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WHO CARDIOVASCULAR DISEASES UNIT 1959-1973

International cooperation in the fight with cardiovascular diseases.
Zdenek Fejfar

THE START

The cardiovascular activity was proposed to the World Health Organization by the Indian Government in 1953. Three years later the decision to promote such a programme was adopted by the World Health Assembly in Minneapolis with the USA financial offer to expand WHO research into this field. The CVD unit was then created and started to function on 15 March 1959 - one cardiologist and one secretary.

The basis to begin with were reports of several meetings - on problems such as atherosclerosis and ischemic heart disease (1955), classification of atherosclerotic lesions (1957), prevention of rheumatic fever and classification and criteria for epidemiological studies of hypertension and coronary heart disease (1958) (Wld.Hlth, Org.tech.Rep.Ser. 1955, No.97, 1957, No.117 and 126, 1958, No.143, 1959, No.168)

The field of epidemiology was considered important for inter national cooperation in cardiovascular research by members of the first scientific group which met in Geneva 16-18 March 1959. Dr.J.Watt, director of the National Heart Institute in Bethesda, was chairman, members included well known epidemiologists such as A.Keys and F.F.Moore, statistician, from the USA, and A.Cochrane and J.M.Morris from the UK, the physicians I.Page (USA), Sir George Pickering (UK), J.Speraksky (USSR) and H.J.Ustvedt (Norway) and the veterinary surgeon D.K.Detweiler (USA). There was also a valuable paper by Paul Wood (UK) suggesting that WHO should eventually also include experimental research of a more fundamental character. For ischemic heart disease, he outlined three main lines: studies of the relation between atherosclerosis and blood lipids; the role of thrombogenic factors in atherogenesis; and behaviour of the intima from the cellular point of view.

We learnt rather quickly that having many good suggestion does not by itself ensure success. Reports published by WHO were more or less buried in ministries of health, and only a few cardiologists knew of them. To disseminate available knowledge about the problems of cardiovascular diseases and about new developments by WHO, required establishing a large circle of cooperating physicians and laboratories throughout the globe. The first task was to establish such cooperation with the leading cardiologists in the International Society of Cardiology (ISC) founded in 1950. Distinguished colleagues were nominated to the WHO panel of experts and, later, the official relation was established between WHO and ISC.

Apart from exchanging and disseminating information and assisting training of physicians in cardiology, our main task was to stimulate, coordinate and carry out research on the pathogenesis, treatment and prevention of cardiovascular diseases of public health importance. At that time, in research measures WHO staff members were free to contact anybody anywhere.

However, knowledge of places from literature was not sufficient to select those who would be the best ones for the cooperative studies into the causes of cardiovascular diseases and into their preventive measures. One had, therefore, to visit places of potential cooperation. All this proved to be very useful. At that time, the WHO cardiologist had to be a clinician, he had to know how to put the catheter into the heart if needed, had to be able to lecture, and no great interest was in the ministries of health in most visited areas.

Research programme was the affair of Headquarters, but all regional directors, when properly briefed, provided good help. During the first 10 years, some regional offices, first of all the European, gradually became our cooperating centres.

PREVENTIVE MEASURES AND TREATMENT

During the first years the main features as to how to treat and prevent major CVD were outlined in several meetings. Cor pulmonale was discussed in 1960, arterial hypertension and ischemic heart disease in 1961, rheumatic fever and rheumatic heart disease in 1966, problems of rehabilitation in 1963. All reports were published in the TRS series. These booklets became the basis for regional meetings, e.g. in Bucharest 1965, in Manila 1968, in Teheran 1972.

It became fairly soon evident that publication of reports only, though written on advice of excellent experts, wasnot sufficient.

It was necessary to prove in smaller pilo studies how to apply the knowledge in a given country. Studies in several countries of different socio-economic levels should show which measures were locally most suitable. Cooperation between outpatient and hospital services and the use of existing structures of health services were the two guiding principles. We never considered to establish special services for cardiac patients outside the local structure and organization of health care.

Programmes for rheumatic fever prevention have been in progress since 1970 in Egypt, Iran, Barbados, Cyprus and the Mongolian Peoples Republic. Both children and adults were sought; the programme was guided by Toma Strasser and data analysis was performed in Geneva Headquarters

The hypertension control programme became possible with advances of hypertension treatment and by finding our that in most populations only a small fraction of hypertensive patients (less than 20%) was adequately treated. The control programme in the early 1970_s organized by Dr. Strasser was carried out in 18 model areas of 13 countries.

In a similar way, the programme for patients with cerebrovascular disease (community stroke registers) started following our meeting in Monaco in 1970; it was headed by Shuichi Hatano.

