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THE EXPANDED PROGRAMME IN IMMUNIZATION AGAINST MEASLES AND POLIOMYELITIS, IRAN'S EXPERIENCE.

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SUMMARY

The expanded programme on mass immunization against measles in a period of 10 years of operation in Iran with locally produced vaccines indicate a clear success in controlling the large epidemics of this infection. While the annual death rate, before immunization programme, was more than ten thousands in rural areas, this rate is now negligible, thanks to a good coverage, exceeding eighty percent of susceptible children. Twenty eight children who had received Sugiyama measles vaccine retained their HI antibody for eight years, the longest time period tested. There is however evidence of a decline in geometric mean of HI antibody titer which plays no role on the immune status of the immunized subjects. Dawson Disease or subacute sclerosing panencephalitis is prevalent in Iran. In 50 cases so far observed none has been vaccinated against measles, on the contrary all have had history of measles infection.

The mass campaigns against poliomyelitis in the past five years in cities and towns on Iran where population exceeds 5000 inhabitants has evidently eliminated poliomyelitis in those areas, However an increase of the number of cases in villages where oral poliovaccine has not been administered was a matter of concern. In order to eliminate the disease, the coverage of all villages throughout the country is being achieved with a great effort.

Introduction

Baby deaths due to diseases preventable by immunization are a great concern of the public health officials throughout the world. In 1974 a resolution calling for the establishment of a worldwide expanded programme of immunization was adopted by the world Health Organization (W. H. O.). The key point in the performance of this important resolution was the search for providing sufficient immunizing agents and to put them at the disposal of the needy countries in developing world. In the Middle-East region, Islamic Republic of Iran, is at present more or less self-sufficient, in regard of

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production of essential immunizing agents. The Razi Institute of Iran has had 40 years experience with manufacture of vaccines and sera and now is the main producer of human biologics, among which DTP is produced, since 1951, enough to meet our own needs. As a result diphtheria and whooping cough which were the main infectious diseases of children during and after the Second world war are now under control. Several field trials during the recent years (9, 18) have shown the efficacy of expanded programmes of mass immunization against these diseases.

Concerning the viral vaccines, this Institute is the main center of the Middle-East, developing a capacity, since 1968, for the production and control of measles and polio vaccines. In this paper we present some results of mass immunization against measles and poliomyelitis in Iran and the present situation regarding control of these diseases.

A) Measles

Measles Morbidity and Mortality

Since the development of the live attenuated measles vaccine by John F. Enders etal (5), Iran was among the countries which have launched mass vaccination campaigns against the diseases. What led to this decision was the high mortality due to measles complications in rural regions of the country, The situation regarding the high incidence of complications of measles infection in urban areas was also a matter of concern. For instance, reports from Children's Hospital of workers community of Tehran City – where the community children are admitted when the complications of measles are severe, showed that infants 5-9 months old, as well as the children aged less than two years were the main victimes of the disease (11). Although accurate statistics before 1967, when vaccination campaigns against measles started in Iran, are unavailable but in 1965 some 150,000 measles cases were reported and more than 10000 deaths due to measles were estimated by the Department of Preventive Medicine of Iranian Ministry of Health (17).

Vaccine Production

a) The Sugiyama vaccine strain of measles virus, BK-78, kindly supplied in 1968 by Dr. S. Hashizume of Chiba Serum Institute of Japan was used. This strain is attenuated in Japan by 78 subcultures in primary calf kidney cells. The vaccine was produced in primary baby calf kidney cells (10).

b) A further attenuated progeny of the same strain, called 5F 100 Clone, was also received from the same Institute in 1971 (12). Since 1972 this strain has been largely used. More than 20 million doses of vaccine were prepared with these strains and were controlled according to the minimum requirements of live attenuated measles vaccine, as formulated by W.H.O. (19).

c) Aik–C vaccine strain (kindly supplied by Dr. S. Makino of Kitasato Institute, Tokyo), an Enders - Edmonston measles virus attenuated in primary sheep - kidney cells and plaques isolated in SPF chick embryo culture (6,7,8) was adapted in our laboratory to Human Diploid Cells (H.D.C.), MRC–5.

