DIPHTHERIA IN DURBAN: MORBIDITY, MORTALITY AND PREVENTION

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In the period 1950 - 1958, 285 residents of Durban died from diphtheria. This unnecessary loss of life, from a disease now so rare in other countries,[1,2] justified an investigation that might lead to its more effective prevention.

MATERIAL AND METHODS

Information on the population and number of notified cases of clinical and fatal diphtheria was extracted from the Annual Reports of the City Medical Officer of Health of Durban.[3] In these, the population is estimated by a formula devised by the Director of Census and Statistics and the notifications are tabulated by race. Excluded from the survey was a small group of patients, domiciled outside the municipal area but treated for diphtheria in Durban ('imported cases'). The data on the extent of prophylactic diphtheria immunization were compiled from questionnaires requesting the following information: (1) child's first name; (2) date and year of birth; (3) residential suburb; (4) length of family residence in Durban; (5) previous history, if any, of diphtheria; (6) immunization against diphtheria, month and year; and (7) immunization by private doctor or at a municipal clinic. This method of investigation presupposes a certain educational level in all sections of the population interrogated. As a whole, it was only the White group which reached the required level. As no other method could be devised for obtaining immunization histories from the other ethnic groups, figures on immunization refer to the White population only. Contact with the children was established through the schools, selected to represent the widest possible cross-section of socio-economic levels in the White population. The questionnaires were distributed early in 1958, filled in by the parents — for both the school child and minor siblings — and returned to the school.

Children under one year of age were excluded from the analysis, since it could be expected that a significant — but unknown — proportion of children in this age group would be less than 6 months old and therefore could not be expected to have been immunized. This made the youngest group smaller, but, on the other hand, it eliminated the uncertainty about their true immunization rate. With this exception, the questionnaires were examined according to criteria given in a previous communication.[4]

RESULTS

Population

The population of Durban (Table I) is classified into the usual 4 major ethnic groups of White, Asian, Coloured and Bantu persons. In 1958, the largest group was Asian, followed by the Bantu, White and Coloured groups. In the last 8 years the population has increased by 42·88%, but the increase in the White section has been considerably slower than in the non-White and, among the non-White groups, the Coloured population has almost doubled itself. As the allocation of prophylactic work between the immunizing organizations is related to race,[5] the shifts in population have a significant bearing on the planning of immunization campaigns.

TABLE I. THE POPULATION OF DURBAN

Year	White	Asian	Coloured	Bantu	Total
1950.. ..	131,932	127,496	12,821	127,496	399,745
1951.. ..	129,380	145,371	14,958	134,451	424,160
1952.. ..	133,261	149,732	15,521	141,174	439,688
1953.. ..	137,253	154,316	17,197	148,230	456,996
1954.. ..	141,370	158,945	17,845	155,642	473,802
1955.. ..	148,800	166,220	18,700	167,500	501,220
1956.. ..	153,260	171,200	19,260	175,880	519,600
1957.. ..	151,678	197,411	23,838	179,157	552,084
1958.. ..	154,763	205,543	25,003	185,835	571,144
% Distribution 1958	27·10	35·99	4·38	32·54	100·01
Increase since 1950	22,831	78,047	12,182	58,339	171,399
Increase as % of 1950 figure ..	17·31	61·22	95·02	45·76	42·88

Notified Diphtheria

The annual number of diphtheria notifications per 100,000 population, hereafter referred to as the 'notification rate', is shown in Fig. 1 and summarized for specified periods in Table II. Until recently diphtheria has been highly prevalent in Durban (Fig. 1). The overall notification rates have declined, somewhat irregularly, from 209·4 per 100,000 in 1944 to 20·1 per 100,000 in 1957. Compared with the remarkably constant level for