A pilot study of the management of acute myocardial infarction was undertaken in 20 areas of 18 countries in Europe, Israel and Australia (dr. Z Pisa, Mr. K. Uemura).

The World Health Day "Your heart is your health" in 1972 was a booster and many countries actively participated, with special stamps, broadcast talks and articles using our documentation. The broadcast series "Round the world with the WHO" also helped considerably.

RESEARCH

In 1959 we considered the globe as a laboratory where one could find contrasting areas regarding the presence and frequency of cardiovascular diseases. The opportunity was to relate the frequency of a disease with different way of living and in different ethnic groups. We learnt, for example, that immigrant Indians had higher morbidity and mortality from ischemic heart diseases than local populations (Kampala, Singapore or Fiji). Searching for such contrasting places was the first task, together with preparations of standardized methodology. Here, unfortunately, the situation was bleak. I learnt with dismay at the famous meeting in Princeton (April 1959) that population studies under way in the USA (Framingham, Albany, Seven Country Study) or in the UK(bus drivers and conductors)) and a few other had been undertaken with various methods, making the eventual comparison and pooling of data very difficult. There was no agreement on such a simple method as the measurement of diastolic blood pressure (the 4th or 5th sound of Korotkov).

We had, first of all therefore, to work out and test comparable methods for epidemiological studies. They involved "Minnesota" coding of the ECG, testing the assessment of ocular fundi, direct and indirect measurement of the blood pressure, working out comparable methods for blood cholesterol estimation. The laboratory of Dr.Cooper in Center of Diseases Control in Atlanta, USA, became the international centre for standardization, and the Institute for Cardiovascular Research, since 1971 part of the Institute for Clinical and Experimental medicine (IKEM) in Prague that for the European Region. The smallest intraobserver and interobserver variability in ECG reading was in those persons who were neither cardiologists nor epidemiologists, pointing to the machine analysis as the best way for ECG coding, unless done in one central laboratory.

The 1960's were indeed the golden age for research. We had funds for supporting cardiovascular projects and started modestly, promoting on advice of Archie Cochrane (UK) the establishment of the MRC Epidemiology Research Unit in Kingston, Jamaica, with Bill Miall in charge. Apart from well known studies, a number of outstanding epidemiologists started their carears there (e.g. Ken Stewart and G. Fodor).

WHO activities were gradually growing in scope and depth. In 1961 a large scale autopsy study of atherosclerosis in the aorta and coronary arteries in subjects of both sexes, aged 10-79 years, who died between 1963-1965, was initiated in Malmö, Prague, Yalta, Riga and Tallin. All samples were collected in a standard way and were processed in the department of pathology in Malmö; data were analyzed periodically in Geneva. Specimens from 17,455 persons were collected covering about 77% of all deaths in the areas. The second study centred on young individuals started twenty-five years later. It will be of interest to learn about changes in populations where coronary mortality has been rising.

Since 1966, the CVD Unit coordinated on primary prevention of ischemic heart disease, attempting to find out to what extent mortality and morbidity from ischemic heart disease would change by lowering serum cholesterol. Clofibrate, known at that time as a drug with neglibible side effects, was chosen for lowering blood cholesterol level. This double blind study was at that time the greatest with 15,000 subjects observed for at least five years in Budapest, Edinburgh and Prague. Statistical analyses were done at the London School of Hygiene and Tropical Medicine. All information on mortality, morbidity and side effects were evaluated by a committee in WHO,

Geneva. The study proved, as the first of its kind, that indeed lowering the serum cholesterol decreased the incidence of myocardial infarction (both fatal and nonfatal). At the same time, however, there was a slightly higher death rate from other causes in subjects taking clofibrate compared to those of placebo. This stirred up rather emotional discussions (see e.g. Editorial in the Lancet 1978, No.25, p.1131) which unfortunately overshadowed the beneficial effect of the drugs and the valuable experience of how to conduct, coordinate and evaluate a large scale preventive trial. As a matter of fact, the so much discussed side effects of clofibrate became apparent only after administration of 38 million capsules of the drug. In how many other therapeutic trials were such amounts ever given?

As said above, the programme was expanding gradually. In a number of developing areas, mostly in the continent of Africa, cardiomyopathies of unclear etiology were described under different names. With the help of consultant pathologists and clinicians, practical classification was made into three main groups (hypertrophic, restrictive and congestive (now called dilated)). WHO groups from four continents became later on the scientific council on cardiomyopathies of (a that time) the International Society of Cardiology.

