IMMUNISATION WITH INFLUENZA VIRUS A VACCINES

COMPARISON OF INTRADERMAL AND SUBCUTANEOUS ROUTES

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EVIDENCE has been brought forward in the U.S.A. to show that influenza virus vaccines are better given intradermally than subcutaneously (Van Gelder et al. 1947, Weller et al. 1948, Bruyn et al. 1949, Rantz and Randall 1949). The advantages claimed for the intradermal route are that it: (1) reduces the risk of serious general reactions; and (2) saves vaccine because an intradermal dose smaller than the usual subcutaneous one produces an equally good antibody response and should therefore be equally effective in immunisation against actual infection.

Bruyn and co-workers (1949) were dealing with the immunisation of children, in whom serious reactions are frequent when virus vaccine is given subcutaneously in the usual concentration. This seems important from the theoretical standpoint of the factors known to be concerned in the antibody response to influenza vaccine. It has been repeatedly shown that the amount of antibody formed in response to a particular quantity of influenza-virus antigen partly depends on the person's pre-immunisation level of antibody. The response to a particular antigen, in terms of the change in titre, may be impressive in people with a low initial level of antibody and negligible in those with a high initial level (Hirst et al. 1942, Eaton and Martin 1942, Henle et al. 1946). In view of the low level of antibodies to the influenza viruses normally found in children, they may be regarded as particularly sensitive indicators of influenza-virus antigens. The amount of antibody response is also governed, within limits, by the quantity of antigen given; and theoretically, because of their lack of pre-existing antibodies, children might therefore respond at least as well to a small dose of antigen as to a large one, whereas adults might respond to large amounts of antigen but not to small amounts. This means that the small dose of vaccine given intradermally to children, which apparently can have as good an antigenic effect as the ten-times larger subcutaneous dose, might be entirely ineffective in adults. There is clearly a need, therefore, for a further comparative trial in adults of influenza-virus vaccine given intradermally and subcutaneously.

METHOD

The plan was to inoculate alternate volunteers intradermally and subcutaneously with a concentrated virus vaccine. Previous experience had shown that the influenza-virus vaccine adsorbed on aluminium phosphate* was an effective antigen with a low rate of general reactions, and this preparation was therefore chosen for the subcutaneous inoculations. However, since vaccines containing aluminium phosphate cause mild irritation when injected into the skin, the intradermal inoculations were done with a concentrate prepared by red-cell adsorption and elution of the virus, using a 5% suspension of fowl red cells. The vaccines were made from similar pools of egg allantoic fluid, infected with the same A-strain of virus. The concentration of virus in each vaccine was equalised, the final level being some ten times as high as in the original allantoic fluids. The doses given were 0·1 ml. intradermally or 1 ml. subcutaneously. Four vaccines were prepared: two from the PR8 strain, and two from the NED/1/49 strain representative of the A prime group. The hæmagglutinin titres were 1/12,800 for the PR8 eluate vaccine and 1/19,200 for the NED eluate. The vaccines adsorbed on to aluminium phosphate were adjusted so that the concentration of hæmagglutinin was about the same as in the eluate vaccines. Formaldehyde in a final concentration of 1 in 4000 was added to all vaccines to inactivate the virus.

The volunteers were nurses of the United Sheffield Hospitals, medical students at the University of Sheffield, and men of the R.A.F. The inoculations were done in April and October, 1950, when there were no recognised outbreaks of influenza A in Great Britain. Three blood samples for the estimation of serum-antibody levels were collected—before inoculation, two weeks after inoculation, and two months after inoculation.

Antibodies were titrated by the Salk technique of agglutination-inhibition, using a concentrated virus antigen with four final hæmagglutinating doses and fowl red cells (0·125% final concentration). The antigens were derived from single batches of red-cell eluates from pooled allantoic fluids infected with the respective virus strains. Titres were expressed as reciprocals of the appropriate serum dilution.

