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Serological studies on infections by respiratory viruses of the inhabitants of Tristan da Cunha

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The volcanic island of Tristan da Cunha, in the South Atlantic, has been inhabited continuously since 1816. It is a barren place remote from seaports and regular shipping routes and is infrequently visited (see Samuels, 1963). In 1961 the volcano became active and the island was therefore evacuated and the 264 inhabitants were brought by ship directly to England with a brief stop at Cape Town on the way. Their origins and their state of health on arrival here have been described elsewhere (Samuels, 1963; Lewis, 1963). They lived for three months in wartime barracks in Surrey and then they were accommodated by families in separate well-built houses in Calshot, Hants (Black, Thacker, Lewis & Thould, 1963).

While on the island some adults had an influenza-like illness in 1950 and there was a severe outbreak of influenza in 1954. After a ship had called there was sometimes a wave of colds (Woolley, 1963). It was known that in 1955 the islanders of all ages had almost no antibodies against poliovirus types 1 and 2, although they had antibodies against type 3. They were therefore given live poliovirus vaccine in 1961 (Gear, personal communication). There had been only one recorded epidemic of measles in which both children and adults were affected. Chicken pox-zoster and infectious hepatitis had also occurred in recent years (Taylor-Robinson & Tyrrell, 1963). It was, nevertheless, thought that these islanders had been to a large extent isolated from contact with respiratory and other viruses and that they might therefore suffer excessively from respiratory diseases as soon as they reached the outside world; this was supported by the fact that although they stopped for only a few days in Cape Town most of them had colds by the time they arrived in Britain.

A few sera taken before the evacuation had been studied previously and had been found to contain antibodies against parainfluenza virus, respiratory syncytial virus and rhinoviruses (Taylor-Robinson & Tyrrell, 1963; J. E. Doggett, personal communication); as the sera lacked antibodies against Asian influenza virus the islanders were given influenza vaccine after they arrived. They continued to suffer from frequent colds and respiratory illnesses during their first months in England and three old people died of pneumonia, the lesions of which on pathological examination resembled virus pneumonia more than a bacterial disease.

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It was not possible to do thorough virus isolation studies, but samples of the sera of many islanders were available and these are listed below. We used these sera to determine what the response to influenza vaccination had been and, as far as possible, what respiratory viruses had infected the islanders after they left Cape Town and during their stay in Britain. The results of these studies are reported below, but as individual records of the illnesses from which the islanders suffered in Britain were not available it has been impossible to correlate individual serological results with individual respiratory tract illnesses.

The main recorded events of the islander's lives which seem to bear on this paper are as follows:

1954	Epidemic of clinical influenza.	
1961	10 October	Volcano erupted. Islanders taken by liner to Cape Town.
	17 October	Islanders reached Cape Town, and visited the City and were bled.
	21 October	Islanders left Cape Town.
	3 November	Reached England and were taken to Pendell Camp.
	21 December	Received influenza vaccine.
1962	6 January	Bled for the first time in England.
	23 January	Moved from barracks to single family, permanent houses at Calshot.
1963	30 April and 10 May	Bled for the second time in England.

MATERIALS AND METHODS

Sera

There were no sera from islanders under 8 years of age, but half or more of all the other age groups were available. The sera were all separated aseptically and stored frozen. The sera were usually diluted 1/5 in cholera filtrate (Phillips) and incubated overnight at 37° and for 30 min. at 56°, and stored at −20° (Tyrrell & Horsfall, 1952). Some sera were diluted in saline and stored at −20° C. There was no apparent loss of antibody titre after repeated freezing and thawing, except on one occasion with sera which had been diluted in saline. Comparisons of the titres of successive sera from each individual were always made on sera which had been diluted at the same time and frozen and thawed in the same way, and control positive human sera were always included in each test and showed no significant changes in the sensitivity of the tests.

Viruses

The following strains of influenza virus were used:

Influenza A Swine—Shope strain.
Influenza A0—MEL.
Influenza A1—Kunz; A/Eng/1/51 and A/Eng/1/53.
Influenza A2—A/Pakistan/1/57.
Influenza B—Lee 1940; B/Eng/10/54; B/Eng/939/59.

All these viruses were grown in the allantoic cavity of embryonated eggs.

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Influenza C—strain 1233 was usually used as amniotic fluid.

