WORLD HEALTH ORGANIZATION

Regional Office for the Eastern Mediterranean

ORGANISATION MONDIALE DE LA SANTÉ

Bureau régional pour la Méditerranée orientale

SEMINAR ON EXPANDED PROGRAMME OF IMMUNIZATION

Alexandria 8 - 14 December 1977

EM/SEM.EPI/17

1 December 1977
ENGLISH ONLY

PAST EXPERIENCE AND RESULTS OF OPERATIONAL RESEARCH - ALTERNATIVE STRATEGIES - THE ROLE OF PILOT STUDIES

by

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PAST EXPERIENCE AND RESULTS OF OPERATIONAL RESEARCH

Let us first define the type of immunization programme we are concerned with in this paper. We wish to deal with one which aims at a high level of coverage at appropriate ages with immunization against the diseases, polio, tuberculosis, measles, diphtheria, pertussis, tetanus and smallpox covered by the EPI programme.

Past experience and the results of operational research in EPI in the developing countries is in fact very little indeed, if we demand evaluation as to coverage, cost, effectiveness of immunization as judged by (a) serum antibody levels or tuberculin sensitivity and (b) reduction in incidence of disease.

In industralized countries we have plenty of experience, but it is all largely irrelevant, because of

(a) high literacy and health motivation of the parents;

(b) relatively high per capita income levels, so that costs of vaccination for the specified diseases are not a constraint;

(c) no problems with cold chain because of the degree of training of health staff and in particular because of widespread reliable electricity supply and good equipment and often a temperate climate;

(d) above all, networks of MCH services which by all other criteria are usually quite efficient i.e. contributing to low infant mortality in general.

No wonder in these circumstances, effective coverage is high, although it should be noted that even with all this some countries still cannot obtain more than 50 to 70 per cent completed coverage, and there are still therefore occasional diphtheria outbreaks, occasional cases of miliary TB or TB meningitis, incomplete control of measles and pertussis and tetanus, and poliomyelitis. The non-attenders are either members of cranky religious sects or health faddists (believing in natural everything, from natural child birth to natural childdeath too, if their children were not protected by the large degree of immunity of the rest of the child population).

Others are frightened by exaggerated publicity of adverse effects in the mass media, but no doubt a substantial portion are the children of the urban and rural poor, immigrants with communication difficulties, problem families and so on.

Nevertheless, the combination of favourable circumstances, such as make high coverage obtainable as a routine part of MCH services, does not usually exist all together in developing countries. The proof that it does not do so lies in the coverage figures of the countries themselves, especially as regards children under 12 or 15 months.

I have been able to identify only three expanded immunization programmes roughly as defined above whose description and evaluation is published or in some other way available. All of them are from Africa.

The first is a description of a programme in the Machakos distric of Kenya as yet unpublished given by J.M. Mahieu at a WHO Headquarters Seminar in 1976. (The paper is included in the background documentation of this Seminar). To mention its drawbacks first, this paper

(i) deals with a programme implemented over a period of two years only,

(ii) it covers an area of only 161,000, but also it makes comparisons with a control area of 76,500 population,

(iii) it unfortunately adopted a two-visit schedule at 6-month interval for triple vaccine with no booster, thus leaving the child unprotected until 9 - 14 months and that doubtfully;

(iv) it makes no attempt to evaluate the effectiveness of the immunization, either by disease incidence reduction or sero - or tuberculin conversion;

(v) it used BCG and smallpox vaccination scars as a maker of completion, it assists that this is time-saving and sufficiently accurate for mass vaccination programmes, but he does not really give evidence of this.

(In fact, what is being evaluated in Mahieu's paper is a rather rigid schedule promoted widely by WHO in 1974-1976 which specifies two triple vaccine shots only, one between 3 and 8 months and one between 9 and 14 months. This schedule influenced a lot of our EMR EPI plans drafted in 1975-1976. We must try to loosen this rigidity in favour of a more flexible approach based on sound epidemiological thinking about the blocking of transmission, on current knowledge rather than pious hope about the immunizing ability of the vaccines, and on the particular circumstances of the particular country, district and project).

