Letters to the Journal

Letters are welcomed and will be published as space permits. Like other material submitted for publication, they should be typewritten, double-spaced, should be of reasonable length, and will be subject to the usual editing. The accuracy of statements of fact contained in these letters is the responsibility of the correspondent.

Views expressed in Letters to the Journal are those of the writers concerned and are NOT to be interpreted as the opinions of The Canadian Medical Association or of the editors.

CHRONOLOGY OF THE THALIDOMIDE STORY

To the Editor:

Last November came the first reports of a sharply rising incidence of phocomelia in some European countries and the possible association of the drug, thalidomide, with these malformations. We at the Wm. S. Merrell Company were deeply and sympathetically concerned. At that time thalidomide, under the Merrell label, was on prescription sale in Canada.

The tragic story of these congenital malformations has received wide publicity. Some of these reports have been confusing and some misleading. For this reason we present the following outline of the facts about thalidomide and our clinical investigation of this product.

The facts, we believe, demonstrate that: (1) Prior to the first report of congenital malformations, Merrell's investigators had every reason to believe that thalidomide was a highly useful, non-toxic substitute for the barbiturates. (2) Subsequent to such reports, Merrell has vigorously pursued a course that was in the best interests of the public welfare, both in terms of human safety and scientific and medical research.

Thalidomide was first synthesized by Chemie Grunenthal G.m.b.H., Stolberg, West Germany, in 1953. The drug was tested in animals and then in humans. The toxicity of thalidomide was extremely low in both animal and clinical testing. No LD_{50} could be established. Of particular importance, an overdose of thalidomide did not induce depression of respiration and heart action, which eliminated the possibility of accidental death or suicide through its use. Clinical reports have been published concerning 17 persons (including small children) who survived following ingestion of excessive amounts of the drug. One intended suicide ingested 144 times the usual dose. No deaths from overdosage are known.

Significant events in the subsequent history of thalidomide are as follows:

1953: Chemie Grunenthal synthesized thalidomide, alpha (N-phthalimide) glutarimide.

1957: Thalidomide was first placed in commercial use in West Germany.

January 1959: Merrell, under a licence covering the U.S. and Canada, commenced its own research investigation of thalidomide. At that time, thalidomide, after five years of testing and widespread use, was accepted as a safe and useful drug in Europe. It had been sold in West Germany for 15 months without necessity for a prescription.

September 8, 1960: Merrell submitted data on animal and clinical findings to the Food and Drug Directorate in Canada. These findings covered more than a year and a half of testing by Merrell.

November 22, 1960: Merrell received notice of compliance from the Canadian Food and Drug Directorate under the new drug law.

February 14, 1961: Merrell, noting letters in the *British Medical Journal* citing instances of peripheral neuritis that possibly represented toxic effects of thalidomide, wrote the licensee for the product, Distillers Limited, asking for details.

March 6, 1961: After exchanges of correspondence concerning the occurrence of peripheral neuritis in patients receiving this drug, Merrell management concluded that we could not get satisfactory answers by mail and sent two Merrell scientists to Europe. They conferred with physicians in England, Scotland, and West Germany about their reports of this side effect.

April 1, 1961: Four months after receipt of notice of compliance from the Canadian authorities, Merrell began marketing thalidomide for prescription sale in Canada under the brand name Kevadon. Initial product information to physicians contained cautions concerning the possible hazard of peripheral neuritis in persons on long-term therapy with this product.

November 29, 1961: Merrell learned for the first time of the possibility of the association of thalidomide with birth defects, in a cable from Grunenthal.

November 30, 1961: Merrell, after verifying this brief message and gathering further information by trans-Atlantic telephone, made an appointment with the Canadian Food and Drug Directorate.

December 1, 1961: Merrell scientists arrived in Ottawa to report what we knew to the Canadian Food and Drug Directorate and to review a warning letter which Merrell proposed to send to Canadian physicians.

December 1, 1961: Two Merrell physicians flew to Germany to obtain at first hand more factual information.

December 2-5, 1961: By Tuesday, December 5, there was mailed to Canadian doctors a letter warning that thalidomide was contraindicated for pregnant women and premenopausal women who might become pregnant.

January 6, 1962: The drug, having been off the market in England for about six weeks, was returned to the market for hospital use.

February 21, 1962: We continued to seek reliable information on the cause of the defects linked with the drug. Following additional reports concerning an increase in congenital defects in Europe we, with the knowledge of the Food and Drug Directorate, followed our first warning letter to physicians in Canada with another letter re-emphasizing the contraindications to the use of this drug.

