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Extraordinary circumstances led me to become an epidemiologist.[1,2] I was a 21-year-old medical student in Warsaw in September 1939 when my father urged me and the rest of our family to 'go east' to escape the Nazi occupation of Poland. My mother objected, convinced that the British and French would come to our rescue. Although my father could not dissuade her, and was not prepared to leave her, he insisted that one of us 'had to survive', so ordered me to leave for the Soviet Union. My parents and my brother remained in Poland until they were deported to the Treblinka extermination camp, where they perished in 1942.

The medical school in Warsaw had been closed by the Nazis, and I was working in a home for Jewish children with severe learning disabilities, mainly Down's syndrome. The director of the home was a communist, and he came up with a plan. The mother of one of the children came from the area of Poland which had been occupied by the Soviet Union. She obtained a permit for herself, her own child and three other children to return there. The director of the home suggested that I should travel with them to help her look after four mentally disabled children during the journey. After tutoring by my mother in how to recite for the German authorities the words written on the Russian travel document, but fictitiously adding my name, the six of us were authorized to leave German-occupied Poland and to remove our 'Star of David' armbands.

A train conveyed us as far as the railhead at Małkinia. From there we had to walk for a few kilometres through a forest, crossing no man's land into Soviet territory at Zaremby Kościelne. It was a Friday evening, and when we spotted candles alight within a house, we asked the Jewish family there for something to drink; but we were refused. We moved on, and eventually arranged for each of the children to be returned to their parents, leaving me free to search for a medical school where I could complete my undergraduate medical training. The medical school at Lvov was already full, partly because of the influx of Polish students who had also fled from the Nazis. However, some friends of mine in that part of Soviet-occupied Poland had highly-placed contacts in Minsk, capital of Soviet Byelorussia. They arranged for me to be admitted to the medical school there, and I qualified in June 1941. It was a special committee of the Ministry of Health which then decided that I was to become an epidemiologist. I had never considered this option (I had wanted to study internal medicine), partly because Jews were ineligible for government jobs in pre-war Poland.

On the day the Germans launched their offensive against the USSR on the 22 June 1941, I volunteered for the Red Army and was made a captain in the Medical Corps. After being wounded in my right leg on the Byelorussian front, I was sent to Molotov – now renamed Perm – in the Urals, where I was appointed head of an anti-epidemic unit. The unit consisted of physicians, paramedics (feldschers), nurses and disinfection personnel, and we had a small mobile laboratory for serological tests.

Typhus in the Soviet Union

In Perm, although we had to deal with outbreaks of typhoid fever, bacillary dysentery, scarlet fever, rubella and measles, our main concern was to prevent or contain outbreaks of epidemic typhus. For example, in 1942 we were confronted with an outbreak in a kolkhoz (collective farm). We went from house to house, looking for typhus-stricken people, grouped them together in a temporary

the International Clearinghouse. Additional material for this article is available from the James Lind Library website (www.jameslindlibrary.org), where it was originally published

hospital set up in a requisitioned school, and disinfected their clothes and home belongings, and the garments of those who had been in contact with sick people, whom we kept under observation. Prevention of typhus was very important because, in those pre-antibiotic days, only symptomatic treatments were available for people who contracted the disease.

In our attempts to trace the source of the epidemic, we looked for information everywhere: among the relatives and neighbours of infected people, teachers, local authority officials, party activists and police officers. Since we lacked notepaper, we used the wallpaper in our office to draw a map of the farm, and to get a picture of the disease's evolution: the location of the index case, and the dates of the first symptoms for the subsequent cases. We traced the outbreak of the epidemic to the house in which a recently released prisoner had first stayed. We then identified other households where he had stayed, and had infected other families. As the man had already left the kolkhoz, we had to discover his whereabouts. The local militia made clear that searching for him on foot was completely unrealistic, so, although I had never previously ridden a horse, I was persuaded to accompany them horseback. We eventually found him and burned his clothes.