On the positive side however, Mathieu's paper is valuable because

(a) He identifies fully and frankly some of the constraints, ranging from endless discussion with other medical officials about the schedule resulting in compromises which damaged evaluation, through transport breakdown because a Landrover was used which had passed its "write-off-date", and delays over failure to pay salaries on time, and lack of independent transport for supervisors, and frequent change of supervisors, to rumours initiated from political malice or based on vaccination incidents elsewhere.

(b) He shows how a comparatively simple mobile team approach can raise completed immunization rates from their former level of about 56 per cent to a new level of about 81 per cent in high and medium density population and from 25% to 57% in low-density population areas.

(c) Mahieu makes a most meticulous analysis of the costs per fully-immunized child, adding together costs of vaccine, manpower, transport, supplies, administration, supervision and coverage assessments. The breakdown is as follows:

Costs per fully immunized child	US $	
Vaccine including Customs, Insurance and Freight	0.75	
Manpower	0.65	
Transport	0.18	
Supply and Administration	0.06	
Supervision and Coverage Assessment	0.09	
	$ 1.73	(Medium population density and using Renaults mainly)

(d) He makes a real contribution by drawing up for this project in Kenya a table of costs of operations (i.e. not including vaccines) per fully immunized child in relation to population density (see foot page 13 of his report).

(e) Another valuable point in Mahieu's paper is that he points out clearly the financial advantages of not using Landrovers when cheap Renaults (ROHOS) will do.

In short, in spite of its limitations Mahieu's paper does make a very useful contribution.

Another useful analysis appears in the paper on "Mass Vaccination Programs in Developing Countries" by William H. Foege and Donald S. Eddins, No. 74 in the list of the special reference material available to you in the Library. The problem with this paper is that the only actual programmes it describes are Measles Control and Smallpox eradication in West Africa and the gobal smallpox eradication programme. However, these are both one-shot vaccines, and leave five of the seven EPI-covered diseases out of the reckoning. On the other hand the paper has a most useful account (page 210 - 217) of operational considerations. This can be summarized as follows·

(a) need for background data on morbidity and mortality by age, and for demographic data, and information of communications and transport, and some sociological data also,

(b) a discussion of house to house versus collecting point mobile campaigns,

(c) a discussion of establishment of vaccine priorities based on the costs in life and money of each immunizable disease versus the cost and feasibility of including the antigen in the campaign,

(d) disease surveillance by means of upgrading the existing system, special "sentinel" system; or by cluster sampling,

(e) observations on advance publicity;

(f) vaccine delivery: discussion of rôle of jet injectors,

(g) age of vaccine recipients,

(h) maintenance of high coverage once the initial phase of the mass vaccination campaign is over,

(i) record keeping at field level tally sheets, weekly summary, weekly inventory form,

(j) shock inventory and supply at central level,

(k) assessment from tally sheets, summaries, special assessment teams, sampling areas for check on scars, or cards, or serum levels or tuberculin sensitivity.

This paper was written in 1973. In 1975/1976 most of these points were incorporated into the WHO EPI Manual in much greater detail. This is I feel the chief testimony to its value.

I can find only one programme of what we would now call EPI in a developing country, covering a large population (about one million) including the six diseases, beginning on a virtually zero base-line, evaluated from point of view of coverage, cost, effectiveness of the immunizations by tuberculin testing, serum conversion, and disease reduction, and followed up for five years and using a strategy conbining mobile teams and fixed units. This was from the period 1965 - 1970,

and was undertaken in Ankole South-West Uganda with foreign aid at first, was then taken over by the district government and continued well until 1974, when it was probably overtaken by the general economic and other difficulties affecting the whole of that country. The programme was also an interesting and deliberate example of the "sequential" development of advocated in WHO Technical Report Series No. 294, 1965, Integration of Mass Campaigns Against Specific Diseases into General Health Services, for it began as an immunization programme, added health and nutrition education, then introduced family planning to the area, expanded into general Young Child Clinics and then added ante-natal care, before finally becoming integrated but still clearly identifiable, in the district health service.

Unfortunately, the development of EPI was not foreseen at that time, and it was never published in its entirety, only aspects or early stages of it in scattered publications by its successive medical officers, Cook, Moffat and Thuriaux. It can be found in its entirety only in the MD theses of Robert Cook and W.M.U. Moffat, which are temporarily added to the reference material in the library specially made available for this seminar.