Parainfluenza virus type 1—Cop 222 or C39 were used; the former was grown in monkey kidney cells and the latter in the allantoic cavity of chick embryos.

Parainfluenza virus type 2—a pool of egg-adapted virus supplied by Dr De Meio, National Drug Company, Philadelphia.

Parainfluenza virus type 3—bovine strain 33 propagated in calf kidney cells.

Reoviruses—type 1 and type 2, prototype strains ECHO 10 and Sue.

Echovirus 11—U virus strain of Philipson; this and the reoviruses were grown in rhesus-monkey cells.

Coxsackievirus A21—a strain isolated in England and usually propagated in human embryo-kidney cells.

All viruses were stored frozen at $-70°$ except for some pools of reovirus which were stored at $-20°$ C.

Titrations

We had barely 0·5 ml. of most of the sera and we wished to perform numerous titrations. Haemagglutination-inhibition tests were therefore performed by the micromethod of Takátsy (Sever, 1962), using 0·025 ml. volumes. Four haemagglutinating (HA) units of virus were allowed to react for 1 hr. at room temperature with serial dilutions of serum before adding 0·025 ml. of 1 % group 0 human red cells. Chicken cells, 0·5 %, were used with parainfluenza type 2. Complete inhibition of haemagglutination was taken as the end-point. The diluent was isotonic sodium chloride buffered at pH 7·1 with 0·01 M sodium phosphate buffer.

Table 1. *Comparison of the efficiency of haemagglutination inhibition and neutralization tests on paired sera from eleven islanders in detecting rising titres of antibody against three influenza A viruses*

	Results of test by		
Test virus	Serum	Neutralization	Haemagglutination-inhibition
MEL A0	57	< 5/10	< 10/40
	62	< 5/80	< 10/40
	191	10/40	< 10/160
	218	< 5/20	< 10/80
A Swine	30	< 5/> 80	< 10/40
	49	< 5/> 80	< 10/160
	131	< 5/> 80	< 10/120
	140	10/80	10/60
Kunz A1 47	218	10/320	5/120
	31	5/60	10/40
	30	< 5/> 320	10/160

It was found that the micromethod gave very reproducible results, and the results agreed well with those of neutralization tests with influenza virus (Table 1). In spite of economy in the use of the sera many became exhausted during the

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course of the investigation and therefore it was not possible to test all specimens with all viruses. At the end of the experiments reported here attempts were made to perform complement-fixation tests, but too many of the remaining sera were anticomplementary for useful results to be obtained.

RESULTS

Influenza viruses

Soon after the epidemics of influenza in 1954, antibodies against influenza A1 and B had been found in the sera of islanders (M. A. Westwood & J. H. S. Gear, personal communication quoted Taylor-Robinson & Tyrrell, 1963). However,

Table 2. *Influenza antibody status on leaving Tristan da Cunha*

		Percentage of sera collected in Cape Town which contained antibody against indicated serotype								
Sera collected	No. of sera tested	A swine	A0 '33	A1 '47	A1 '51	A1 '53	A2 '57	B '40	B '42	B '59
October 1961	103–129	0	0	0	25	9	0	0	2	0

Inhibiting haemagglutination at the initial dilution of 1/10 or greater.

Table 3. *Initial response to influenza vaccine containing A2 and B' 59 strain*

		Percentage of islanders with rising titres against indicated virus							
Sera collected	No. of pairs tested*	A swine	A0 '33	A1 '47	A1 '51	A1 '53	A2 '57	B '40	B '59
October 1961 and January 1962	132–138	43	52	80	95	92	83	17	85

* According to records nine Islanders who were supposed to have received vaccine did not get it. However, as one of these had an antibody rise against Influenza A2 all the serum pairs have been included in this analysis.

by October 1961 only low titres could be detected (Table 2) in about a quarter of the sera collected in Cape Town. In December 1961 the islanders received at 1 week intervals two injections of 1 ml. of a formalin-inactivated vaccine containing 7500 HA units of the strain of A2/Singapore/1/59 and 5000 units of B/England/59/59 suspended in saline (manufactured by Pfizer Ltd., Sandwich, Kent). The islanders were bled thereafter in December 1961 and January 1962, and most of them showed antibody against viruses of the type present in the vaccine. However, in addition, most of them developed antibodies against viruses of the A1 types which had been prevalent at the time of the epidemics on the island (Table 3). Furthermore, many developed antibodies against the A Swine, A0 and B Lee viruses which had been prevalent before the recorded outbreaks of influenza.

