Modern Concepts in Tuberculosis Control

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It is great honor and privilege for me to attend this meeting and address to your distinguished members of the Academic Society of Tuberculosis here today. It is a very significant and gratifying fact indeed that so many distinguished physicians in the county have gathered here in this room to discuss about tuberculosis on such days when medical profession is losing interest in tuberculosis in many other countries. This fact itself gives promise for the future success in tuberculosis control in this country.

My subject today is 'modern concepts in tuberculosis control'. By choosing this subject, I do not intend to introduce you something very new or something astonishing, but I am just going to summarize the concepts which we have been becoming more and more familiar with during the past decade or so and express them in a rather clear-cut way, or simply bring up something vague in our mind to speak out in language only. By doing so, I hope you will understand more the underlining concepts of what your Government is going to do or what WHO is going to help your Government in the combat against tuberculosis.

After the successful conduct of the first prevalence survey of tuberculosis in 1965, the extent of tuberculosis problem in Korea has been clearly defined, and the distribution of this disease among the population has become clearly known. Tuberculosis problem is very serious in Korea; this is no longer a guess work but a true fact, which should deserve grave concern of both the Government and the public.

5.1% of the population aged 5 years and above have active pulmonary tuberculosis. This means that we have a TB population of one and a quarter million, almost the same size of the population as in Pusan City. Among these, 226,000 are infectious cases, and more than a half of them are not known to the health authorities and spreading the germs to their surrounding fellows, especially to young children, so that by the time they enter the primary school, about 30% of them will have got tuberculosis infection. All age groups as a whole, 65% of the urban and 58% of the rural population are tuberculin positive and we are bound to have hundreds of thousand of new cases to be developed among this infected population in the future.

So the problem is very serious but if you are not brave enough to face this fact and take immediate actions, you will lose further in the fight against this disease. To solve the problem of this magnitude, what do we have in our hands? We have the knowledge of control measures, we have technical personnel, and we have some resources although rather limited. The problem is how to organize a tuberculosis control system, how to plan a national tuberculosis programme, how to select priorities for application and how to utilize the limited resources to a maximum extent.

From what I have said above I believe you would agree with me in saying that tuberculosis is not only a problem of individual sufferers but at the same time it is a social suffering. Therefore, to solve the problem we ought to employ a community approach and not an individual approach. In other words, we have to rely on a public health approach in stead of clinical approach, if our purpose is to solve the problem.

It is much easier to start with the traditional patient-doctor relationship than with the more abstract problem-resource relationship, but as far as our purpose is to solve the problem, the national tuberculosis programme should aim at the specific and systematic reduction of tuberculosis problem within the resources at our disposal in the country. With this as an objective, the national tuberculosis

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programme should take a set of organized actions today and tomorrow......not in the next century or even not in the next decade, because the problem is so serious and so urgent.

In this respect, we should not be confused and identify the hospitals, clinics, rehabilitation centres, research projects, or these combined together as a national tuberculosis programme. We cannot deny their places in the total frame of the national tuberculosis programme, but they should be recognized as the microsystems of the total programme.

After the magnitude of the problem and the implication of the national tuberculosis programme are made clear, I should like to discuss the three phases of tuberculosis control from the problem-resource standpoint, namely, first case-finding, then treatment, and finally prevention.

Let me start with case-finding. It was a great mistake in the history of medicine that for almost 70 years after the discovery of tubercle bacilli in 1882, search for tubercle bacilli as a means of diagnosis, especially as a means of case-finding, has not been given proper weight and fully utilized. During the early days of this century physicians thought that they could make diagnosis of tuberculosis with a stethoscope. Later it was replaced by radiological examination. Especially during World War II, mass photofluorography was extensively used for case-finding, and this has become an almost established standard method of case-finding in many advanced countries. People believe that tuberculosis can be detected by X-ray examination and they think they can look into the chest of a person to find out pathological changes. But in this way we are totally misled; what we see on the X-ray films are, in fact, neither tubercle bacilli nor histological changes, but merely shadows of something abnormal. How can we tell these shadows are tuberculous and not other type of pathology? In other words, the radiological shadows are not pathognomonic at all.