Another example illustrates the problems that confronted us. One day, a coded telegram arrived notifying us of an outbreak of epidemic typhus in one of the new coalmining locations. By 1942 the huge coal fields in the Ukraine were under German occupation, and the Soviet government had started to explore new coal fields in the east of the country, including the Urals. After our anti-epidemic unit's arrival there, I went first to meet the local chief medical officer. The outbreak was putting at risk tens of thousand of workers who had been brought there from the Caucasian Soviet Republics to create new coal mines.

Very unsatisfactory provision had been made for this influx of workers; the housing, lavatories, showers, facilities for washing clothing, and so on were hopelessly inadequate. After visiting the provisional hospital and the arrangements for quarantining typhus contacts I sent an urgent coded telegram to the Regional Department of Health, asking for an immediate supply of medicines, soap, beds, mattresses, clothing and special facilities for washing and disinfection.

The next step was to meet the director general of the new coalmine, a high-ranking man in his late forties. He listened politely as I described the epidemiological situation and asked him why he had not prepared accommodation and other facilities before the arrival of tens of thousands of workers. Did he not understand that without adequate living facilities and basic sanitary arrangements, outbreaks of communicable diseases were to be expected?

The director general said he agreed with me, but asked whether I realized that the Soviet Union would be unable to fight the fascists without coal for the country's industry in general, and for military industry in particular. 'Before I left Moscow,' he said, 'I was summoned to the Kremlin and instructed personally by comrade Stalin to produce coal in very great quantities and to start the enterprise immediately. This was an order! And for your information, I am obliged to report daily to comrade Molotov how much coal we have produced. Now, please tell me what I can do. If I do not achieve the production target I shall be tried and face a death sentence. I may choose to be sent to one of the punitive battalions on the front line. If I survive there I shall be a hero; but as you may know, the chances of survival there are almost zero. And by the way, if the outbreak of epidemic typhus spreads and there are many fatal cases, I will be blamed for that as well.' After this very sad conversation, the director general invited me for a dinner of caviar, different kinds of sausages and meats and vodka. We were alone apart from a young woman who served us. He did not pressure me to write a dishonest report.

I stayed at the coalmine with my unit for some weeks. We tried our best to prevent further spread of the outbreak, but our efforts were only partly successful. After returning to Perm, I prepared a report, and, as far as I know, the regional authorities and the Regional Party Executive sent it to the Regional Prosecutor. I do not know what the outcome was.

In June 1943, I was sent to Moscow for postgraduate training by the best epidemiologists in the country, including Professor Lev Gromashevski, the master of Soviet epidemiology. By the end of 1943, some parts of eastern Byelorussia had been liberated from the Nazis and I was appointed chief epidemiologist of the Byelorussian Republic. The masses of refugees, the hundreds of thousands of

wounded, the hunger, cold and poor sanitary conditions, all created a fertile ground for epidemics. Epidemic typhus remained our main concern, but, as in Perm, we also had to deal with epidemics of typhoid fever, bacillary dysentery, scarlet fever, rubella and measles. In addition, there was an outbreak of malaria in one district, and scabies was everywhere.

Towards the end of the war, I witnessed how the retreating German army used epidemic typhus as a weapon. In 1944, in the Mozyr region of Byelorussia, the Nazi troops put tens of thousands of unaffected Soviet citizens in a detention camp they were evacuating where epidemic typhus was raging. The Germans knew that the Red Army would try to rescue these people, and this was a way of targeting it. We were charged with the task of isolating the sick and quarantining those who had had contact with affected individuals. In this way, we succeeded in preventing contamination of the Red Army.

Today, sociologists and social anthropologists urge medical scientists in general and epidemiologists in particular to acknowledge the potential contribution of the social sciences to epidemiological research. Although I was unfamiliar with the term 'social anthropology' at the time, I recognize in retrospect that my epidemiological work during the war by necessity had to encompass sociological investigations. I remember an outbreak of typhoid fever in a Muslim village in the Perm region. I knew nothing about Islam or Muslim culture, but on inquiry, we found that the outbreak was connected somehow to the funeral of the community leader, the mullah. Since people were unwilling to talk to us about their traditional practices, we remained in the dark until the village teacher, who was a party member, told us about the local purification funerary rites, which included manual cleaning of the rectum. This explained how the disease had spread after the mullah's death.