Together with Jack Davis, pathologist fro the UK, working for a number od years in Kampala (Uganda), whose name became connected with endomyocardial fibrosis, I studied, from a clinician's point of view, Chagas' heart disease in Latin America. Our report stimulated and renewed interest for further work by PAHO (Pan American GHealth Organization, the WHO Regional Office for the Continent).

We explored and critically assessed at meeting in Israel immunological and electronmicroscopic methods for furthering research into the pathogenesis of congestive cardiomyopathies.
The high altitude areas became another point of interest in view of the high frequency of patent ductus arteriosus and arterial septal defect, both often with high pulmonary artery pressure. There were also reports about a rather low prevaence of systemic hypertension, ischemic heart disease and vascular thrombosis. Research teams from Geneva University, headed by Pierre Moret, investigated in Bolivia cardiac metabolism and at a meeting organized jointly with George Lambert in la Paz in 1972, the broad spectrum of high altitude cardiological problems was presented.
We also attempted to open the more or less closed classifica

tion of lipoproteins (Fredrickson and Levy) by proposing to separate group II into IIa and IIb. The suggestion came from L.Carlsson (see Beaumot and Cooper, Bull. WHO, 1970, 43. 891-915). The classification, meant originally as "working" for a few years, is still in use.

Our attempt to expand activity into the problem of arterial thrombosis in relation to atherogenesis and coronary heart disease was not realised because of the lack of time in the early seventies. By 1972, there were 131 institutes throughout the world cooperating with the CVD Unit of the World Health Organization:
10 in the African regions, 22 in the regions of Americas, 11 in the Eastern Mediterranean region, 72 in the European region, 3 in South-East Asia and 13 in the Western Pacific region.

We did not finish, as we wished, the investigation into the role of trace elements (methodological problems).

In cooperation with the International Society of Cardiology, we sponsored and organized symposia on outstanding problems - - such as the metabolism of the hypoxic and ischemic myocardium; myocardial blood flow, neural and psychological mechanisms in cardiovascular diseases (see bibliography in WHO Chronicle 1974, 28, 55-64).

At a WHO meeting on worldwide cooperative efforts to control cardiovascular diseases held in Geneva (30 April - 4 May 1973), the 14 years of work was evaluated by 22 experts (theoreticians, epidemiologists, clinicians) from 19 countries, and an intensified programme for 1973-1980 was outlined. In included the establishment of nationwide community programmes for comprehensive control of cardiovascular diseases as distinct from single disease control; continuation in creating the global network of cooperating national and regional laboratories, institutes and institutions to cooperate in research investigations and to apply rapidly the new knowledge into general practice; to concentrate more effort on early phases of cardiovascular diseases, some of which begin in childhood; to work out thus programmes for improvement of cardiovascular health starting in the first years of life and continuing throughout the life span until old age. Details can be found in WHO Chronicle 1974, 28, pp. 55-64, 116-125 and 190-199).

ACHIEVEMENTS AND FAILURES

WHO's activity on the available measures for CVD prevention and methodology for population studies soon became known to the cardiological world. The cooperation with the international Society of Cardiology (ISC) became fruitful for both organizations. During the IV. World Congress of Cardiology in 1962 in Mexico City, Lars Werkö, Kempton Maddox and myself suggested the enlargement of the

Scientific Committee of ISC by other specialists, apart from epidemiologists. This then became the nucleus of the Scientific Councils. They were created later (1966) when the danger of splitting the ISC into several specialized separate societies arose. The president of the Society, Pierre W. Duchosal, prepared, with my help, during 1964-1966, a proposal for the creation of the Scientific Board, composed of the chairmen of the Scientific Councils (Hypertension, Epidemiology, Clinical cardiology, Thrombosis, Cardiomyopathies, etc.) enabling the ISC and the later International Society and Federation of Cardiology (ISFC) to put under its umbrella any new specialized society.

The proposal was accepted by representatives of the national societies of cardiology during the Vth World Congress of
Cardiology in New Delhi 1966. Later on, the permanent Secretariat of the Society was established in Geneva, mainly to be close to WHO. It became a tradition to invite the chief of the CVD Unit to all sessions of the Committeee of the Society and its Scientific Board.

We enjoyed excellent cooperation with cardiologists and other
scientists all over the world. No one ever refused to come to give advice, write a paper or do a study. Our financial support. Though small (usually one dollar from WHO for 20 of the other partners) enabled a number of good laboratories to expand or start new work. In countries with soft currency the need was for purchase of equipment, in othersto pay the salaries. Our reputation gradually grew and it became customery to say and write "according to the WHO classification, or standardization, or methodology".
We were, of course, lucky to have in my time a broadminded
great personage as Director General, M.G.Candau from Brazil
had an enormous international reputation. He favoured our work and the Advisory Committee for Medical Research (several members were Nobel Prize winners) after sharp discussion, viewed our programme with friendly eyes. There was a good spirit of cooperation within the Organization. We could, for example, use to full extent in early seventies the new computing facilities for our atuopsy study of atherosclerosis.