There was no evidence that Influenza A or B were active in the south of England at that time and attempts to isolate influenza virus from a number of islanders

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suffering from influenza-like illnesses were unsuccessful (G. Cook, personal communication).

It was possible that the rises in the titre of antibody against 'old' influenza strains were due to the recall of antibody which had been induced by infection during unrecorded or unrecognized epidemics on the island before 1950. A previous serological survey (see Taylor-Robinson & Tyrrell, 1963) had shown that there were antibodies to 'earlier' serotypes in sera collected in 1955, but only in subjects

Table 4. *Changes in titres of antibody against influenza virus in 76 pairs of sera collected after vaccination and before departure from Britain*

		Percentage of subjects with indicated finding					
Sera collected		A swine	A0 '33	A1 '47	A2 '57	B '40	B '59
January 1962	Antibody present	17	61	89	83	40	85
May 1963	Antibody present	3	3	72	100	83	99
	Rises*	1	0	0	51	13	30
	Falls*	7	26	57	9	3	0

* Rising or falling titres of fourfold or greater.

Table 5. *Relationship between antibody titres after vaccination and further rises in titre against influenza A and B viruses presumably due to natural infection*

Virus used in test	Antibody titre after vaccination	No. of islanders	Percentage of islanders with rising titres against
Influenza B '59	< 10	11	91
	10	6	83
	20	12	67
	40	40	8
	80 or 160	6	0
Influenza A2 '57	< 10	14	93
	10	2	(100)
	20	11	100
	40	23	17
	80 or 160	26	0

over 16 years of age at that time, and it was thought then that there might have been an epidemic of influenza A in 1934 or of B in 1938. If that were so it was expected that antibody following vaccination in 1961 would be recalled only in those who were alive at the time of prevalence of the earlier serotypes, i.e. those over 15 years in the case of A viruses and probably over 30 years in the case of A Swine viruses. The antibody titres were therefore arranged according to the ages of the donors, and the results are shown in Fig. 1. These graphs demonstrate clearly that at all ages the antibody response to the A1 strain A/Eng/1/51 was as great as that to the A2 serotype given in the vaccine (Fig. 1*a*, *b*). No specimens were obtained from children under eight who might not have been sensitized to the

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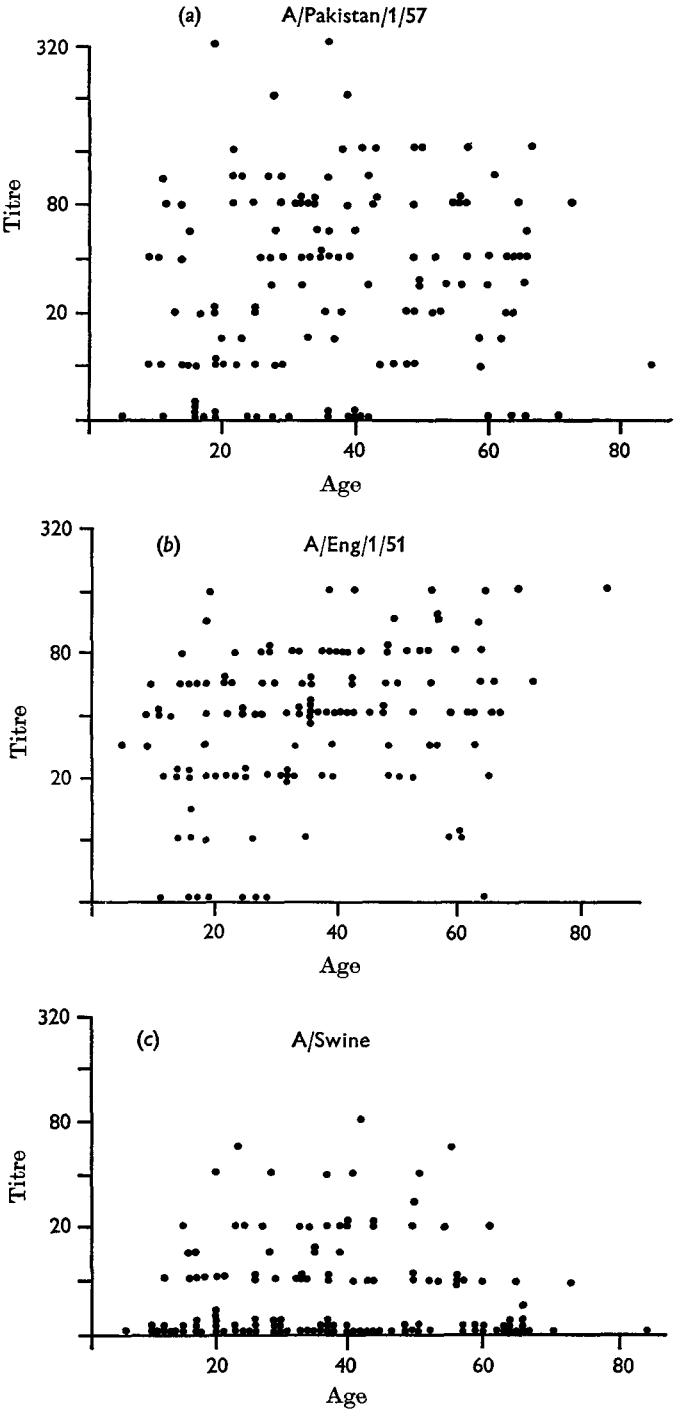