Another case illustrating the importance of familiarity with the community's social practices concerned an unknown disease which caused vomiting, diarrhoea and haemorrhages, and had a high fatality rate. Initially it was suspected that it was an infectious disease, but local doctors had never previously witnessed a similar epidemic. Nor did the pattern fit an infectious disease epidemic: whole families were sick, yet their neighbours and other people with whom they had contact were not affected. Our investigation revealed that wheat stocks of the affected families had run out during the winter. Harvest had been difficult because the men and many of the young women of the village were serving in the Red Army, or were working in factories. Those remaining in the kolkhoz were old people, children and invalids. As a result, it had only been possible for them to harvest some of the wheat. When the spring sun melted the snow, those who had run out of wheat reserves had gone to the fields to collect the unharvested wheat, which had rotted in the meantime. After we had ordered the villagers to stop eating it, the epidemic came to an abrupt end. This was another example of many in history of the way that effective public health action can be taken without a complete understanding of aetiology. I learned after the war that the disease was alimentary toxic aleukia, or septic angina, which is a form of mycotoxicosis associated with the ingestion of grain contaminated with fungi containing trichothecenes.

Israel: from infectious disease epidemiology to epidemiological teratology

After the war, I returned to Poland for about two years as a deputy high commissioner in the Ministry of Health, doing anti-epidemic work. However, in 1948, because (apart from me) one cousin was the only member of my family who had survived the Nazis, I decided to emigrate to Israel. In Israel, I worked in increasingly senior positions in the Division of Preventive Medicine in the Office of the Surgeon General of Israel Defence Forces. In the 1950s, we encountered outbreaks of another disease of unknown origin, which came to be known as West Nile Fever. We were the first to describe its natural history, epidemiological distribution, clinical presentation and laboratory findings, which we reported in a series of papers published in the *American Journal of Hygiene* (now the *American Journal of Epidemiology*) and elsewhere.[3,4] I left my position as director and chief epidemiologist in the Israel Defence Forces in 1953, after being appointed to direct the military Medical Research Laboratories, and in 1957, I finally left the army to become the deputy scientific director of the Israel Institute for Biological Research, at Ness Ziona.

As I have explained, I was confronted during the war with outbreaks of non-infectious diseases, as in the case of the mycotoxin, but my work as an epidemiologist in the Soviet Union had mainly been on infectious diseases. In 1951, however, I was introduced by John Gordon, then head of the Department of Epidemiology at the Harvard School of Public Health, to the use of epidemiology for problems other than infections. He was studying the epidemiology of traffic accidents; and he also mentioned Donald Reid's studies of the epidemiology of hearing loss in the UK.[5] Not only were these examples outside the traditional uses of epidemiology, but the former had nothing to do with what I then conceived as medical questions.

In 1962, I went on a two-year sabbatical to the Henry Phipps Institute in Philadelphia, and I came to realize there that infectious disease epidemiology had become a peripheral discipline within the developed world. It was at the Institute that Professor Theodor Ingalls persuaded me not to pursue my interest in infectious diseases and urged me instead to collaborate with him in epidemiological investigations of congenital malformations. Although reluctant at first, it did not take long for me to swallow the bait and to start working enthusiastically on the subject. My interest was aroused particularly by McBride's 1961 *Lancet* letter about thalidomide,[6] as well as the protracted subsequent correspondence between him and Ingalls. With the information gathered after the tragic consequences on the equivocal effects of thalidomide on chick, mouse, rat, guinea pig and rabbit embryos, it would have hardly been possible to arrive at the conclusion that thalidomide was a threat to the human embryo. At that time, only very high doses given to pregnant New Zealand rabbits produced limb reduction deformities,[7] and we were dubious about applying findings in animals to humans. To support our insistence on the need for monitoring human populations, Ingalls and I[8,9] quoted JG Wilson's view stated a decade earlier that society must 'depend upon an actual human experiment to detect teratogenic effects of new agents in women'.[10] We and others concluded that surveillance and registration of congenital malformations in newborn human populations were essential.

