Was the thalidomide tragedy preventable?

Sir—Ann Dally's question (April 18, p 1197)[1] is both provocative and rhetorical, and she assembles a *mélange* of science, history, and feminism to suggest an affirmative answer. Perhaps most surprisingly, after quoting a 1960 report about thalidomide and peripheral neuritis,[2] she writes, "Yet there was already evidence of its teratogenic potential". No reference is given to support this statement. The first published suggestion of teratogenicity in man was McBride's letter in 1961.[3]

Experimental animal teratology was pioneered in France and the USA from the 1930s, and a vast literature developed. Experiments with the use of drugs or dietary manipulation used such extreme measures that it was impossible to know whether the results had any bearing on human malformations. Indeed, to this day it is impossible to predict which animal model most accurately reflects the human response. To say that "Routine testing of new drugs on pregnant animals was perfunctory or non-existent" is to apply today's standards to events 40 years ago. We must remember that the ability of drugs to cross the placenta can be of therapeutic value, and that some drugs (eg, aspirin, antibiotics) are teratogenic in some animals but not in human beings.

As regards the placenta "as a perfect barrier", Dally believes she was taught that, "the human placenta . . . was impervious to toxic substances except in such large doses that they killed the mother". At the 1st International Conference on Congenital Malformations, in London in July, 1960, James Wilson[4] gave as one of the general principles of experimental teratology, "An agent which is very damaging to the embryo may be relatively harmless to the mother". In January, 1960, almost 2 years before McBride's letter,[3] a Ciba Foundation Symposium on Congenital Malformations was held, also in London.[5] These two meetings illustrate the interest in congenital malformations before thalidomide hit the headlines.

Medical minds in 1960 may not have been as wide open as Dally would have liked, and thalidomide could have been withdrawn from the market more promptly than it was, but I see no evidence that the tragedy was wholly preventable, except with hindsight.

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1 Dally A. Thalidomide: was the tragedy preventable? *Lancet* 1998; **351:** 1197–99.
2 Leslie FA. Is thalidomide to blame? *BMJ* 1960; ii: 1954.
3 McBride WG. Thalidomide and congenital abnormalities. *Lancet* 1961; ii: 1358.
4 Wilson JG. General principles in experimental teratology. In: Fishbein M, ed. Proceedings of the 1st International Conference on Congenital Malformations. Philadelphia: Lippincott, 1961: 191.
5 Wolstenholme GEW, O'Connor CM, eds. Ciba Foundation Symposium on Congenital Malformations. Boston: Little Brown & Co, 1960.

Sir—Ann Dally[1] leaves several issues unaddressed. Even during the thalidomide epidemic, not every mother of an affected child was found to have taken the drug. Other drugs, such as valproic acid, have occasionally been implicated and there is always the possibility that other medicaments, nostrums, toxins, or genetic mutation, may have been responsible. The incidence of phocomelia in the past was not quoted. Her index case, Thomas Inglefield, was born without arms or legs in 1769.

Sarah Biffin, the first UK artist who painted with her mouth was phocomelic, only 37 in in height, and mentioned in several works by Dickens, Hood, Surtees, and Thackeray.[2] She was born in 1784. Was phocomelia endemic about that time and could the aetiology, as has been suggested, be related to a cottage industry such as blanket making? To a medical historian, the sociomedical implications of deformities such as phocomelia are particularly absorbing. In an age when even twin births were thought to be unnatural and those with deformities were encouraged to die, Sarah was the middle of five children of a farm labourer, and was baptised with her mother's Christian name 6 days later.[3] In later life, she appeared as an educated and responsible person, speaking well and sensibly.[4] She was adopted by a painter when in her teens and aged 15 toured the fairgrounds exhibiting her art, and skill at needlecraft and writing. After she was discovered at St Bartholomew's Fair by the Earl of Morton, George III decreed that she should be taught miniature painting by the court miniaturist, William Craig. Besides painting miniatures of members of the Royal Family, she exhibited at the Royal Academy and had a social clientele.

She died in poverty aged 66 after a lengthy illness with difficulty breathing. The cause of death was given as "disordered stomach, breaking up of the constitution". From what is known of the associated defects that co-exist with phocomelia, a reasonable supposition is that she had a congenital weakness of the diaphragm with resultant herniation of the abdominal contents upwards into the thorax. More recent victims of phocomelia and thalidomide have also become mouth-painting artists.[5]

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1 Dally A. Thalidomide: was the tragedy preventable? *Lancet* 1998; **351:** 1197–99.
2 Leybourne W. Sarah Biffin, miniaturist. *The Dickensian* 1997; **93:** 165–84.
3 Ayres J, ed. Paupers and pig killers. The diary of William Holland. A Somerset parson 1799–1818. Gloucester: Alan Sutton, 1984.
4 Hardy G. Freak show to court favourite. Sarah Biffin, miniature painter 1784–1850. *Country Life* Sept 19, 1985: 822–23.
5 Critchley EMR. The motivation and shared experience of foot and mouth painting artists. *J R Soc Med* 1994; **87:** 457–60.

Patent protection for medical technologies

Sir—David Meltzer's report (Feb 14, p 518)[1] manages to avoid even a passing mention of one of the strongest arguments against the patenting of medical procedures. Many useful advances in medicine have their origins in informal conversations at conferences, or in bars and restaurants after the conference has ended. The ability to have such conversations, unhindered by legal or financial considerations, is one of the delights and strengths of medicine as currently organised and practised, especially in its more academic manifestations. My own specialty—addiction medicine—is witnessing some exciting developments in treatment and I receive frequent requests for information. I do not want to see a situation in which I have to reply: "I can't help you because my department is trying to patent this procedure".

Patenting also increases the likelihood that adverse effects of new treatments will be concealed for financial reasons by aspiring patent holders. Recently, with colleagues, I drew attention[2] to attempts to patent rapid opiate detoxification under anaesthesia (RODA) and its unethical promotion by the CITA organisation.[2] Our letter was widely reported in Spain and several Spanish newspapers interviewed the psychologist, Juan Legarda, who has applied for a patent. Despite unequivocal evidence of at least one death in a CITA clinic, Legarda denied that any CITA patient had died.[3]