

# Commentary: Epidemiology, iodine deficiency and the power of multidisciplinary sufficiency

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It is pleasing to see this article<sup>1</sup> being accorded ‘classic’ status. I am also glad to be able to offer comment on it since, by coincidence, I was ‘on the sidelines’ during the development of several stages of what became a multidisciplinary research-and-intervention odyssey, spanning the 1960s to the 1980s. Around 1970, Basil Hetzel, Foundation Professor of Social and Preventive Medicine at Monash University, Melbourne, Australia—and supervisor of my (unrelated) PhD—saw clearly the need and opportunity to pursue a programme of research for which this classic article is the prime foundation.

The programme sought, via epidemiological research and then animal experimental studies, a fuller understanding of the developmental and health consequences of lifelong iodine deficiency. Whereas goitre (sometimes associated with cretinism) had been known to medicine in Europe and China for many centuries, its usual causation by micronutrient deficiency was not understood and neither was its linkage with a wider range of disabilities. Hence the importance of research to achieve, first, the elaboration of the full spectrum of iodine deficiency disorders (IDDs), and, second, the mobilization of international agency support for large-scale population interventions and evaluations.

Basil Hetzel was Professor of Medicine during my undergraduate clinical years (1964–66) at the University of Adelaide. I knew nothing, then, of his nascent interest in the problem of iodine deficiency and goitre in the Papua New Guinea (PNG) highlands. In describing the source of his interest, he has noted in his autobiographical book, *Chance and Commitment: Memoirs of a Medical Scientist* (2005),<sup>2</sup> the role of serendipity in one’s research life—in this case, his being asked to review a journal paper, in 1963, on an exploratory study of goitre prevention in PNG.

During my first 2 years in the Department of Social and Preventive Medicine at Monash University, there were occasional frissons of excitement relating to the ongoing randomized controlled trial of cretinism prevention in newborns in a sample of villages in the

PNG highlands. The intervention, in 1966, entailed intramuscular injection of reproductive-aged, alternate, women with iodized oil or saline. Follow-up of pregnancy outcome occurred over the next 3 years, via copious boot-leather epidemiology in the mountainous PNG highlands.

This classically experimental study was a relatively novel epidemiological research design in the late 1960s—and especially so for non-communicable disease outcomes. (Further, of course, it was carried out at a time when the process of research ethical review was a much lesser source of delay and frustration than is now the case.) Interestingly, at that time, the concepts and terminology of epidemiological research, especially for non-communicable diseases, were in a rather intuitive and unsystematized state. The leading epidemiology textbook of the day, by McMahon and Pugh,<sup>3</sup> did not mention the actual word ‘confounding’. (When I arrived in 1972 at the highly regarded Department of Epidemiology, University of North Carolina, the senior academics there referred to case-control studies as ‘association studies’).

Hetzel was fortunate to have able and energetic field-working colleagues, well-attuned to tramping around the PNG highlands—Drs Ian Butfield and, especially, Peter Pharoah. The support from the PNG Department of Public Health was also invaluable.

Meanwhile, back in Australia, the other side of the ‘iodine coin’ was causing public health concern. Tasmania, with its long-standing problem of iodine deficiency and adult goitre, had introduced iodine-supplemented bread in 1966. At that same time, coincidentally, iodine-based sterilizers (iodophors) were introduced into the dairy industry to ensure a safe milk supply. This became a second, unintended, source of iodine supplementation in the diet. A subsequent rise in thyrotoxicosis occurred due to over-exposure to supplementary iodine and, hence, overactive thyroid glands. Hetzel was called in as an advisor. Here was further confirmation of a central role for dietary iodine imbalance as a source of various human health disorders.

Few in the epidemiology research arena have the chance to test and elaborate their ideas in the realm of animal experimental research. In 1975, Basil Hetzel took the opportunity to take over as head of a revamped branch of the Australian Government's CSIRO (Commonwealth Scientific and Industrial Research Organization). This now became the Division of Human Nutrition, based in Adelaide, South Australia. Coincidentally, in the latter 1970s and early 1980s, I found myself (as convenor of the Division's epidemiology research group) working in proximity to the animal experimental phase of this programme of research into iodine deficiency.

A sequence of experimental studies of iodine deficiency in pre-pregnant animals was carried out first in sheep and then in marmoset monkeys. This stage of the research story made clear that the iodine deficiency caused abnormal development of the fetal cortex and cerebellum, growth retardation and stillbirths and abortion. (Meanwhile, our epidemiology group identified an increase in the rate of stillbirths in Tasmania that had occurred during the abovementioned thyrotoxicosis episode.<sup>4</sup>)

Following Hetzel's clarification of the syndrome of IDD in the early 1980s,<sup>5</sup> IDD prevention became part of modern, global, public health architecture. This 'translational' step is where the really hard work often begins. How to actually prevent disorders and diseases for which there is now clear empirical evidence of major risk factors? Hetzel and colleagues saw that, in the long haul, it was going to be necessary to establish an authoritative body to deal with international agencies and national governments. In 1985, they established an international NGO, the International Council for the Control of Iodine Deficiency Disorders (ICCIDDs).

In the wake of successful lobbying and negotiation at international level, with the WHO and UNICEF in particular, the ICCIDD was then able to assist in the development of a global programme of elimination of IDDs. Basil Hetzel was executive director during 1985–95, and then chairman during 1995–2001. Today, the ICCIDD comprises a network of 700

professionals from 100 countries. This network includes epidemiologists, endocrinologists, salt chemists, media experts and others.

The ongoing programme of iodine supplementation, led by WHO, has not been a straightforward path to continuing prevention. Cultures and governmental capacities differ, and population diets and environmental conditions change over time. In 2007, WHO therefore took action to require countries to monitor and report on their IDD control programmes. Even so, iodine deficiency has been reappearing in various parts of the world in recent years, including in some locations in Australia. As ever with environmental health, there is need for continuing vigilance—especially as expanding populations farm on increasingly marginal land and deplete iodine from the soil.

The 1971 paper is itself a 'classic' of epidemiology. More important, though, its significance has grown over time via systematic exploration of this research question through further human and animal studies, leading to coordinated population scale intervention in countries around the world. Risk assessment by epidemiologists is never self-sufficient; risk management is the necessary complementary activity.

**Conflict of interest:** None declared.

## References

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