Fig. 1. Haemagglutination-inhibiting antibody titres against influenza viruses in the sera of islanders of various ages bled in January 1962 after being vaccinated with influenza A2/Sing/1/57 and influenza B/Eng/59/59. The distribution of antibody titres against para-influenza viruses was rather similar to that of antibodies against A/Eng/1/51.

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A strain, but it is quite clear that the antibodies to the A Swine and A strains were found in subjects of all ages, although the titre and the frequency of antibody were less against the 'older' strain A 0, and least against the 'oldest' strain, A Swine (Fig. 1 c). The best explanation of these findings is that the islanders had been sensitized to a wide range of antigens and produced a fairly 'broad' antibody response. The fact that they reacted in the same way irrespective of age suggests that they had all had the same antigenic experience in the past; this is consistent both with the reports that epidemic influenza appeared on the island only in recent years and that antibodies were found in most sera collected in 1955.

Further sera were collected in 1963 and where possible these were compared with the sera collected immediately after vaccination. The results are summarized in Table 4, which shows that while antibody against 'old' strains of influenza A declined, further rises in antibody titres against influenza A 2 and B occurred. These were observed only in subjects with low antibody titres after vaccination (Table 5), and as both viruses were known to be prevalent in Britain between 1961 and 1963, it is assumed that they are due to natural infections with influenza A 2 and B viruses. Antibody to a titre of about 1/40 was apparently able to prevent infection with these viruses. Antibody titres against the A 1 1947, A 0 and A Swine viruses, on the other hand, declined and there was no evidence that the antibodies against the A 1 1947 or earlier strains were boosted by natural infections with the recent A 2 strains, although they had been boosted by vaccination. There were, however, some increases in titre against influenza B strains, possibly because the antigens are more closely related to current antigen than those of the A 2 serotypes and influenza A 1 strains. In the end, virtually all the islanders acquired antibody against the current serotypes of influenza A and B.

Table 6. *Age distribution of* 76 *subjects tested for rising titres against parainfluenza* 1 *and* 3 *viruses*

Age (years)	No. of subjects	Age (years)	No. of subjects
0–5	1	31–40	19
6–10	3	41–50	12
11–15	6	51–60	6
16–20	7	61–70	9
21–30	11	Over 70	2

Antibody responses to other respiratory viruses

The sera were next titrated against other haemagglutinating viruses which are certainly or possibly associated with upper respiratory tract disease. The age distribution of the donors of the paired sera tested appears in Table 6 because of the surprising finding that most adults were apparently infected with parainfluenza 3 virus, which usually affects infants and children in this country. The results of the serological tests are shown in Table 7, together with some results on unpaired sera. In many tests it was possible to titrate paired sera from about one-third of the islanders, but owing to shortage of sera or antigens the numbers

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Table 7. *Presence of H.I. antibodies against other respiratory viruses and changes in titre*