The staffing of the Unit was at high technical and moral level. Andy Burgess jr. from the USA worked 18 months on
standardizatioon of methods, and on return to the USA became mem
ber of Ruttstein's department of preventive medicine at Harvard University. Aubrey Kagan, originally taking part in J.N.Morris's bus drivers and conductors study, was responsible for testing epidemiological methods and for the autopsy study of atherosclerosis. He left WHO for Stockholm to work with L.levy on psychosomatic medicine.Igor Shkvatshabayia started work on the hypertension programme and on return home became director of Mjasnikov's Institute of Cardiology in Moscow. Toma Strasse from Beograd did an enormous amount of work since 1969, when became in charge of rheumatic fever prevention and hypertension control programme. He continued as secretary general of the World Hypertension League and published several important books on this topic, including that on cardiovascular diseases in old age. Shuichi Harano, who was in charge of the cerebrovascular diseases programme, became one of the leaders in the Institute of Public Health in Tokyo. Don Badger worked with us as scientist for a couple of years, and on return home to the USA , became professor of physiology at the University of Illinois. Robertto Masironi tried first to do research on trace elements and is now responsible for WHO's programme on smoking control.

There was also a WHO CVD research team in Africa, in Kampala and later in Accra. Dr. Paret, followed by Dr. A. Ikeme (laterthe Dean of the university in Jos) and Dr. Pole coming from Perth, all did fine work under sometimes difficult circumstances.
Medical people joining WHO with different cultural backgrounds would be rather behlpless without good secretaries. At the start in 1959 it was Isabelle Mundy who took care of everything and everybody in the Unit. Since 1963, Barbara Pumfrey, and later on an excellent team - Mary-Jane Watson, Bunty Müller and Margaret Eddison - helped very much in carrying out all tasks.

I am also happy to mention the close cooperation with the Department of Cardiology at Geneva University, headed at that time by Professor P.W.Duchosal. I had the opportunity of taking part in the life of his department and to lecture to students.

A long term training programme was also satisfactory. Apart from traditional fellowships at the request of governments, the cardiovascular programme received research training grants given to WHO by the Swedish Society against Chest and Heart Diseases since 1959. Several young persons, later leading cardiologists in their countries, spent each a profitable year in Sweden. An annual advanced course in cardiology for physicians from developing countries was organized for several years in Copenhagen by Prof. A. Tybjaerg Hansen and Prof. Olesen. Financial support was from the Danish International Agency.
The World health Day 1972 "Your heart is your health" and the World Heart Month were successful in informing the general public.

We might of course have done better. The start was slow. I had no experience in international work or in epidemiology, and my knowledge about the distribution of major cardiovascu lar diseases was scanty. The first large meeting on cardiovascular epidemiology was held in Princeton three weeks after my arrival in Geneva.

Apart from Ancel Keys' Seven Country Study there was no experience from cooperative investigations. There was no other information about the prevalence of major cardiovascular di¡ì seases. When cooperative studies were undertaken, it became necessary for the participants to meet regularly to get to know each other and to improve the quality of work. However, funds were lacking for such gatherings unless local support was provided. For there reasons, we were able to coordinate directly for several years only two big studies (atherosclerosis and clsofibrate).
It has not been easy to orientate cardiologists towards prevention, rather than to the customery diagnostics and treatment of patients with established disease, and to change their attitudes from preferring rarities to common conditions.

The public in the early sixties was not prepared for an optmistic view. Cardiovascular diseases were considered in the developed world as more or less diseases of old age and not

preventable. Besides, preventive measures are in general accepted slowly if they require continuing efforts, compared to one single activity such as vaccination. In the USA, for example, the first big effort to combat smoking in 1964 resulted within a year in the forced departure of the cardiologist, Luther Terry, from the post of surgeon general. The effect, however, is clear now, 25 years later.

The principal cause of delay im implementing several good projects were insufficient financial resources. In 1973, the funds for CVD programme projects represented 0.60% of the total effective working budget (1 dollar at that time = 4,31 SF). We failed at that time to create an International Institute similar to Cancer Research Institute in Lyon.

My time in WHO ended with Dr. Candau's departure. The long term programmee I was prevented from building up in later years remained on paper.