The programme is briefly described in my letter to the Lancet of 12 December 1970 provided as a background document. The salient points are as follows:

1. It was a programme based in its mass campaign period 1965 - 1967 on 3 mobile teams, twenty fixed units including one mission hospital, two mission clinics, and one mobile supervising, supplying team.

2. It had a three-visit schedule for children 0 to 5 years.

1st visit: BCG, Smallpox, 1st DPT, 1st TOPV (trivalent oral polio vaccine)

2nd visit: Inspection of scars, 2nd DPT, 2nd TOPV, Measles vaccine (9 - 35 months only)

3rd visit· 3rd DPT, 3rd TOPV.

Intervals between 1st and 2nd visit were from just over four weeks to just under 8 weeks; between 2nd and 3rd always 4 weeks.

3. Records· Small card for each patient

Register one per sub-country. This was done only because it was a pilot project. Normally (as was done later) a tally sheet alone would suffice.

4. Administration of vaccines. DPT: By multidose syringe in the first year, then by disposable syringe, then this was abandoned in favour of Ped-O-Jet. BCG· By dermojet. Our experience with these, I spoke of earlier in the Seminar. Measles vaccine: by disposable syringe, then by dermojet. Smallpox: multiple pressure method.

5. Sterilization· Domestic pressure cooker, at base, taken to the field sterile.

6. Cold Chain. Measles and polio vaccines transported in CO_2 snow, met at airport and taken streight to district level refrigerators. To field daily in cold-boxes. Or in electric or kerosine refrigerators of fixed units checked monthly. Probably the latter, looked at in retrospect, may have been a weak point. As far as the mobile teams were concerned efficiency of cold chain was proved by sero-conversion to measles and polio vaccine and tuberculin conversion with BCG.

7. The static clinics and the mobile teams used as much as possible the same schedules and records and vaccines.

8. Coverage

(a) Immunizations Performed

See Table 1. This gives the totals for a four year period.

(b) A more sure indication is by examination of immunization cards retained at home and by scar examination in surveys random - sampling two counties which contained one-third of the population. Reference shoudl be made to the schedule page 6 point 2 .

The conclusion to be drawn from this is (a) that as of March 1967 about 78% of eligibles had been for at least the first visit and 63% of eligibles had completed the 3-visit schedule. BCG-scars were a little less than the total of 1st visits being about 62% in both 1967 and 1969, the latter by independent assessors.

9. Results of Immunization: Tuberculin or serum conversion

(a) BCG. See WHO/TB/72.93 by W.M.U. Moffatt and R. Cook, BCG Vaccination by Jet Injector and Syringe. "Using a slightly more concentrated vaccine from a (60 doses from a 100-dose vial) the dermojet compared favourably with the standard dilution given by syringe, both in regard to resulting tuberculin allergy and size and nature of the BCG lesions".

(b) Measles. Although we used in an attempt at economy an experimental intradermal injection of 200-400 $TCID_{50}$ by dermojet, we obtained 74 per cent sero-conversion (West and Makuye 1967), the same as the intradermal injection of 200 $TCID_{50}$ in Hong Kong by syringe and needle. Nevertheless, it was in one sense worthwhile, because for each million $TCID_{50}$ available we were able to immunize successfully 1850 children instead of 950 - 980, had we used the recommended dose of 1000 $TCID_{50}$. Although the result was the best possible at the time, now that measles vaccine is 12 cents a dose instead of a dollar, the use of fractional doses does not arise any more.

(c) Polio. The results of the polio immunization are summarized in Table 4 , compiled from West et al. (1966). The results as regards Type 1 and Type 2 were quite satisfactory. Type 3 was somewhat disappointing. Natural infection was higher to begin with, and sero-conversion less than for the other types, an experience not at all unusual in developing countries.

10. Lastly, the only really sure evaluation is control of the diseases themselves. The usual constraints of inadequate reporting obtained.

We have two sources of data, the district hospital and the returns from the dispensaries.

Table 5 shows the percentages of hospital admissions and deaths due to 5 of the immunizable diseases (diphtheria, nil). A definite decrease is noted in all except measles.

Table 6 compares hospital admissions in the district and the two neighbouring districts for pertussis.