		Percentage of subjects showing indicated findings								
		Parainfluenza							Reovirus	
Sera collected		1	2	3	Mumps	Influenza C	Coxsackie A 21	Echovirus 11	1	2
October 1961	Antibody present	23 (128)	50 (12)	48 (128)	—	69 (68)	13 (86)	—	—	—
January 1962	Antibody present	80 (76)	100 (20)	99 (76)	85 (35)	91 (75)	14 (76)	12 (137)	0 (76)	0 (76)
May 1963	Antibody present	72 (76)	100 (15)	100 (76)	83 (36)	54 (72)	25 (76)	—	0 (76)	3 (76)
First period (October 1961–January 1962)	Rises*	83 (80)	50 (12)	95 (80)	—	10 (68)	7 (86)	1 (137)	—	—
Second period (January 1961–May 1963)	Rises	1 (76)	20 (15)	1 (76)	3 (35)	0 (71)	5 (76)	—	0 (76)	0 (76)
Second period	Falls	72	20	26	0	18	3	—	0	0

Number of sera or serum pairs shown in parentheses.

* Fourfold or greater rises or falls.

were reduced in some of the later tests. Nevertheless, certain quite striking facts emerged. For instance, in the first period of study, almost all the islanders showed antibody rises against parainfluenza 3, many against parainfluenza 1 and some against type 2. During the second period there were many falls in antibody against type 3 and both rises and falls against type 2. There were also antibody rises against influenza C in the first period and some falls in the second. Mumps antibody was detected although the disease had not been reported on the Island (Samuels, 1963). Some rising titres were also detected against coxsackievirus A 21 in both periods of study. On the other hand, antibodies against the reoviruses were infrequent and no rising titres were detected. Since very different frequencies of antibody rises were noted using different viruses as antigens it is unlikely that the results were due to loss of antibody during the storage of the sera collected in Cape Town; these sera were in any case handled with great care and stored almost as long as the next sera by the time some of the tests were made.

We wondered if these antibody results were not specific, but it has been shown that the HI titres as measured in this laboratory give results which agree well with those of specific homologous neutralizing antibody to parainfluenza 1, 2 and 3 (Taylor-Robinson, 1965; Taylor-Robinson & Bynoe, 1963), reoviruses (Brown & Taylor-Robinson, 1966), echovirus 11 (Buckland, Bynoe, Philipson & Tyrrell, 1959) and coxsackievirus A 21 (Buckland, Bynoe & Tyrrell, 1965).

Table 8. *Relationship between antibody titre in first serum of a pair and the presence of a rising titre*

Virus used in test	Antibody titre of first specimen	No. of sera	Percentage of paired sera showing rising titre
Parainfluenza 2	< 10	6	100
	10	7	63
	20	6	17
	40	8	0
Influenza C	< 10	29	24
	10	40	18
	20	29	3
	40	2	0
Coxsackie A 21	< 10	67	15
	10	8	0
	20	4	0
	40	3	0

The apparent correlations between low antibody titre and the appearance of a rise are statistically significant.

It was, of course, possible that some of the antibody responses were due to cross-reactions between the antigens; for instance, it is likely that the antibody responses to parainfluenza 1 were due to infection with the type 3 virus or vice versa. However, for both the periods of study it was found that, as in the case of the influenza antibodies, rising titres against parainfluenza 2, influenza C and cox-

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sackievirus A21 occurred almost entirely in persons without detectable antibody or with only low titres (Table 8); there is other evidence that antibody rises against coxsackievirus A21 are not induced by several other biologically related picornaviruses (Doggett, Buckland & Tyrrell, 1964). As the proportion of antibody responses to the other viruses, such as parainfluenza 3 or reoviruses, was either almost 100% or nil, it was not possible in these cases to detect a correlation between antibody titre and the occurrence of a subsequent rise. We nevertheless believe that the rises observed were due to infection with viruses closely related antigenically to those used in the tests.

In populous areas such as Britain and the U.S.A. antibody rises against parainfluenza viruses or isolations of these agents are only common among infants and young children with respiratory disease (Chanock & Parrott, 1965) and the titres of normal adults persist at a high level (Taylor-Robinson, 1965); it is therefore remarkable that in this investigation rising titres of antibody were found in subjects of all ages. The antibody distribution resembled the uniform response of islanders of all ages to influenza vaccine which is seen in Fig. 1*a* and *b*. In one respect, however, the pattern of antibody responses did resemble that seen in populous areas. It can be seen from Table 7 that infections seemed to occur earlier with parainfluenza virus types 3 and 1 and later with type 2, and this is exactly the pattern seen in children in the first few years of life in Britain (Stark, Heath & Peto, 1964). It also looks as though coxsackievirus A21 spread inefficiently and slowly even under barrack conditions and this is consistent with what is known of its behaviour in civilians and servicemen in Britain (McDonald, Miller, Zuckerman & Pereira, 1962; Pereira & Pereira, 1959). It might therefore be said that, like infants who have lost their maternal antibody, these islanders acted as a sentinel population; they picked up those viruses which were circulating in the area, and picked up most frequently those which are known to be readily transmitted among children.