Let me start from a different angle. Suppose a patient has his sputum examined without prior X-ray examination and the result comes out to be positive. Then are you not going to approve that he is a genuine case of tuberculosis? Yes, you certainly would. He is not only a definite case of tuberculosis but also infectious and active, and therefore, needs immediate actions including health education, drug treatment, examination of his family contacts, and so on. We call this measure of case-finding primary sputum test. This is so easy, so cheap and so clear-cut, so there is no reason why we do not use this measure as a means of case-finding. We have been using this method for 10 years in Taiwan which contributed to the discovery of about two thirds of the total number of infectious cases discovered each year, and a very significant fact is that this has been done by non-professional, so-called health workers in the rural health stations. It requires only one or two days to train them in this particular item of work. The discovery rate is usually around 5-10%. The cost of discovering a case of tuberculosis by this means is only 1.5 US dollars while that by mass X-ray with subsequent sputum examination is 26 dollars, almost 17 times expensive, and taking into account the cost of one microscope being only 60 dollars as compared with 20,000 dollars for a mobile X-ray unit, there is no reason why we do not take this primary sputum test as a standard method of case-finding as far as our present target is to discover all existing infectious cases in the communities.

By what I said above I do not intend to underestimate the value of X-ray examination. Certainly X-ray has its own advantages. The problem is that X-ray equipment is too expensive for us to buy and very expensive too to maintain. Furthermore, mass X-ray examination would discover so many insignificant cases for us to take care of. In so far as our primary purpose is detection of all infectious cases, discovery and treatment of hundreds or thousands of non-infectious, insignificant cases, so-called TB suspects, simply would cause competition in drug consumption with infectious cases and affect the intensity of supervision of the latter group in view of the limited amount of fund for drug procurement and the rather heavy work-load in the peripheral health units at present. Mass X-ray examination, or so-called community-wide case-finding campaign by X-ray, would bring about 10% of those examined for us to make bacteriological examination because of pulmonary abnormalities, and from this group we would find about 10% bacteriologically positives or 1% of the total X-ray examined. This means that to discover one case of tuberculosis out of one hundred persons the remaining 99 persons are given X-ray examination. This is indeed a waste of time, money and manpower in the light of our resources at this stage so it should be discouraged.

Therefore, WHO is recommending more selective way
of X-ray examination, if such facilities are available. This is more productive because it is more selective. Sociological surveys in several developing countries have shown that 90% of reliably diagnosed active cases of tuberculosis were conscious of symptoms suggestive of tuberculosis; that more than 70% of these spontaneously expressed worry over these symptoms; and that more than 50% not only were conscious and worried, but indeed had taken action to search for alleviation of their suffering, but mostly in vain. So why not make such limited X-ray services available to all those who already suffer and who are prepared to accept help, and let them have such services at their own communities.

On the basis of this concept, we have organized the so-called mobile clinic services in Taiwan, using the existing mobile X-ray units, attached with a laboratory technician to each of them. These units visit each township once every six months in rotation. The local health station workers have to locate persons with respiratory symptoms and keep their names registered. Of course, they have to collect sputum from them and examine it on microscopy. If the result is positive, they will be given treatment right away and have a X-ray film taken when the X-ray unit comes. If the result is repeatedly negative and the symptoms persist, they are informed to come to the health station on the day of visit of the X-ray unit to take X-ray and have sputum and or laryngeal swab taken for culture. In a prefecture where this type of case-finding was conducted as a trial, such a mobile clinic discovered during its first round of visits 22.7% of radiological suspects of tuberculosis, and the discovery rate of infectious cases was 3.8%. During the second round of visits the corresponding rates were 13.6% and 2.5%, respectively. In view of such a high yield of cases which is considered to be much more productive than the ordinary community-wide X-ray campaign, this type of mobile clinic services has now been extended to the whole province of Taiwan.

What then are the possibilities for matching rational case-finding with effective treatment? The last WHO Export Committee on Tuberculosis recommended that, as there was no evidence that special benefits resulted from hospitalization, all financial resources and manpower available for tuberculosis control in the developing countries should be concentrated on organizing efficient ambulatory services, and not on running or constructing new beds. Then it is said, ......it is for any developing country to choose between a modern, scientifically proved treatment approach costing a few dollars per case treated, or traditional practice demanding prolonged hospitalization costing hundreds of dollars per case.

Then someone may ask whether bed-rest, diet and individual sanatorium care in the past were useless. I would not say they were entirely useless, but so far nobody has proved their effectiveness in a scientific way, and even if they had some merit in the past, it was so slim that in the light of so effective, so powerful chemotherapeutic drugs we have now they are almost negligible today. I used to tell the medical students at home when I was giving lectures to them that the effect of those traditional methods may be well compared with a street lamp in the darkness of the night. It is certainly of some help to the people during night, but as soon as the day breaks and the sun comes up, nobody would notice whether the lamp is still lit or not.

Let's detach from such a sentiment and let's be more realistic and more practical. We have a rather limited amount of fund for treatment. This fund should not be spent for the care of a small number of privileged persons, but should procure drugs for tens of thousand of infectious cases to be discovered.