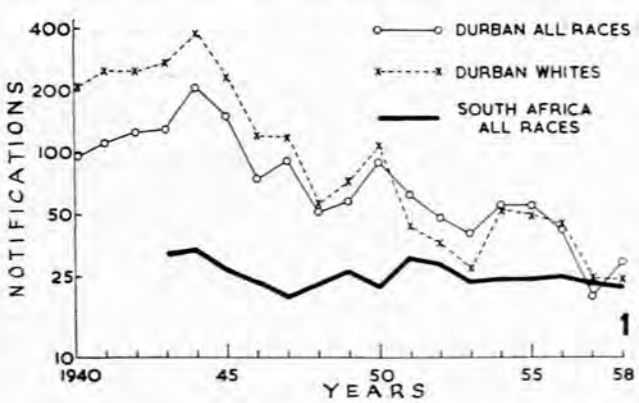

Fig. 1. Annual notifications per 100,000 population in Durban and South Africa.

the Union,[1,5] it appears that the Durban Municipality is succeeding in suppressing a focus of infection in the Union. The disease is encountered in all ethnic groups, illustrated in Table II, which, in its first section, gives

TABLE II. OBSERVED MEAN DIPHTHERIA MORBIDITY AND MORTALITY PER ANNUM IN SPECIFIED PERIODS

Years	Mean annual number of notified cases per 100,000 population				
	White	Asian	Coloured	Bantu	Total
1940 - 44	272·38	20·55	386·94	65·70	136·40
1945 - 49	122·00	31·41	176·00	93·21	86·72
1950 - 54	54·89	36·02	128·95	80·75	59·64
1955 - 58	36·42	31·90	73·58	39·61	37·30

Years	Mean annual number of notified deaths per 100,000 population				
	White	Asian	Coloured	Bantu	Total
1940 - 44	5·08	1·49	7·50	8·61	4·82
1945 - 49	3·01	4·78	11·49	9·82	5·76
1950 - 54	1·50	6·26	13·85	14·22	7·63
1955 - 58	2·13	6·21	3·97	8·09	5·55

Years	Deaths as % of notifications				
	White	Asian	Coloured	Bantu	Total
1940 - 44	1·87	7·25	1·94	13·11	3·54
1945 - 49	2·47	15·22	6·53	10·54	6·64
1950 - 54	2·73	17·38	10·74	17·61	12·79
1955 - 58	5·85	19·47	5·40	20·42	14·87

the mean notification rates by race in 3 periods of 5 years and 1 of 4 years. This method of calculation was considered advantageous since it eliminates annual fluctuations, and emphasizes trends. The table shows that proportionately more cases of diphtheria were reported from the Coloured than from the other groups.

Furthermore, the notification rates in the White and Coloured groups followed the general trend of decline. Preceded by a substantial increase in the notification rate in the earlier periods, proportionately highest in the Asian group, the same pattern of decline has also prevailed among the other ethnic groups in recent years. These comforting observations should not lead to the conclusion that the menace of diphtheria is over. It must be emphasized that the disease in Durban, and in South Africa as a whole, is still common when compared with overseas countries,[1,5] and that it still causes severe loss of life, which is illustrated in the central section of Table II. Probably the most striking feature is that the death rate has remained about 5 per 100,000 population *per annum*, being highest in the Bantu, followed by the Coloured, Asian and White groups. In recent years, however, it would appear that diphtheria has been more malignant in the Bantu and the Asian groups than in other races.

A downward trend in the notification rate, together with an unchanged death rate, is inevitably associated with a deterioration of the case prognosis *quoad vitam*. As is seen from the last section of Table II, the observed overall case mortality has increased approximately 4 times (from 3·54% to 14·87%). In all groups, except the Coloured group, it has increased steadily, and in recent years about 20% of observed diphtheria cases in Bantu and Asian patients ended in death. The possible causes for this striking case mortality will be discussed below.

Immunization Survey

Out of about 4,500 (90%) questionnaires returned, some were excluded because of their incomprehensive content and others, as pointed out above, because they were completed for children under 1 year of age. In 92 (2·14%) cases the individuals were said to have suffered from clinical diphtheria. Since their post-infectious antibody levels were unknown, it was impossible to determine their need for prophylactic immunization, for which reasons also they were omitted from the analysis. After these adjustments the material was reduced to 4,201 questionnaires suitable for tabulation. Assuming age distribution of the White population in Durban and Johannesburg[6] to be identical, our sample represents about 7% of the group investigated, i.e. White persons between 1 and 20 years of age.