March, 1962: With the knowledge of the Canadian Food and Drug Directorate, Kevadon sale in Canada was suspended and all supplies were recalled. Another firm marketing the drug withdrew it at the same time.

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We have pledged the full co-operation and resources of Merrell in the present evaluation of thalidomide's potential teratogenicity and in the search both for other causal factors and, if possible, for preventive measures.

At present scientists in more than 100 laboratories are being furnished with thalidomide for animal experimentation, and at the same time we have expanded our own laboratory research program in the teratogenic effects of various agents. Much remains to be learned in this area, most specifically in regard to thalidomide itself, but also with regard to the development of reliable test techniques.

We have not at any time minimized the possible relationship between thalidomide and congenital malformations. We hope that this series of events will lead to better scientific understanding of the development of the human embryo and to progress in preventing fetal abnormalities whatever the cause.

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THE HAMMER AND THE HERITAGE

To the Editor:

In his letter Dr. Robert Bradley (*Canad. Med. Ass. J.*, 87: 679, 1962) seems more concerned with the mote in the eye of his professional brethren than with the beam in his own. He describes the phrase "monstrous nonsense", which appeared in the Journal's editorial (*Ibid.*, 87: 303, 1962) in the following context: "The monstrous nonsense that 'health is too important to be entrusted to doctors' should be scotched", as "unhelpful extravagant language, open to misunderstanding, contributing nothing towards the improved atmosphere . . ." This comment comes from the man who, in a television interview, described the provision of Emergency Medical Care as "an obscene act". The Concise Oxford Dictionary defines obscene as "repulsive, filthy, loathsome, (archaic); indecent, lewd."

One might think that the application of this epithet to a comprehensive service provided to the people of this province, free of charge, as a protest by an entirely voluntary group of professional men, might also be termed extravagant, etc.

I applaud the sentiments of Dr. Bradley's last paragraph and would recommend that he, to follow his own advice, "remove the cause of the criticism" and minister tenderly to himself with the delicate tools of self-examination.

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MENTAL RETARDATION TODAY

To the Editor:

I would like to congratulate Dr. Zarfas on his fine article on mental retardation which recently appeared in your Journal (*Canad. Med. Ass. J.*, 87: 479, 1962).

As a parent of a mongoloid child and having lived in half a dozen communities in the United States and Canada, I have had opportunities for discussion with many parents and physicians. Informal opinion polling of the parents has produced comments along the following lines.

The diagnostic and counselling area seems to be a real jungle. The majority of parents (with one or two exceptions) want a precise, early diagnosis; they want a clear picture of the capabilities and limitations of the child. Some physicians are knowledgeable enough to handle this. Unfortunately, many are not. The doctor should be aware of his limitations and, where necessary, refer the family immediately to an informed physician or special clinic. Inept counselling is widespread. Parents are agreed that hinting by the physician that something is not as it should be but "let's wait and see how things turn out" is a crude procedure.

Some parents complain that the medical needs of the child are neglected, or grudgingly given, by the physician. Recently, at the suggestion of an eye specialist who warned us that our boy would lose the sight of one eye if corrective surgery was not performed, this was done. The general practitioner said: "Why bother with this child? He will end up in an institution anyway." Parents don't want special favours, but they won't accept anything less than normal medical care for these children. If the child is comfortable, the family is comfortable.

Parents need the co-operation of the medical profession in breaking down the "wilderness" pattern in the location and design of Canadian institutions. Smaller residences are required, close to the home community. This helps to avoid the "institutionalization" of both the child and the staff. These children benefit from community contact.

Many private medical care plans refuse to accept the retarded—this is another area where improvement is needed.

Either in or out of an institution, my observation has been that many of these children can live contented lives if the community cares. If the community doesn't care, they are the most forlorn section of the population.

MRS. J. D. MCNEELY

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Toronto.

THE JOURNAL IN THE MISSION FIELDS

To the Editor:

I have much appreciated receiving the Journal during many years of medical missionary service in Korea, first in the north, latterly in Wonju, Kangwon Province. Now having completed 40 years with the United Church Mission, I am to be automatically retired at the end of my present furlough.

However, I am returning for a two-year term with the Mission to Lepers, Taegu, Korea, and if your generosity will extend to sending the Journal to me while in the service of this international organization, I shall appreciate it greatly.

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(For many years The Canadian Medical Association has endeavoured to provide its journal to Canadian physicians working in mission fields throughout the world. This is usually accomplished by re-directing to them the subscriptions of members of The Association to whom the Journal is readily available from other sources. Dr. Murray's letter is published as tangible evidence of the appreciation with which such complimentary subscriptions are received by Canada's medical missionaries.—Editor)