REACTIONS

The PR8-virus vaccines were used for 40 nurses and 18 R.A.F. men, half of each group receiving one vaccine,

TABLE I—ANTIBODY TITRES AFTER IMMUNISATION WITH INFLUENZA-A VACCINES (PR8 STRAIN) (HOMOLOGOUS VIRUS)

Case no.	Intradermal		Case no.	Subcutaneous	
	Mean initial titre	Mean post-vaccination titre		Mean initial titre	Mean post-vaccination titre
22	213	213	25	12	1440
23	133	373	28	267	2133
24	27	640	29	360	400
26	120	200	31	93	2133
27	480	800	32	160	1920
30	240	1920	33	13	107
34	40	240	36	120	640
35	60	960	37	60	3840
38	20	160	46	160	320
39	100	1920	48	60	640
40	120	480	50	187	5120
41	27	2133	51	53	2133
42	20	160	54	120	1280
43	187	3413	55	100	1600
44	400	400	56	15	7680
45	50	480	57	80	8533
47	25	160	58	40	160
49	240	320	59	40	640
52	120	240	60	120	320
53	173	3413	61	133	6827
143	120	320	146	120	1920
145	160	480	148	60	2560
151	27	4267	150	60	960
155	120	120	152	15	7680
157	240	400	154	107	7680
158	80	240	156	40	640
160	160	2560	159	10	240
163	10	160	164	20	1920
165	160	960	169	20	960
Geometric mean titre	83	540	..	57	1350
Antibody rise ..	× 6·5		..	× 23·6	

* These vaccines were prepared by one of us (F. H.) by adsorbing the virus from allantoic fluids on to aluminium phosphate. The final preparations were adjusted to contain 6 mg. of aluminium phosphate per ml. and 1 part of 'Merthiolate' per 10,000, in addition to the required amount of virus (inactivated with formalin 1 in 4000), in neutral *M*/10 phosphate buffer solution.

and half the other. There were no febrile reactions in any of the nurses. Of the 20 nurses inoculated subcutaneously, 6 complained of transient tiredness, aching, or dizziness in the next 24 hours, and 1 had a severe headache and was off duty for a day; 15 had trifling and 1 moderate local reactions with œdema and tenderness at the site of injection. Of the 20 nurses inoculated intradermally, 2 complained of tiredness or aching in the next 24 hours, and 2 had trifling local reactions. The 18 R.A.F. men were not examined in detail, but none of them reported a severe general or local reaction.

The NED-virus vaccines were given to 45 student volunteers, of whom 23 were injected intradermally and 22 subcutaneously. No severe general reaction was encountered, but 1 student in each group complained of slight headache in the evening after the injection. Mild local reactions, with redness and tenderness at the site of injection were noted in 9 students who had subcutaneous vaccine and in 2 who had intradermal vaccine. The remainder of the 45 students either had no reaction at all or only trifling local changes.

TABLE II—ANTIBODY TITRES AFTER IMMUNISATION WITH INFLUENZA-A PRIME VACCINES (NED/1/49 STRAIN) (HOMOLOGOUS)

Case no.	Intradermal		Case no.	Subcutaneous	
	Mean initial titre	Mean post-vaccination titre		Mean initial titre	Mean post-vaccination titre
1	20	160	24	40	120
2	30	240	25	60	240
3	40	80	26	10	240
4	20	80	27	40	320
5	60	240	28	120	240
6	15	120	29	15	1920
7	20	80	30	20	960
8	20	160	31	30	50
9	40	80	32	15	80
10	25	60	33	30	240
11	20	80	34	60	240
12	60	80	35	20	853
13	60	120	36	50	120
14	40	160	37	80	160
15	20	80	38	50	120
16	37	320	39	80	640
17	20	47	40	40	160
18	80	80	41	10	80
19	40	80	42	80	320
20	40	160	43	40	240
21	60	120	44	10	160
22	30	80	45	20	640
23	40	40	..	..	..
Geometric mean titre	33	104	..	33	242
Antibody rise ..	× 3·1		..	× 7·3	

ANTIBODY RESPONSE TO HOMOLOGOUS VIRUS

PR8-virus vaccines

The antibody responses were determined by comparing the antibody level before vaccination with that two weeks afterwards, both pairs of sera being titrated at the same time on more than one occasion. Table I gives the arithmetic means of the duplicate or triplicate estimations for each serum. Log mean titres are about normally distributed in a population; so the statistical analysis has been done on the logarithms of these averages, and the final results have been transformed back to the original units. Accordingly it is the geometrical mean titre that has been given for each group in table I.

The range of initial titres for those receiving vaccine either intradermally or subcutaneously was similar, and lay between 10 and 480 for the intradermal group and 10 and 360 for the subcutaneous group. The geometric means of the initial titres were 83 for the intradermal and 57 for the subcutaneous group. The range of post-vaccination titres lay between 120 and 4267 for the intradermal group and between 107 and 8533 for the subcutaneous group. The geometric means were 540 and 1350 respectively, and the 95% confidence limits for the post-vaccination groups were calculated as shown in table III. The post-vaccination geometrical mean titre was significantly greater in the subcutaneous than in the intradermal group ('t' with 56 degrees of freedom was 3·07, and the probability of this being exceeded by chance is less than 1/100).