"Figure 8" shows the quarterly pertussis returns for 10 fixed health units showing that the epidemic of 1969/1970 was much less than that of 1964/1966, whereas in the neighbouring districts of Masaka and Kigeji which had slightly smaller populations than Ankole quarterly notifications in 1970 hit peaks of 2117 and 2164 cases respectively, compared with Ankole's peak of less than 400.

"Figure 6" and Table 7 confirm that there was no visible effect on measles incidence.

This all amounts to many thousand cases of pertussis, probably several hundreds of tuberculosis, tetanus and poliomyelitis, but no visible effect on measles.

In fact, what has happened with measles is this: About 30,000 doses were given to children aged 9 to 35 months of urban one third were already immune. Thus 20,000 doses were given to non-immune children, but almost all were "economical fractional doses with 70% sero-conversion. So approximately 14,000 children were protected. But 42,000 children each year were born. Very little measles vaccine was given at all after September 1967 for lack of money. Surely some 10,000 - 15,000 cases probably were prevented but this is only ten per cent of the cases expected to occur 1968 - 1970, and too small to detect by crude returns like this. It is only when we get over 50 per cent reductions, as we have every reason to expect in TB, pertussis, polio and tetanus (other than neonatorum) that we can easily see the results even in crude statistics.

One thing quite missing from our prototype EPI in Uganda was immunization of women of child-bearing age to prevent neonatal and maternal tetanus. We simply had not then (1966) realized how important this disease could be, and how tetanus immunization of potential mothers could prevent much of it. You are referred to Berggrens paper (1974) for an account of how this measure at Deschapelles , Haiti, prevented with a programme costing US $ 67,000, 41,140 days of hospital care which would have cost $ 494,000, most of which would have been wasted since tetanus case fatality is very high indeed and most of the patients would have died anyway.

11. Cost

The cost of the immunizations in the mass campaign 1965 - 1967 was fairly accurately calculated at £27,300 or US $ 70,000. Leaving aside all who completed only one visit (receiving BCG, smallpox 1st DPT and 1st Polio) or two visits receiving as well as measles (only if right age) and 2nd DPT and 2nd Polio, there were 85,000 children who completed the 3-visit schedule.

The cost per completely immunized (7 diseases) child was therefore $ 0.82, including vaccines which in fact were donated and about 20 out of the 82 cents which returned to Government in the form of petrol tax, import tax on vehicles and four kinds of taxes on incomes of the staff. Nevertheless if we call it 82 cents, it compares quite closely with Mahieu's cost of about $ 1.73 per completely immunized child in Kenya, allowing for inflation between 1967 and 1974.

	Cook, Uganda, 1965-67 $	Mahieu, Kenya, 1974-76 $
Vaccine	0.21	0.75
Manpower including supervision and coverage assessment	0.34	0.74
Transport	0.21	0.18
Supply and administration	0.06	0.06
Total	0.82	1.73

ALTERNATIVE STRATEGIES AND THE ROLE OF PILOT STUDIES

We have reviewed then (something of) the measles/smallpox campaign in West Africa, Mahieu's EPI study in Keny 1974-1976 and the EPI part of the "EPI-plus" project of Cook, Moffat and Thuriaux in Uganda 1965-1970.

Really we can draw lessons from them, but some of them are not unexpected, their experiences having passed indirectly into the WHO EPI Manual itself. One is the importance of the cold chain. Another is the destructive effect of the lack of government committment (one country that "could not afford" ± 400,000 a year for measles vaccine which would have sufficed all its child population nevertheless "could afford" to buy in those same years sixteen jet-fighters and quintuple the size of its army and double their pay.

Another lesson is the common one, how little it costs to perform immunization in comparison to the cost treatment of the diseases, leaving aside any humanitarian considerations.

Issues which are raised and still not yet fully decided include:

(a) the two-visit versus three-visit. I personally believe that is settled until we have better vaccines and some proof that a two-visit schedule will suffice for pertussis and polio immunization. It is a pity that the 2-visit schedule gained a wholly premature acceptance.

(b) Only one of these projects attempted all forms of evaluation, coverage by total and by sample; efficacy of immunization by serum or tuberculin conversion; achievement of objective of reduction of incidence; and cost. Each of these four evaluations has serious problems, but each <u>is</u> possible and there is no alternative to carrying them out, <u>at least in pilot projects</u>, and preferably continously. We must refine our methods.