Then it will be naturally clear about what drug regimens should be chosen? The choice among the first-line drugs ranges from the cheapest combination costing 3 dollars and giving 80 to 90%, to the most expensive one costing 50 dollars and giving 95 to 100% cure. Suppose we have 30,000 dollars in hand for procurement of drugs, and suppose by utilizing our existing public health services and all clinics and hospitals we can discover 10,000 infectious cases a year. Shall we choose the first one, namely the cheapest combination to treat all of them or choose the second one, namely the idealist one, to apply to only 600 cases and leave the remaining 9,400 discovered cases untreated? Of course, we know that the first one is a little inferior to the second one and would result in about 2,000 cases of treatment failure who might be discharging drug resistant organisms. Is this more dangerous than leaving 9,400 fresh cases untreated? Certainly it is not. This is indeed a very realistic problem. We have to remember that our countries are less resourceful at this stage and our problem is so serious that time does not permit us to wait for five years until
our next five year economic development plan is completed. So there is no room for saying 'like' or 'dislike'. What we have to do right now is just to accelerate discovery of infectious cases and treat all of them completely.

Treatment failure certainly is a great drawback in our mass chemotherapy programme, but these treatment failure cases are not necessarily all due to incapability of the simple drug regimen, but rather due to insufficient and irregular treatment in the past. This is the case in our health centres. When the patients come for the first time to the health centre, a certain proportion of them would say that they have already received treatment somewhere before, but it was irregular and incomplete because nobody told them how to take drugs and for how long, or they might be too poor to go to the physician's clinic to receive treatment continuously because they just couldn't afford to do so. In this group of retreatment patients naturally we cannot expect a good result. Therefore, the problem is not which drug regimen is better than the others but how regularly the drugs can be administered for at least one year during the period of initial chemotherapy. Once this period is lost, probably the chance of cure will never come back. Therefore, I should like to make a plea that unless you are sure you can treat continuously for at least full one year, 'you had better not treat the fresh cases of tuberculosis and simply refer them to the place where free treatment and adequate supervision can be given.

It is of course the responsibility of the Government to establish efficient ambulatory treatment services, in which collection and administration of drugs are well supervised. For this purpose we are exploiting the human resources in our communities to strengthen this aspect of the programme. Employment of follow-up workers at the health centres and auxiliary nurses at the Myon level is the feature of the Korean national tuberculosis programme while their equivalents in Taiwan are called TB health workers and lay home visitors. With a few weeks of training, these lay workers can carry out quite satisfactorily such items of work as sputum collection, microscopic examination, registration of cases, drug distribution, home visiting, tracing of defaulters, etc.

Utilizing such lay workers for the purpose of case-finding and treatment of tuberculosis, one cannot avoid to hear some criticisms from the side of medical profession. They may say that TB patients are human beings and not mosquitoes. As far as they are human beings, they should be seen by doctors and treatment given by doctors, too. But how many doctors do we have? Are the doctors interested in such simple monotonous work? Without doctors, can't we find and cure patients? Of course we can! In Taiwan we had 1.5 million of malaria cases in 1947 when the malaria control programme was started, but owing to organized efforts in malaria control for 15 years, malaria has been completely eradicated. Of course the vectors, mosquitoes, were killed by DDT, but how about the infectious source, human cases of malaria? Were they all treated by doctors? Certainly not! The great majority of them were discovered by lay malaria workers with blood smears and also treated by them. It is anti-malarial drugs that cured the patients. The same applies to tuberculosis. Without seeing the doctors, I am sure, tuberculosis can also be cured. It is not doctors nor the lay workers but it is anti-tuberculous drugs which are given and taken regularly that cure the patients. As far as a certain level of serum concentration of these drugs can be constantly maintained for at least one year, I am quite sure that the great majority of patients would be cured and it doesn't matter whether the drugs are dispensed by doctors or by lay workers.

However, I am not intending to degrade the value of doctors and not trying to say that doctors are useless in the national tuberculosis programme. Just the contrary, because doctors are so valuable, they should be reserved at the higher level of echelon and work as programmers, organizers, tutors, supervisors and assessors.