Since 1977 this vaccine is mainly used in mass campaigns (13).

The vaccine is packaged in 10–dose vials and freeze dried. These are sealed under high vacuum and stored at - 20°C. It is normally packed in dry ice and air–transported to the main cities from where it is sent to the smaller cities and towns. In most of the health centers, electricity-run refrigerators are available. The vaccine is routinly stored at cold for gradual uses.

Mass Campaigns

At the begining, there was a period (1966 - 1970) during which the programme was applied as field trials, at limited scale, in rural areas where measles was the main concern. In this period, measles vaccine was imported and the high cost of vaccine was a constraint for development of the programme. The situation changed quickly in 1971 when locally produced vaccine was available. The Department of Preventive Medicine of the Ministry of Health, planned immunization schemes for a high coverage of susceptible children. The remarkable effect of the mass vaccination programme in reducing morbidity and mortality in rural parts of Iran became soon apparent. At the end of 1971 when a coverage of only 37–percent was achieved, there was a 56 percent reduction in morbidity and a dramatic fall in mortality due to measles (11). From 1971 to the present time the national coverage is maintained by health teams all over the country. As a result, measles is no more a problem in rural regions of the country. Fig 1 illustres the morbidity cases from 1966 (before mass immunization), to 1971 (1 year after performance of expanded programme) and to 1981 when an 80 percent coverage (in most of rural areas) was achieved.

At the moment, waves of measles epidemics are no more observed as it was the case several years ago.

Frequency of the Late Measles Complications

The association of Dawson disease or subacute sclerosing panencephalitis (SSPE) with measles infection is now well documented. Various investigations have shown that laboratory confirmed cases occur throughout the world. In this country, pediatricians have clearly described the disease in the past. However, due to the shortcomings of laboratory diagnosis of SSPE, the true incidence of the disease was not known. During the recent years, in collaboration with a team of neurosurgeons of a children's hospital in Tehran, we have been able to diagnose some 50 cases of SSPE. Out of 7 brain

biopsies, 3 measles like viruses have been isolated (2,3,15). So for all cases have been observed among young patients, 8 to 22 years old of both sexes. Most patients had positive measles history but none have been vaccinated against the disease in previous years.

Persistence of Antibody After Vaccination

Children of the personnel of the Razi Institute, aged 1–2 years without preexisting natural measles antibody have been immunized in 1970 with 1000 TCID50/ dose of Sugiyama vaccine BK–78 (10). Reaction to the vaccine was mild, seroconversion in this group was 100% and geometric mean (G.M.) titer of hemagglutination inhibition (H.I.) antibody was 6.7, 8 years after vaccination 28 children aged 9 to 10 years of the above mentioned group were selected for control of persistence of antibody. Description of vaccine and collection of finger blood specimens and technique of HI test have been published earlier (10,12). Veinous blood was collected for test when HI titer was less than 1:8. Table 2 shows the measles HI antibody of children, 8 years post-immunization. The individual HI titers, 4 weeks after vaccination, are not available but the G.M was 6.7. The decline of the G.M. titer to 4.2 is most probably due to the loss of circulating antibody during 8 years time. Absence of detectable HI antibody does not necessarily mean susceptibility of children to measles infection since cellular immunity plays an important role in preventing the disease. Our findings are in accordance with those of other investigators who have shown persistence of measles antibody, 15 years after immunization (1).

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The official public health annual reports of Iran so far indicate the efficiency of expanded immunization programme against measles infection. This success is probably due to the following facts:

1) Plans to accumulate and store sufficient vaccine with high quality before starting any programme of vaccination.
2) The existing vaccine production facilities in the country which satisfied the anticipated demands.
3) The efficacy of the cold chain from the laboratory to the centers where vaccine was stored and distributed for expanded programme.
4) Availability of trained personnel and financial support of the Ministry of Health for extending geographical coverage.

B) Poliomyelitis

Poliomyelitis is an endemic disease in Iran. The disease became a public health problem since 1962 and thereafter, several hundred of paralytic cases

were reported annually. The reported cases reflected in Table No. 3 are mainly based on clinical diagnosis without laboratory confirmation. Since 1975 attention is paid to reporting the laboratory confirmed cases as well.