Later during their stay the antibody titres of the islanders against parainfluenza and influenza C viruses declined (Table 7) and few further rises were detected, which suggests that these viruses did not attack the community again.

Relation between blood groups and virus infection

It was shown by McDonald & Zuckerman (1962) that in the R.A.F. relatively more men with blood group O than with group A were admitted to hospital with serologically recognized influenza A2 infections. However, they had no means of determining whether subjects of known antibody status were more likely to become infected with an influenza virus if they belonged to blood group O, or whether the antibody response on which they diagnosed the disease was more likely to occur in subjects of group A than of group O. As the Tristan islanders were of a different racial origin and as we knew their antibody status while in Britain, we wished to correlate their antibody responses with their blood groups in order to extend the observations of McDonald & Zuckerman. The blood groups of the islanders were kindly supplied to us by Dr A. E. Mourant and our results were analysed in order to see whether there was any correlation between the blood

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groups and the presence of antibody on arrival in Britain or the acquisition of antibody afterwards.

As shown in Table 9, on arrival in Britain more of the islanders who had antibody against influenza A1/51 belonged to group A than to group O and the difference was statistically significant. This finding might have been due to subjects of group A being more susceptible to infection with influenza A1 virus when the virus was epidemic on the island. The possibility was also considered that the differences might be due to the production of differing amounts of antibody to

Table 9. *Frequency of antibodies against influenza* A/Eng/1/51 *in sera collected on arriving in Cape Town from persons of various blood groups*

	No. of persons in blood group				
Antibody	A	O	B	AB	All groups
Present	19	1	2	2	24
Absent	23	27	3	2	55
Total	42	28	5	4	79

Table 10. *Frequency of rising titres of antibody in subjects with antibody titres of* 20 *or less*

	Number of pairs of sera showing antibody rises—classified by blood group				
Virus used	A	O	B	AB	All groups
Influenza B/Eng/59	*13/17	6/9	2/2	2/2	23/30
Influenza C	4/12	3/14	0/1	0/2	7/29
Coxsackie A21	5/30	3/30	1/5	1/1	10/66
Totals	22/59	12/53	3/8	3/5	40/125
	37%	23%			32%

* Numerator = number of pairs in which a rising titre was observed. Denominator = number of pairs tested.

the same infection; however, further analysis showed that when exposed to an identical 'new' antigenic stimulus, namely vaccination with influenza A2, the frequency and height of the antibody response was the same in subjects of both blood groups to all the influenza A and B strains. An attempt was therefore made to detect the postulated difference in susceptibility to infection by studying a small number of subjects who were without protective levels of antibody at either the first or second bleeding. It was shown (Table 10) that a relatively higher proportion of those in Group A than those in group O developed antibody, presumably due to infection with one of the three viruses used in the test. The difference was almost significant at the level $P = 0{\cdot}05$. Antibody against influenza C was not apparently related to blood group and the titre of antibody against influenza A and B was not apparently related to the presence of M and N blood groups. It seemed that the ABO blood group was related in some way to resistance to infection, but nevertheless the presence of antibody was a much more important factor.

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DISCUSSION

Recent serological surveys from this laboratory have shown that a high proportion of sera collected from normal subjects living in cities or in remote and isolated villages in many parts of the world, contain antibodies against the common respiratory viruses, such as influenza, parainfluenza, respiratory syncytial virus, reoviruses and rhinoviruses (Taylor-Robinson, 1965; Doggett, 1965; Brown & Taylor-Robinson, 1966). This implies that all these viruses are able to spread in human communities in very varied conditions of climate, housing and standard of living. The extreme degree of physical isolation of Tristan da Cunha was, however, apparently sufficient to reduce detectably the degree to which the inhabitants were exposed to viruses and immunized against them.