The findings are summarized in Table III which shows that about 22% were unimmunized or unable to

TABLE III. DIPHTHERIA IMMUNIZATION AMONG 4,201 WHITE PERSONS UNDER 20 YEARS OF AGE

	Age groups					
	1 - 4	5 - 9	10 - 14	15 - 19	Total	%
Number of observations	253	1,781	1,606	561	4,201	100
Immunization uncertain or not done ..	64	319	361	187	931	22·16
Primary course	189	1,462	1,245	374	3,270	77·84
Primary course as %	74·70	82·09	77·52	66·67	77·84	
Booster ..	8	695	655	164	1,522	36·23
Booster as % ..	3·16	39·02	40·78	29·23	36·23	

give a convincing immunization history. On the whole, just over 77% had received a primary course, with a slightly increasing trend with falling age, except in the youngest group. This does not necessarily indicate a deterioration of preventive efforts, but is rather a reflection of the late administration of the primary course in some of the children.[2,4] Only about a third of all children, equivalent to about half of those who had had a primary immunization course, received a booster injection. There is little difference in the booster rate in children over 5 years of age, whereas the youngest age group, more in need of a booster, seldom received it early enough. The low booster rates are most unfortunate since the advantage gained by the primary course[7] is not followed up.

As pointed out previously, early administration of the prophylactic is of major importance in the prevention of diphtheria.[4] This aspect, in regard to the time for the administration of the primary course, has been examined and the results are presented in Table IV and in Fig. 2. It

TABLE IV. PRIMARY COURSE OF DIPHTHERIA PROPHYLACTIC IN WHITE CHILDREN UNDER 2 YEARS OF AGE

Age groups (years)	Total observation	Immunized under 2 years of age	
		Number	%
1 - 4	253	179	70·75
5 - 9	1,781	1,074	60·30
10 - 14	1,606	695	43·27
15 - 19	561	140	24·96

emerges that throughout the observation period there has been an increasing tendency towards earlier immunization, which closely resembles that observed in Johannesburg.[2,4] A comparison of Figs. 1 and 2 shows that the initial

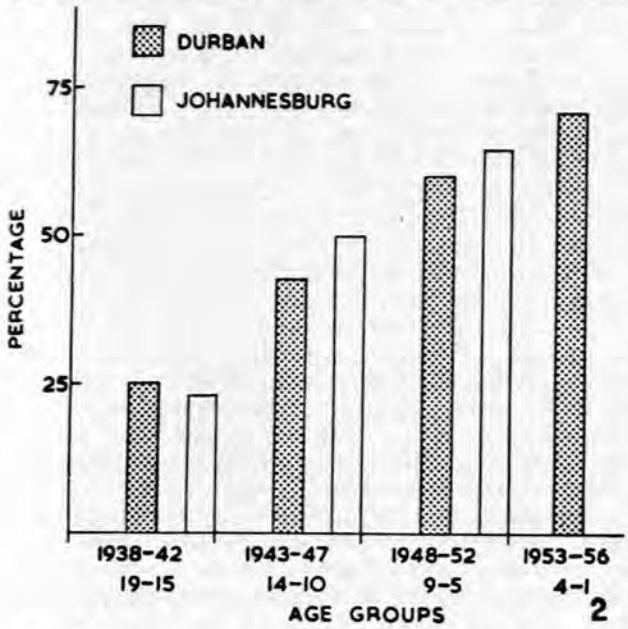

Fig. 2. Immunization in White children before 2 years of age in Durban and Johannesburg.

decline in the notification rates in the White group coincided with the immunization of approximately 50% of the children under 2 years of age. Although this should not be taken as proof of a causal relationship,[8] it is interesting to recall that similar observations have been made in previous investigations.[4]

It has been suggested that one of the reasons for the unsatisfactory immunization rates in Durban might be the influx of a considerable number of unimmunized children into the municipal area. By sorting out the questionnaires according to length of domicile in Durban, it was found that only 172 children had lived in the city for less than 1 year. A tabulation of these revealed that the age distribution corresponded closely to that of the total material, and that 58·50% had received a primary course, given in most cases before their arrival in Durban. Their inclusion, therefore, did not distort the general picture.