The mass campaigns with oral polio vaccine had a marked effect in the cities of the country. However due to the lack of mass use of vaccine in the villages there are still some foci of continued paralytic activity of the naturally occuring poliovirus. To illustrate the situation we refer to the report of Dr. Sabet Saidi (personal communication) of Department of Preventive Medicine of the Ministry of Health, who has analysed 68 confirmed cases in Central Children's Hospital of Tehran where children of migrating farmers or those of central district villagers are hospitalized. As shown by table No. 3, 84% of cases are those who had no history of oral vaccine, 14% have been fed onc with Sabin trivalent oral polio vaccine (TOPV) and only 2% have received this vaccine twice.

Mass Campaigns

The vaccination against the disease was encouraged in private clinics by imported Salk vaccine, normally combined with DTP. TOPV was also imported and used in different cities in fixed centers where people were asked to bring their children for vaccine administration. Table N.. 4 shows the number of doses of vaccine used from 1970 to 1974. Since 1975 the health authorities who were worried about the expansion of poliomyelitis in the country planned mass campaigns in all cities and towns where total population exceeds 5000. For these campaigns TOPV manufactured by the Razi Institute in Human Diploid Cells (HDC) was used (14). Some 25 million doses of this vaccine of which the quality was found satisfactory by two reference laboratories of WHO were stored frozen for such campaigns. It is worth mentioning that, according to the demographic book of the Ministry of Health the number of population at risk in 1977, based on 35 millions population of the country, for 0–2 years was 3463322 or 10,31 percent of total population. The mass campaigns were carried out in winter time. Children 3 months to 5 years of age regardless of previous administration of vaccine were fed, mostly 3 times, 6 to 8 week apart. The campaign was arranged for 1 or 2 days by numerous mobile teams who administered vaccine, though either house-to-house callings or getting localized in schools, mosques or other public places where children were brought for receiving vaccine. The response of people to the government request for vaccination was very satisfactory. Table 5 illustrates the TOPY used during these three years. Booster doses were normally given to the children attending kindergarden or at the first year of primary school. This programme has been followed in 1978 and 1979.

Poliomyelitis in Villages

Following mass campaigns in cities and towns a dramatic fall in number

of polio cases was noticed. In cities of one million or more inhabitants in 1978 and 1979 a few cases, not confirmed by laboratory test were reported. On the contrary an increase in reported cases from villages of two provinces of the country. Hamadan in West and Gorgan in North of Iran, was reported. All villages of these two provinces were covered by a mass campaign in January-March 1980.

Serological Surveys

The efficacy of TOPV produced in HDC was studied in 3000 susceptible children who were immunized with three doses of vaccine at 4–6 weeks interval. The serological survey was undertaken by applying the microneutralization test (4) with blood samples collected on filter paper discs after three times of oral administration vaccine. In 300 children of the same age groups, not receiving vaccine, it was noted that while only 10 percent had neutralizing antibody (NA) against all three types of polio viruses, 41 percent were free of NA against any of the three types of viruses. After administration of vaccine 80 to 90 percent of children have shown NA at a detectable level (16).

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Although repeated mass campaigns against poliomyelitis have been carried out in all cities and towns of Iran, but still sporadic cases of paralytic poliomyelitis are observed because of insufficient coverage in remote villages and also due to the migration of the unvaccinated children from such villages where poliomyelitis is prevalent to the cities and towns.