The antibody responses of the group to influenza vaccination were remarkable, but not unique for islanders have been found in the Pacific who had apparently never been exposed to infection with influenza viruses (Brown, Gajdusek & Morris, 1966), but it must still be very rare to find a whole community which has apparently been exposed to only two epidemics of influenza virus and to administer a uniform antigenic stimulus to all of them. The Eskimos studied by Reinhard & Gerloff (1960) and Reinhard (1962) were probably less isolated than the inhabitants of Tristan da Cunha. The Tristan islanders of all ages apparently responded mainly to the viruses prevalent when the epidemics occurred on the island and this can be interpreted as a striking natural experiment in confirmation of the ideas of Davenport and his colleagues (Davenport & Hennessey, 1957). They believe that the broadness and altered specificity of the response of older subjects to vaccination with monospecific vaccines is due to their 'experience' of more and different influenza antigens and not to any hypothetical ageing process. On the other hand, it should be noted that although the islanders were apparently exposed to only two serotypes of influenza A virus there were many antibody responses to viruses only distantly related to these. It may be significant that these antibodies declined rather rapidly and did not seem to be recalled by natural infection. It is likely therefore that they were not really comparable with those found in the sera of old subjects who have not been vaccinated and carry antibody against viruses to which they were probably exposed only in early life. Experiments in rabbits show that the dosage of virus given to an animal already sensitized to a distantly related virus may decide whether the animal produces more of an older type of antibody or gives a primary type response against the 'new' antigen (Fazekas de St Groth & Webster, 1966). In the case of the islanders it is, however, theoretically possible that after a long period without reinforcement their immunological 'memory' might fade. If it had been possible to apply the technique of Drescher (Drescher, Hennessey & Davenport, 1962) or to perform adsorption experiments, one might have demonstrated whether the antibodies were directed primarily against the old viruses or the newer ones.

There is little need to comment further on the results with the other respiratory viruses. The remains of the sera were in too poor condition to do successful complement-fixation tests otherwise we might have tried to detect infection with

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adenovirus or R.S. virus. It is likely that the influenza vaccine gave some useful protection and if an effective vaccine against parainfluenza viruses had been available the islanders might have been protected against these viruses. The data suggest that, with the technique used, antibody to a titre of 1/40 or more protected almost all subjects against influenza infections, and this titre apparently protected volunteers against infection with influenza A 2 and B viruses (Bell *et al.* 1957; Buckland, Bynoe & Tyrrell, unpublished); a titre of 1/20 might have protected them against parainfluenza 2 infection (Table 8). The results draw attention again to the mysteries of the clinical significance, if any, of antibodies against influenza C virus, an agent which is almost never isolated in Britain, although it seems to be associated with respiratory disease. Antibodies against reoviruses are found in sera of British residents, but these viruses are not known to be associated with disease here, they are rarely isolated and were not apparently transmitted to the islanders.

We were rather surprised by the results of our analysis of the relation between infection and blood groups which seem to show that subjects with blood group A are more likely to be infected with influenza and some other viruses than those of group O. This is the opposite of what we expected on the basis of the work of McDonald & Zuckerman (1962). There seem to be two possible explanations. One is that there may be two opposing effects of the blood groups—the possession of group A for example may render a subject both more likely to be infected by influenza A 2, and less likely to be made ill by it. This is difficult to believe. The other alternative is that this is not an effect of blood groups at all, but of some other factor which, in the case of natives of Britain, is linked with blood groups O and A in one way, and in the islanders in the opposite way. This resistance appeared to be effective against a number of viruses in our study although only the combined data approached statistical significance. Sheddon & Potter (1964) also found a correlation between the frequency of antibodies against 'epidemic' adenoviruses and the blood groups of children in Sheffield. On the other hand, Downie *et al.* (1965) could find no support for a suggestion that the frequency or severity of smallpox in India might be correlated with the possession of A, B and O blood groups.

SUMMARY

Sera were obtained from about half of the Tristan da Cunha islanders on reaching Cape Town in October 1961, a few months after reaching Britain and before returning to the Island in 1963.

After vaccination against current influenza A 2 and B serotypes antibodies were evoked against earlier serotypes, in particular against influenza A 1 of 1951 with which the islanders had almost certainly been infected. Those who failed to develop antibody against A 2 and B after vaccination developed it later presumably owing to natural infection.

Almost all islanders developed antibodies against parainfluenza 3 and 1 and some against parainfluenza 2 and coxsackie A 21 viruses. There were no antibody rises against reoviruses.

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There was some evidence that islanders belonging to blood group A were more susceptible to infection with influenza and coxsackie viruses than were those belonging to blood group O.

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