(c) One issue is the age of the target population. Some hold by a schedule of 1st visit for children aged 3-8 months, 2nd for children 9-14 months, 3rd (if any 3rd)thereafter. Apart from the fact that this is partly useless for pertussis in its most dangerous age, and for much of polio too, it is also too restrictive. Such experience as we have in industrialized countries and in the Ankole project, too strongly favours that schedule suggested page 14 of the Report on the Damascus WHO EMR Seminar in 1975, provided to you. Moreover, there is much to be said for immunizing all the children under 5 years old in the first phase of an EPI, then retracting to the immunization of non-immunes (mainly newborn) in subsequent phases. To fail to do so is (a) to defer impact by three to four years by failing to block transmission and (b) to risk raising the cost per non-immune child fully-immunized. As a counterweight to this strategy however we must recognize that the younger the child the more important he is as a target for pertussis and polio vaccination and once past 9 months for measles vaccination.
Two of the projects discussed did gain valuable experience in the use of jet injectors, clearly in my view refuting much of the apprehension and doubt which surrounds their use.

Lastly the issue of immunization from fixed units or from mobile teams. This is a bogus issue. There is no alternative strategy for most developing countries today. The answer is mobile outreach to all physically accessible children and, simultaneously, making all fixed units efficient immunizing facilities. This latter, the fixed unit, is easy to give lip service to, but actually it needs real trouble and time and resources to be devoted to it, over and above what at present clearly does not suffice. It gives, however, the only hope that, one day, the same system as in industrialized centres will be possible in developing countries too.

As to the rôle of pilot projects, they are quite essential. All the above projects were innovative. Every programme must have a pilot phase when new methods are tried out, where we discover how applicable in this particular area are methods used in other programmes and other countries. In fact Sir Francis Bacon expressed the essence of the matter more than three hundred years ago when he wrote:

"It would be an unsound fancy to expect that things which have never yet been done can be done, except by methods which have never yet been tried".

"Never yet been done" includes nation-wide high coverage of effective poly-immunization of young children in almost all developing countries.

TABLE 1

Immunizations Performed May 1965 - Sept 1967 and July 1968 - June 1969 and Last Quarter of 1970.* Children under 5. (Measles 9-35m only). Ankole

	Moblie Immunization or YCC Teams	Static Units	Total
Smallpox**	74.129	20.358	94.487
BCG	137.837	26.125	163.962
DPT 1	139.188	55.618	194.806
DPT 2	104.721 (75.3%)	36.879 (66 3%)	141.600
DPT 3	73.426 (52.7%)	27.601 (49.6%)	101.027
DPT Booster	3.381	1.851	5.232
POLIO 1	132.886	49 249	182.135
POLIO 2	94.130 (70.8%)	34.314 (69.7%)	128 444
POLIO 3	65.926 (49.6%)	25.092 (50.9%)	91.018
POLIO Booster	10.851 (8.2%)	1 199	12.050
Measles	32.919	-	32 919

*Period of 48 months all told. Missing periods were transitions between medical officers Activities went on as before but complete records were not available. An average of 42.000 children a year born, and an average number of children 0-5 each year of 176.000.

** Mainly primary, and excluding special smallpox eradication programme vaccinations.

TABLE 2

March 1967 House to House random sample survey in two counties

Production of cards. Children 1-7

Full 3 - visit completed	190/300	63.3%
2 visits only	26/300	8.7%
1 visit only	17/300	5.7%
Cannot produce any card and no scars	64/300	21.3%

TABLE 3

BCG scars children 0 - 5 years

	March 1965	March 1967	April 1969
	House to House Random Scar survey (Cook) (2 counties)	House to House Random Scar survey (Cook) (2 counties)	House to House Random Scar survey (WHO) All Ankole (10 counties)
BCG	0/301	188/306	514/829
	-	61.4%	62.0%

TABLE 4

POLIO ANTIBODIES IN UNVACCINATED
COMPARED WITH VACCINATED CHILDREN

Age	Type	UNVACINNATED Nos	UNVACINNATED Percentages	VACCINATED Nos.	VACCINATED Percentages	DIFFERENCE
1-23 months	1	14/88	15 9%	69/92	75.0%	59.1%
	2	18/88	20 5	69/93	74.2	53.7
	3	37/90	41.1	61/93	65.6	24.5
24-59 months	1	59/211	28.0%	172/211	81.5	53.5%
	2	63/211	30.0	178/213	83.6	53.6
	3	88/205	42.9	161/210	76.7	33.8
	1	73/299	24.4%	241/303	79.5	55.1%
	2	81/299	27.1	247/306	80.7	53.6
	3	125/295	42.4	222/303	73.3	30.9