Fig.1-Effect of Vaccination on Reported Measles Cases in Rural Regions of IRAN

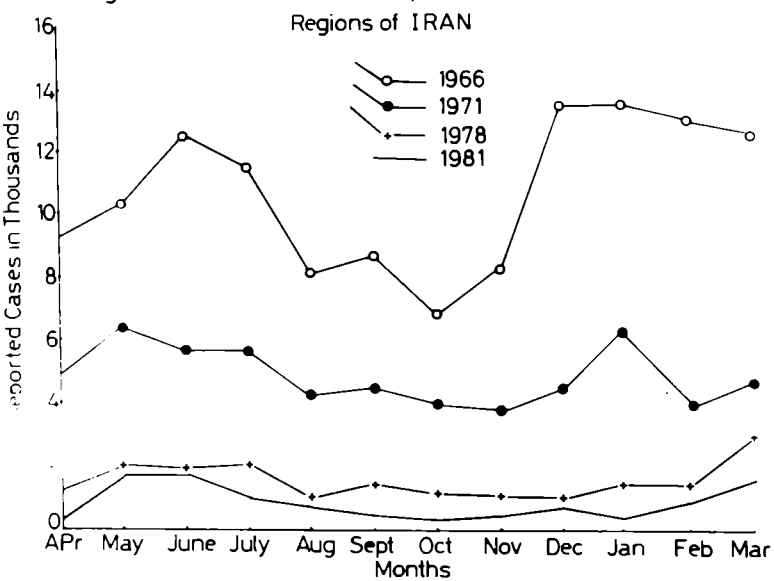

Table 2 - Distribution of HI antibody Titers in 28 Children 8years after Immunization with Sugiyama Live attenuated Measles Vaccine

HI Titer	No of Children	Geometric Mean Titer (Log2)	
		One month after vaccination	8years after vaccination
512	4		
128	2		
64	2		
32	2	6.7	4.2
16	6		
8	6		
4	2		
2	2		
(2	2		

Table No3- Poliomyelitis in IRAN (1962 -1979)

Vaccine Used	Year	No Reported *
None	1962	416
	1963	471
	1964	609
	1965	296
	1966	268
	1967	606
	1968	644
	1969	1693
Limited use of Inactivated Vaccine	1970	549
	1971	608
	1972	484
	1973	572
	1974	731
SABIN Trivalent Oral Vaccine	1975	178
	1976	544
	1977	231(68Confirmed)
	1978	59(24Confirmed)
	1979	91(68Confirmed)

* Mostly not Confirmed by Laboratory Test

REFERENCES

1. Buynak, E.B. etal (1976). Proc. Soc. Exp. Biol. and Med. **153,** 441–443.
2. Derakhshan, I., Mirchamsy, H. and Shafyi, A. (1979). Europ. Neurol. **18,** 79–83.
3. Derakhshan, I. etal (1979). J. Neurol. **221,** 169–180.
4. Dömök, I. and Magrath, D.I. (1979). W.H.O. Offset Publication No. 46.
5. Enders, J.F., Katz, S.L., Milovanovic, M.V. and Halloway, A. (1960). New Engl. J. Med. **263,** 153–184.
6. Makino, S., Sasaki, K. and Nakamura, N. (1973). Jap. J. Microbiol. **17,** 75–79.
7. Makino, S., Sasaki, K. and Nakamura, N. (1973). Kitasato Arch. Exp. Med. **46,** 83–92.
8. Makino, S., Sasaki, K. and Nakamura, N. (1974). Kitasato Arch. Exp. Med. **47,** 13–21.
9. Mirchamsy, H. etal (1968). Bull. of W.H.O. **38,** 665–671.
10. Mirchamsy, H. etal (1971). Jap. J. Exp. Med. **41,** 39–48.
11. Mirchamsy, H., Manteghi, A. and Saleh, H. (1973). Proc. Symp. Field Trials of Vaccines, Yugoslav Acad. of Sci and Arts Zagreb. 123–130.
12. Mirchamsy, H. etal (1974). J. Hyg. Camb. **72,** 273–279.
13. Mirchamsy, H. etal (1977). J. Biol. Stand. **5,** 1–18.
14. Mirchamsy, H. etal. Wold Health Organ. Poliomyelitis Committee. Document BLG/Polio 77.14, Geneva, 10–12 Oct. 1977.
15. Mirchamsy, H. etal (1978). Intervirology. **9,** 106–118.
16. Mirchamsy, H., Shafyi, A. and Sassani, A. (1980). In preparation.
17. Nafyci, K., Saidi, S. and Nategh, R. (1967). Arch. Ges. Virusforsch. **22,** 11–22.
18. Nazari, F. etal (1976). J. Biol. Stand. **4,** 329–333.
19. W.H.O. Expert Committee on Biological Standardization. Technical Report Series No. 329, 60–77 (1966).