Last but not least let us not overlook the preventive tools. For obvious financial and manpower reasons, it is impossible to keep the hundreds of million of infected persons under periodical diagnostic follow-up or under cover of drugs in order to reduce the unavoidable consequences of infection that takes place before the case is discovered in a realistic case-finding programme. But through BCG immunization we have a treatment of bacilli at the very moment they are producing a potential case of tuberculosis. There is very little argument now in regard to the effectiveness of BCG vaccination. The controlled study made by the British Medical Research Council has clearly proved that BCG vaccination gives 80% of protection and during the 10 year observation period,
there was no substantial reduction of its protective value. The effectiveness of BCG vaccination has also been well demonstrated by the Korean Prevalence Tuberculosis Survey. The prevalence rate of active pulmonary tuberculosis cases was 1.4% among the examinees with previous BCG scars as compared with 6.0% among those without BCG scars, while the prevalence rate of bacteriologically proven cases among these two groups was 0.11%, and 1.07% respectively. So the problem is how to apply such an effective preventive measure to the most valuable, therefore, the most needy group of population. In Taiwan, TB meningitis mortality is still high among the youngest age group although it is declining. Therefore, if TB meningitis is to be prevented, BCG vaccination should be given as early as possible in infancy. On the other hand, almost 20% of the children are found to have been infected when BCG vaccination is going to be given at the school entrance, and to this 20% of infected children BCG is no longer of any help and their future consequences in tuberculosis are just subject to its natural course. Therefore, if we want to make best use of BCG vaccination as a preventive measure, again it should be given as early as possible, preferably to all newborn babies, but if this is difficult, it should be given at least before 12 months of age so that such an artificial infection will not lose its chance in the race with the natural infection.

However, this is operationally difficult. Infants are not organized and their residences are widely scattered throughout the communities. On the other hand, our health stations are short of staff and complaining of ever increasing work load by the creation of new projects. Therefore, consideration was given to BCG vaccination in conjunction with other immunizations so that the staff of the health stations might not be further overloaded by the introduction of an additional vaccination into their work schedule. One particularly attractive possibility that presented itself was the simultaneous administration of smallpox and BCG vaccines. This should enable BCG vaccination to reach as wide an infant population as smallpox vaccination; now the latter is very popular and well accepted by practically all parents in Taiwan, and simultaneous administration would involve very little additional staff time and labour.

However, experimental data were needed to show whether these two vaccines could be given simultaneously without mutual interference on protective effects and without an increase in complications. So far the literature contained nothing but speculations leading to conflicting views. Therefore a controlled study was conducted in the Taipei TB Centre in 1962, in order to test the efficacy of simultaneous administration of these two vaccines. The results clearly proved that there is no mutual interference and that such simultaneous vaccination caused no more complications than the individual vaccinations given separately.

On the basis of this experimental study, simultaneous BCG and smallpox vaccination was applied in the field for the first time in Taiwan in the spring of 1965. After this successful trial, it was put in full operation throughout the province of Taiwan. At each drive of such simultaneous vaccination in spring and autumn each year, the coverage of smallpox vaccination usually reached 90% of eligible infants, and the coverage of BCG vaccination about 80—85% of these smallpox vaccinated, or around 75% of total eligible. As the experience increases, these ratios are becoming greater, and it is expected that it will reach 100% eventually, that is, for every smallpox vaccination there will be a BCG vaccination simultaneously performed.

Thus, the first line of defense against the invasion of tuberculosis has now been firmly established in Taiwan. This alone will be able to reduce to a minimum the morbidity and mortality of TB meningitis and other types of post-primary complication, and if the second line of defense at school entrance is well maintained, our young generations will be able to live in greater safety as far as tuberculosis is concerned.

I have elaborated a little too much in detail for the the case of the development of simultaneous BCG and smallpox vaccination in Taiwan. By doing so, I was trying to illustrate how the need can be met by reorienting the current practice and exploiting the existing resources without much additional cost.

The Korean national tuberculosis programme is relatively new as compared with ours in Taiwan. However, these two countries have many similarities, such as socio-economic status, epidemiological situation of tuberculosis, health facilities, etc. During the past five years, your national workers accomplished a great deal in tuberculosis control and the basis of the national tuberculosis programme has already been laid down. One of
The features of your programme which you should be proud of is good co-operation between the government agencies, voluntary agencies, and teaching institutions. I was very much impressed by seeing that so many men and women representing different organizations are working so closely in a very harmonious atmosphere for one purpose, namely, effective control of tuberculosis. It is also gratifying to note that your Government is now determined to push the battle against tuberculosis to a full swing and has increased the national budget by four times and reorganized the administrative structure of the programme. Both WHO and UNICEF are anxious to help your Government further in the conduct of your programme, and I am very glad that I am here at your service and sincerely hope that my past experience in Taiwan will be of some help to your programme.

Mr. President, ladies and gentlemen! Once again I wish to express my hearty congratulation for the success of this biannual meeting of your Academic Society of Tuberculosis and thank you very much for giving me this opportunity to address to you.