TABLE 5

Admissions and deaths from the immunizable diseases as a percentage of all admissions and deaths, Mbarara Hospital, Ankole
Children 0-6 years

	Admissions		Deaths	
	Nov. 63 June 66	July 67 June 68	Nov. 63 June 66	July 67 June 68
Total Nos.	3.703	1469	282	147
Measles and post-measles pneumonia	15.3%	18.2%	8.5%	7.5%
Pertussis	3.8%	0.8%	4.3%	0.7%
Tb. all forms	4.1%	1.8%	7.8%	5.4%
Tetanus	0.3%	0.1%	2.8%	0.7%
Acute polio	0.4%	0	0.7%	0

TABLE 6

Pertussis. Admissions Ankole and the hospitals of the districts immediately neighbouring to north and east. 1964 - 66 = 100

	1964-6	1966-7	1967-8	1968-9
Ankole	100	11	16	40
Masaka	100	58	96	39
Toro	100	38	40	50

Fig. 8.

PERTUSSIS QUARTERLY RETURNS

10 Health Units in Ankole

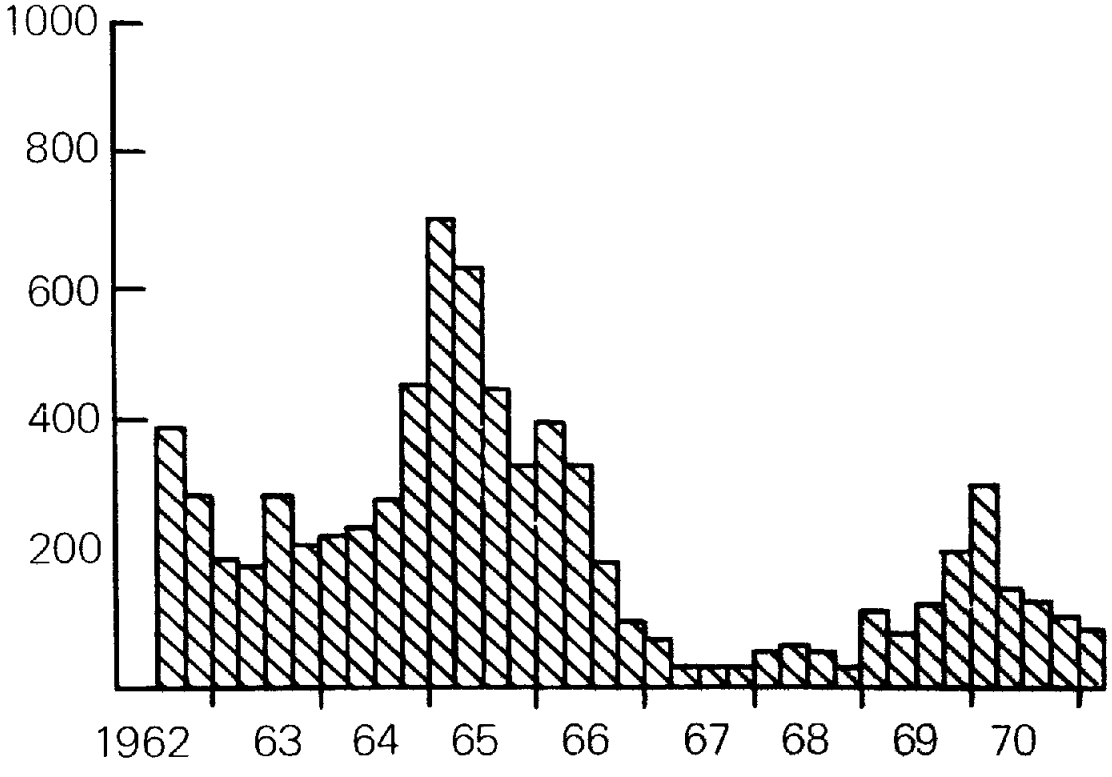

Figure 6 MEASLES Quarterly Returns, 10 Health Units, Ankole July 1962 – Dec 1967

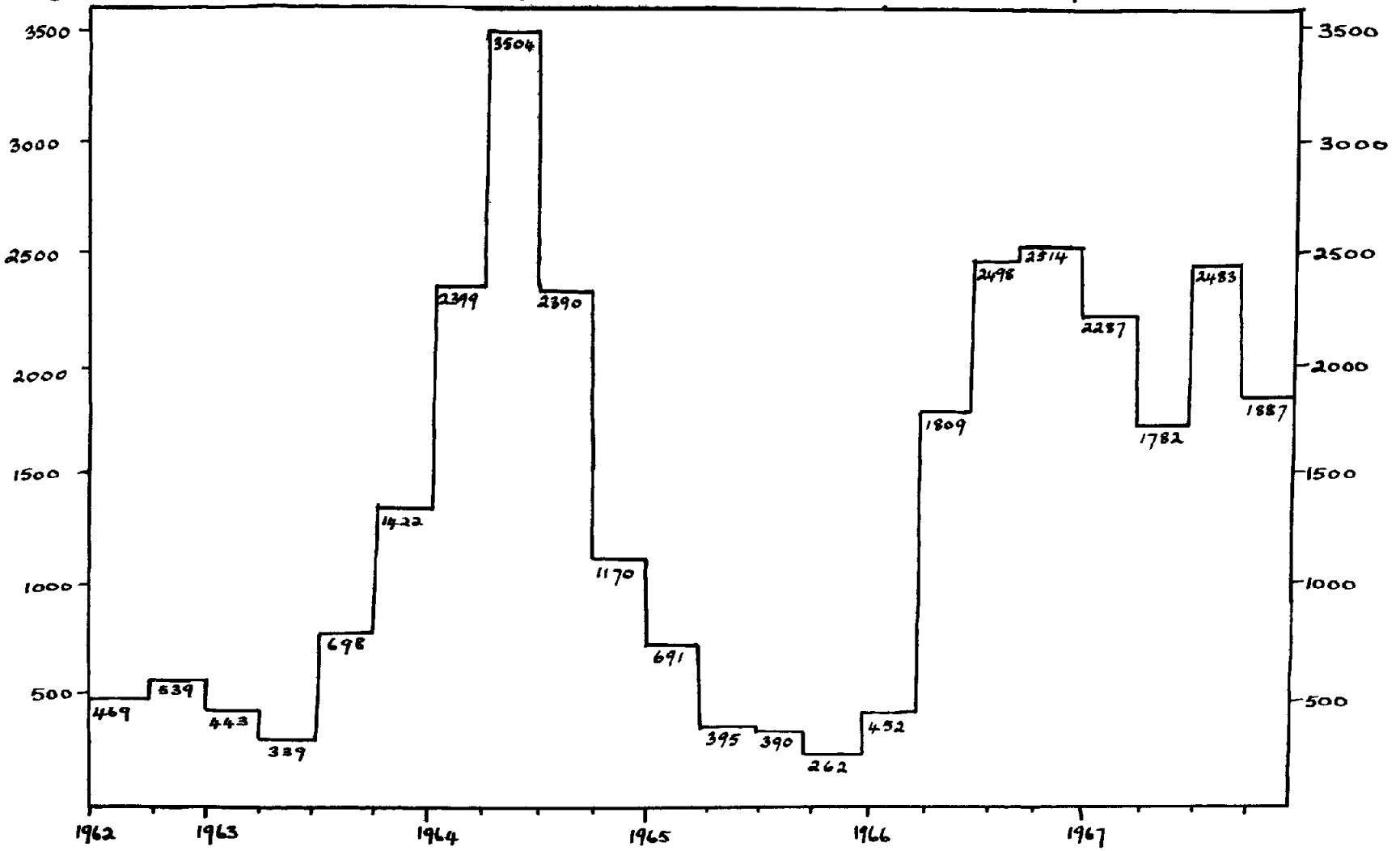

TABLE 7

Additional to "Figure 6"

Further quarterly returns of measles cases after 1 Jan. 1968
10 health units Ankole

1st quarter	1968	1883
2nd		2645
3rd		3246
4th		2381
1st	1969	3875
2nd		3665

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