In conclusion it may be stated that the prevention of diphtheria in the White population of Durban, though not satisfactory, compares favourably with Johannesburg, both with regard to the extent and time of administration of the primary course and to booster injections.[2,4]

Distribution of Work

Prophylactic injections may be given by general practitioners and at the municipal clinics. From Table V it appears that White children receive slightly more prophylactic injections from the general practitioners than from the municipal authorities. The higher percentage given by general practitioners to those in the youngest age

TABLE V. IMMUNIZATION IN WHITE PERSONS BY GENERAL PRACTITIONER OR MUNICIPAL CLINIC

	Immunized			
	by general practitioner		*at municipal clinic*	
Age groups (years)	*Number*	*%*	*Number*	*%*
1 - 4 ..	123	69·10	55	30·90
5 - 9 ..	791	55·01	647	45·99
10 - 14 ..	636	51·33	603	48·67
15 - 19 ..	213	56·95	161	43·05
Total ..	1,763	54·60	1,466	45·40

group is hardly a sign of a new attitude towards immunization, but probably indicates that the general practitioner does the bulk of early prophylactic immunization and the municipal clinics most of the later. This could be the result of several factors. Firstly, the general practitioner has easier access to the child in its preschool years. Secondly, mothers, actively interested in the protection of their children, are often more inclined to use a private doctor. Thirdly, the gathering of children at school furnishes the municipal authorities with an excellent opportunity for mass immunization.

DISCUSSION

The findings presented have posed 2 major, though closely related, problems. In the first place, what is the cause of the increase in observed case mortality in recent years, and why does diphtheria appear to be more malignant in certain races? Secondly, how accurately do the notification rates reflect the incidence, and can an approximate estimate of the occurrence in the population be ascertained?

With regard to the first problem, a rising case mortality may be the result of one or more of the following factors: (1) enhanced pathogenicity of the infecting strains; (2) delayed treatment; (3) lower resistance of the patient; and (4) under-notification of the disease.

Corynebacterium diphtheriae

Notwithstanding the possibility of variations in pathogenicity of the same type, it is generally accepted that gravis types are more malignant than mitis types.[9,10] Although we have no records of the diphtheria types occurring in Durban, we have no reason to suspect that the gravis type is prevalent. In support of this, the still moderate case mortality among the White population, and the fact that the alteration in case mortality has been gradual, may be mentioned — observations compatible with predominant mitis infections.[9,10] Furthermore, periodical surveys into the types found in other parts of the country[11-13] have shown that about 90% of the recovered strains are of the mitis type and 4% of the gravis type, a distribution that was essentially the same in 1942[11] and 1956.[12] Lastly, the case mortality of diphtheria in Johannesburg,[2] where the mitis strain is prevalent, is of the same order as in Durban.

To explain the differences in racial case mortality, it would be irrational to assume that the races living in close geographical proximity and occupational contact would be exposed for any significant period of time to infections that differ distinctly in regard to distribution of types. Thus, it is improbable that the infecting type

of *C. diphtheriae* can explain either the apparently greater malignancy of diphtheria in the Asian and Bantu groups or the increased case mortality in recent years. It would, however, be desirable to check this hypothesis by systematic typing of recovered strains.

Late Treatment

The probability of fatal termination of diphtheria increases with delay in treatment.[14] In a predominantly mitis-infected group of White patients, a maximum case mortality of about 10% is reached on the 4th - 5th day of illness.[14] It is possible that a delay in treatment may have contributed both to the higher case mortality in the Asian and Bantu groups and to the general rise in recent years. The delay may be the result of a reluctance to seek medical assistance and/or a misinterpretation of early symptoms. Reluctance to seek medical aid is probably of greater significance in the non-White races[15] but, as a single factor, it is incapable of explaining case mortalities as high as 20%. In regard to misinterpretation of symptoms, it is commonly observed that, as a disease becomes less frequent, it presents greater diagnostic difficulties, particularly in its early stages. This may result in some delay in treatment which, in turn, will increase the case mortality. It is difficult to assess the contribution of this factor, but, while it is probably safe to assume that it is comparatively small and independent of race, it may well be that it will become an increasing factor as less and less clinical diphtheria is seen by students and practitioners.