We started working using certificates of births, stillbirths and infant deaths. This was possible because in Philadelphia, as in many other communities, certificates had a specific space for recording congenital malformations detected at birth.[8,9] Indeed, we discovered that the only case of thalidomide embryopathy encountered in Philadelphia between 1961 and 1963 had been so designated on the birth certificate: under the heading 'Complications of Pregnancy', an astute physician had noted 'thalidomide ingestion in first trimester'.

The International Clearinghouse for Birth Defects Monitoring Systems

During the 15 years following the identification of thalidomide as a teratogen, researchers working in various congenital malformation monitoring programmes communicated informally, but all of us felt the need for more systematic collaboration. The original idea behind the Clearinghouse was to make monitoring of congenital malformations more sensitive by collecting data from a large population from different parts of the world. One wanted to detect a new thalidomide situation as quickly as possible even if the infants with a rare malformation or a combination of malformations, caused by the new teratogen, were born in different areas.[11]

In 1974, at a meeting in Helsinki, the March of Dimes Birth Defects Foundation sponsored the organization of the International Clearinghouse for Birth Defects Monitoring Systems. In addition to the involvement of the World Health Organization (WHO), the meeting was attended by representatives of monitoring systems in nine countries: Canada (Philip Banister), England–Wales (Josephine Weatherall), Finland (A Härö), France (Madeleine Dessemond), Hungary (Andrew Czeizel), Israel (me), Norway (Tor Bjerkedal), Sweden (Bengt Källén), and the United States (William Flint). Many other countries subsequently joined the Clearinghouse.

There were several schools of thought about how to build up the International Clearinghouse. The main division of opinion was between those who wanted the responsibility for collecting, pooling and analysing raw data to be with a central body, such as WHO, and others who conceived the Clearinghouse as a communication tool, to promote the sharing of data collected using agreed standard methods and formats. The majority supported the latter point of view.

In 1977, those involved in establishing the Clearinghouse decided to try to achieve Non-Governmental Organization (NGO) status for it with WHO (it was not until 1986 that it succeeded). By 1980, after analysing monitoring activities in the various individual programmes, 11 specific malformations were selected by consensus for use in the regular exchange of incidence data: anencephaly; spina bifida; hydrocephaly; cleft palate; total cleft lip; tracheo-oesophageal fistula; oesophageal atresia and stenosis; rectal and anal stresia and stenosis; hypospadias; reduction deformity of limbs; and omphalocoele. Down's syndrome was also included.

While I was preparing this account, Bengt Källén kindly sent me some observations on the work of the Clearinghouse (personal communication). He noted in these that:

> *'In order to have everyone to look at his/her data regularly, we wanted quarterly reporting of the agreed "standard" malformations but also a list of unusual conditions which we had not seen so often before. Most members could produce the former tables but many were reluctant to report the latter, because "there is no suitable code for them".'*
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> *'In order to keep up the interest, we tried to use the routinely collected material for various epidemiological analyses. Although the material as a whole could usually not be used, a group of interested people got together to analyse not only the common malformations like hypospadias, but also extremely unusual conditions.'*[11,12]
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> *'Quite early in the history of the Clearinghouse, we stressed the importance of an analysis of infants with multiple malformations and we tried to get people to report these with verbal descriptions. Most of the recognized human teratogens caused multiple damage so it seemed logical to concentrate on multi-malformed infants. After some discussion, we decided how to analyse this material to look for patterns of similar malformations … We decided to test our proposed method by describing three (fictitious) infants with similar – but not identical – malformations, and then submitted these descriptions to our colleagues for assessment. One of them detected the "cluster", and was very excited until we told him that it had been faked.'*
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> *'Another idea we tried was to increase the power of monitoring by combining outcome (malformations) with exposures (maternal drug use). Many programs routinely collected interview information on maternal use of drugs, with or without controls. My idea was that one should compare the reported maternal drug associated with different malformations, adjusting for reporting programme and, for instance, maternal age, in order to identify associations between specific drug use and specific "common" malformations. Again only some of the Clearinghouse programs participated. The system was called MADRE and some publications from it have appeared. The basic idea was to get a signal system, not to use this material for epidemiological research. If a signal appeared, one would have to look more carefully into it.'*
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> *'However, none of our efforts identified a new teratogenic drug. Indeed, the identification of valproic acid as a teratogen was the result not of the monitoring activity, but rather of the observations of an alert clinician (Elisabeth Robert) who found the association during her routine interviews with women who had infants with spina bifida.'*[13–15]

