-introduced into the chest. We reported a case of a self-inflicted sewing needle introduced into the myocardium in 1949,[2] and at that time we found an additional similar previous report. It is of interest that Berg's[1] case as well as ours showed evidence of pericarditis. It is regrettable that the current report omits electrocardiographic findings.

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Who Was First?

To the Editor.—Probably the commonest error to be found in the case report throughout the literature is the claim of precedence: ie, "this is the third reported case of . . ."; "the association of these three lesions has not previously been emphasized in the