Lower Resistance

To explain a high case mortality in terms of low resistance will require the consideration of agents of non-specific nature since diphtheria rarely terminates fatally in individuals with a demonstrable, though low, level of circulating antitoxin.[14,16,17] Such agents must interfere comparatively little with the susceptibility to diphtheria while they enhance the severity of already established infections. They may be sought either in environment or in racial characteristics. Under the former heading we may consider climate, malnutrition, avitaminosis, debility, predisposing diseases, etc. However, it is difficult to discover where such a deterioration could have occurred in recent years that would have caused an increased case mortality, particularly in the White population. Although none of the factors mentioned seems to fulfil the criteria for acceptance, the proposition cannot be entirely dismissed. Thus, it would be of interest to follow the case prognosis in the malnourished patients who are predominantly of Bantu origin.

Since it seems equally difficult to ascribe differences in racial case mortality to dissimilarities in environment, it is reasonable to consider the possibility of racial differences in the ability to overcome the already established infection, i.e. a lower resistance in the Bantu. But such a view would clash with Murray's assumption,[18] that the Bantu have a racial resistance to diphtheria. He suggested that this racial immunity is based on a greater ability of the Bantu to form antitoxin, which may be genetically or environmentally determined. From this theory it follows that the Bantu should be in a better position to overcome the infection and consequently have a better case prognosis than White patients — the reverse of what we actually found. It is quite possible that neither view is correct, that is to say, the Bantu are not particularly susceptible to the established infection, but the other factors must be responsible for the high case mortality. Nor are the Bantu particularly resistant; a view that was based on the controversial assumption that notification rates are accurate measures of incidence.

The same arguments apply to the Asian group; considering their high case mortality it would appear that they had a low resistance to diphtheria, but an inquiry into the antitoxin levels among unimmunized Asian children in Natal revealed that an unexpectedly high proportion possessed protective quantities of antibodies.[19]

Notifications

The calculated case mortality depends on the accuracy of notifications. As a rule, the more severe the disease the greater the need for medical attention and the easier the diagnosis. This implies that the reliability of notifications augments with increasing gravity and it may reasonably be assumed that in a community like Durban very few deaths from diphtheria will remain unreported. It also follows that the milder the disease the easier it escapes notification. To this may be added that as the rôle of a disease decreases so does the awareness of its existence, thus leading to an undernotification of milder cases with an inverse effect on the observed case mortality. Considering the notification rates in the White population in Durban, it is apparent that they have fallen considerably during the observation period and may have caused a disproportionate reduction in the reporting of cases. This is probably the most important single factor in the explanation of the increased case mortality in the White, Bantu and Asian groups, while the Coloured group is so small that no inference should be drawn from the figures concerning its members.

The persistently higher case mortality which has been observed in certain ethnic groups, for example, in the Bantu, may be related partly to the inadequate medical facilities offered them and partly to their reluctance to seek medical attention at an early stage of the disease. In this connection we are concerned about the possible retarding effect which the introduction in certain areas of a clinic fee may have on the treatment of diphtheria. The possibility exists that a higher proportion of patients may die and that milder, but still detectable, cases may add to the number of foci from which the infection may spread to other sections of the community.

Estimation of the Incidence

This problem is related to the reliability of the population figures and the accuracy of notifications. The basic population figures were estimated by periodical census, which were considered reliable for the White, but somewhat defective for the non-White population. On these figures the population groups were estimated in the years between the census. Admittedly this assessment carries a certain error, which probably does not exceed 10% and is thus of minor importance in the calculation of rates.

Inaccuracies in notifications may be the result of either

erroneous reporting or the existence of unobserved cases. According to McComb[20] it is likely that failure to notify far outweighs erroneous reporting and thus results in an under-estimation of incidence. This agrees with our argument above. The figures given do not permit an accurate assessment of the incidence rate, the order of which may be estimated from a study of case-mortality rates.