Seveso

It was because of my work with the International Clearinghouse for Birth Defects Monitoring Systems that I was contacted in the summer of 1976 by Professor Gaetano Maria Fara, from Milan. On Saturday 10 July 1976, there had been an explosion in a factory in Meda operated by Industrie Chimiche Meda Società Azionaria, a subsidiary of Givaudan, which in turn was a subsidiary of Hoffmann-La Roche. As a result, the population in Meda and neighbouring towns, the largest among which was Seveso, had been exposed to dioxin (2,3,7,8-tetrachlorodibenzo-p-dioxin – TCDD). Professor Fara wanted me to chair a symposium two months later (on the first day of the 5th Conference of the European Teratology Society, in Gargnano, Italy) to assess the possible teratogenic risks resulting from dioxin exposure. I agreed to do so, and, as I was totally ignorant about dioxin, I asked him to send me all the papers available on the topic. In addition, I asked some chemists in the Ness Ziona Institute to provide me with information about the chemical.

Soon after the symposium, the Lombardy Regional government asked me to serve as a consultant epidemiologist to investigate the health effects of the dioxin exposure and assess whether it had any impact on either mortality or birth defects in

the population of the Seveso area. Later, the Italian government appointed an International Scientific Steering Committee for the Seveso incident (Comitato dei garanti), members of which included Irving Selikoff, Nathan Mantel, Donald Young and Robert Miller (I was elected chairman).

We established an epidemiological monitoring system for the total population of 220,000 inhabitants. Apart from 193 cases of chloracne, some very serious, we did not detect other adverse effects during the first few years following the Seveso incident. To avoid political pressure, we held our meetings *in camera*, and only after finalizing our recommendations did we disclose them to the *Uficio Speciale* of the incident, in the presence of the media. The Seveso incident resulted in standardized industrial safety regulations in the European Union, which are known as the Seveso II Directive (http://ec.europa.eu/environment/seveso/index.htm).

Reflections

After my return from the United States most of my epidemiological research was on congenital malformations, but I did not abandon my initial 'epidemiological love' for studies of infectious diseases. In 1965, I received a five-year contract from the USA Army Medical Corps to study recrudescent typhus, and this was followed by a further five-year contract to research spotted fever. Ironically, I was the first scientist at the Ness Ziona Institute to be awarded a grant by the US military. I also contributed to studies of influenza surveillance and immunization, and rubella vaccination.

With these research interests, and as head of the department of Preventive and Social Medicine at Tel Aviv University, my professional life was very full – until 19 January 1983, the day my scientific career ended abruptly.[2] On that day I was secretly arrested, interrogated harshly, tried in camera, and sentenced to a 20-year prison term, because I had provided highly secret scientific information to the Soviet Union. For the first 10 years of my 20-year sentence I was held in solitary confinement, in a high security prison, under a false name and a fabricated profession. In spite of my suffering during this long imprisonment, I have never regretted my modest attempt during the Cold War to undermine what I believed to be the dangers associated with imbalances in scientific knowledge. My feelings about this remain with me despite the fall of the Soviet Union – a country to which not only I owe my life, as well as my career in epidemiology and my most useful work; but, above all, the opportunity to fight fascism.

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