In Northern Europe, between 1930 and 1935, the case mortality from mitis infections was 2 - 3%,[9] which was identical to the findings in Copenhagen a few years later.[10] In untreated cases of mitis infections in White patients in South Africa, we have observed a maximum case mortality of 10%.[14] Thus, assuming that practically all diphtheria infections in the White population of Durban were caused by the mitis type and that the delay in treatment had remained unchanged, we would expect a case mortality of about 3%. In the non-White population, the assumed delay in treatment will tend to increase the case mortality, but not to figures exceeding 10%, provided the infection is of the mitis type.[10] Since it is generally agreed that a proportion of non-White patients are treated timeously, it would probably be fair to assume that the case mortality would be about 6%. This is twice the rate in White patients and allows for a considerable, but not excessive, delay in treatment. On this basis we have attempted to calculate the incidence per 100,000 population per year in specified periods (Table VI). Under these circumstances, it appears that diphtheria is particularly

TABLE VI. ESTIMATION OF INCIDENCE PER 100,000 POPULATION PER YEAR, BASED ON ASSESSED CASE-MORTALITY RATES

	Period	*White*	*Asian*	*Coloured*	*Bantu*
Assessed case-mortality rate	1940 - 58	3%	6%	6%	6%
Estimated incidence	1940 - 44	169·32	24·84	125·03	143·53
	1945 - 49	100·32	79·68	191·54	163·70
	1950 - 54	50·00	104·35	230·88	237·04
	1955 - 58	70·99	103·52	66·18	134·86

prevalent in the Bantu and Asian groups and that it is far more common than the notification rates show (Table II). Contrary to observations, the main focus seems not to be in the Coloured but in the Bantu, among whom only 1 out of 3 cases is reported. If this reasoning is correct, it would be rewarding to encourage the population, particularly the non-White groups, to have children with sore throats and allied disorders medically examined. A systematic clinical and bacteriological investigation should detect a diphtheritic aetiology in many cases that otherwise would have been missed.

Prophylactic Immunization

In planning an immunization campaign, it is essential to realize the importance of immunizing a very high proportion of young susceptible individuals, preferably when the children are about 4 - 6 months old.[1,4] In other countries it has been possible to immunize 90 - 100% of the children,[6,21,22] but spectacular results have also been achieved in South Africa. In Johannesburg, for example, all children born since 1950 in the richer districts were immunized before the age of 2 years.[2] This reflects the parents' positive attitude to preventive measures, together with effective administration of the prophylactic. Immunization rates in other income groups were of a lower order[2] and, in some cases, could not be expected to have much influence on the morbidity.[1,4]

In Durban, in recent years, the tendency among White persons has been to immunize a higher proportion of their children before the age of 2 years, but the pace of progress has slowed down considerably (Table IV). With the birth of approximately 3,200 White children per year,[3] and a 70% immunization rate of children at the age of 2 years, 960 will reach this age annually without having been protected against diphtheria. This cannot be ascribed to lack of immunizing facilities but rather to the irresponsibility of the parents. Consequently, the campaign should be intensified, but in doing so it should be remembered that the need for immunization in the poorer White classes is likely to surpass substantially the average deficit of 30%[2,4] and that the propaganda should reach families with infants.[1,4,14] Should the response be unsatisfactory, it might be relevant to consider the introduction of a card system, as suggested in a previous communication.[2]

Unfortunately we are ignorant of the immunization rates among the non-White groups. But from the observed morbidity and mortality figures (Table II), as well as from the estimated incidence (Table VI), it is clear that they are in urgent need of protection against diphtheria. In agreement with the findings in Johannesburg,[2] it must be expected that their immunization rates are lower than in the White group and that the bulk of the work will fall on the municipal health authorities. The propaganda among the non-White population must be adjusted to their educational level and their background of customs, folk-lore and idiom. Although loudspeaker talks, group talks and leaflets have been extensively used, it is felt that some striking form of visual aid must be used to achieve effective propaganda. A card system[2] would probably not be of great value because of the low educational standard of most members of the group. If the campaign succeeded, it would be of the greatest administrative value to immunize according to a system based on regular availability of service and the age of the child. Under such circumstances it would be possible to dispense with individual immunization records and thus minimize bookkeeping, avoid several interpreters and increase the efficiency of the team. In this way the cost of immunization could be kept low without interfering with the effectiveness of the work.

SUMMARY

From the notification rates observed, it appears that a focus of diphtheria has existed in Durban, compared with the Union in general. Since 1944 the rates have diminished gradually so that, in 1958, the overall notification rate was similar to that of the Union and comparable, race to race. The findings have been discussed and in view of the rise in observed case mortality, which was excessive in certain groups, the conclusion was reached that the incidence of diphtheria has fallen less sharply than indicated by the notification rates. In fact, it is likely that, in the Bantu, only 1 out of 3 cases has been reported. This conclusion is based on the assumption that mitis infections

predominate and that racial and environmental factors are of no importance in the case prognosis. It is recommended that strains of *C. diphtheriae* should be typed and the course of the disease in malnourished patients studied. If diphtheria is as prevalent as suggested by the present study, it would be profitable to extend the clinical and bacteriological investigations of conditions which may be the less obvious manifestations of the disease.

An examination of immunization rates in the White population showed that there has been an increasing tendency towards early administration of the prophylactic. In 1955 - 1958 about 70% of the children were immunized at the age of 2 years. The failure to protect the remaining 30% seems to be due to indifference of parents; various suggestions have been outlined in this connection.

The need for immunization among the non-White population is believed to be even greater. In these groups, continuous immunization presents special difficulties, partly because of their lower educational level and partly because most of the work will fall on the municipal health authorities. However, if the cooperation of the people can be ensured it is possible to devise rational and fairly inexpensive methods for the immunization.

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REFERENCES

1. Bokkenheuser, V. and Heymann, C. S. (1954): S. Afr. Med. J., **28**, 685.
2. Bokkenheuser, V. and Smith, A. H. (1960): *Ibid.*, **34**, 928.
3. City Medical Officer of Health, Durban (1950-1958): Annual Reports.
4. Bokkenheuser, V. (1955): S. Afr. Med. J., **29**, 1249.
5. *Idem*: Unpublished data.
6. *Idem*: S. Afr. J. Med. Sci. (in press).
7. Scheibel, I., Tulinius, S., Rasch, G., Bojlen, K. and Petersen, C. B. (1948): Acta path. microbiol. scand., **25**, 319.
8. Madsen, Th. and Madsen, S. (1956): Dan. med. Bull., **3**, 112.
9. Cooper, K. E., Happold, F. C., McLeod, J. W. and Woodcock, H. E. de C. (1936): Proc. Roy. Soc. Med., **29**, 1029.
10. Annual Report of the Commissioner of Health (1952): *State of Health in Copenhagen*. Copenhagen: Public Health Department.
11. Murray, J. F. (1942): S. Afr. Med. J., **11**, 247.
12. Bokkenheuser, V., von Haebler, T. and Jackson, A. L. (1956): Med. Proc., **2**, 484.
13. Emmerson, N. (1941): S. Afr. J. Med. Sci., **6**, 51.
14. Bokkenheuser, V. (1955): S. Afr. Med. J., **29**, 461.
15. *Idem* (1959): Leech, **24**, 167.
16. Hartley, P. *et al.* (1950): Special Rep. Ser. Med. Res. Coun. (London), no. 272.
17. Ammundsen, E. *et al.* (1948): Acta med. scand., **129**, 415.
18. Murray, J. F. (1943): J. Hyg. (Camb.), **43**, 159.
19. Mason, J. H., Robinson, M. and English, G. D. (1957): S. Afr. Med. J., **31**, 644.
20. McComb, J. A. (1953): New Engl. J. Med., **249**, 120.
21. Noergaard, A. (1959): Dan. med. Bull., **6**, 94.
22. Annual Report of the Commissioner of Health (1958): *State of Health in Copenhagen*. Copenhagen: Public Health Department.