TABLE III—SUMMARY OF RESULTS

Vaccine	Vaccination group	No. of cases	G.M. initial titre	G.M. post-vaccination titre
PR8	Intradermal	29	83 (57, 122)	538 (364, 796)
	Subcutaneous	29	57 (41, 82)	1352 (861, 2123)
NED/1/49	Intradermal	23	33 (27, 40)	104 (83, 123)
	Subcutaneous	22	33 (24, 45)	242 (165, 355)

The figures in parentheses give the 95% confidence limits for the geometric means, being transformed from the expressions (arithmetic mean ± 2 s.e.) in the logarithmic units.

Because a variation in antibody response to a vaccine has been ascribed to different initial antibody titres, the distribution of initial titres in the two groups was examined more closely. There were 16 persons with initial titres of 80 or less in the subcutaneous group, compared with 11 persons in the intradermal group. However, the antibody response in the intradermal group was far below that obtained in the subcutaneous group. With the intradermal vaccine, 11 persons with a geometric mean initial titre of 30 gave a post-vaccination mean titre of 433. The corresponding post-vaccination figure for the 16 subcutaneously immunised persons with a geometric mean initial titre of 30 was 1234.

Even in the persons with low initial titres a better antibody response was therefore induced by subcutaneous vaccine than by intradermal vaccine.

NED-virus Vaccine

Table II gives the antibody titres in the two groups receiving NED-virus vaccine intradermally or subcutaneously. The geometric mean initial titre for each group was 33, and the post-vaccination was 104 in the intradermal group and 242 in the subcutaneous group—a difference which is again statistically significant ('t' for 43 degrees of freedom being 3·9, $P < 1/1000$). The antibody response was therefore greater in the volunteers receiving vaccine subcutaneously than in those inoculated intradermally. The distribution of initial titres in both series was substantially the same, the numbers with low titres being actually slightly greater in the intradermal group; hence the greater antibody response in the subcutaneous group was unlikely to have been due to this factor.

Decline in Antibody Response

The antibody levels two months after vaccination were compared with those found after two weeks in each of the four groups. Sera were tested from 26 of the volunteers receiving PR8 vaccines intradermally and 24 receiving vaccine subcutaneously. The tests were carried out on the same day with the pairs of serum from each person collected two weeks and two months after vaccination. The serum pairs from 14 of the intradermal and from 10 of the subcutaneous group gave identical titres, but lower titres were found in the serum collected after two months in 8 intradermally and 14 subcutaneously immunised persons. The fall in titre was to a quarter or half of that encountered two weeks after vaccination, except in 1 case. The serum titre of this person, who had received vaccine intradermally, declined from 1/3840 to 1/80. Possibly a mistake had occurred in the serum sampling in this case.

In no case in the subcutaneous group did the titre increase but in 4 of the intradermal group the titre

increased twofold in two months. The geometric mean titre of the two-month serum samples was still statistically greater in the subcutaneous group (750) than that in the intradermal group (290).

In the NED-vaccinated series serum was obtained two months after inoculation from 16 of the intradermal and 20 of the subcutaneous group. Identical titres were found in the pairs of sera from the same persons two weeks and two months after inoculation in 13 of the intradermal and 14 of the subcutaneous group. 3 of the intradermal and 6 of the subcutaneous group showed a fall in titre to half of that present two weeks after inoculation. No rises in antibody were found in either group.

It was concluded that in most people the antibody titre present two months after vaccination was the same as that present two weeks after injection with either strain of virus. In a few people, however, antibody levels had declined to a quarter or half of those present two weeks after inoculation. It mattered but little whether the vaccine was given subcutaneously or intradermally.

Response to Heterologous Virus

Tests were made of sera from people in the various groups with a virus strain other than that utilised in the preparation of the vaccine. Thus pairs of sera from 25 people immunised with PR8 vaccine either intradermally or subcutaneously were tested against the NED virus. The sera were chosen as being representative of the various ranges in antibody response to PR8, and the titre of the post-vaccination specimens varied from 120 times the pre-vaccination titre down to identical values. The titres of the pre- and post-vaccination sera against the NED virus were identical with each other in 23 pairs and showed only a twofold increase in titre in the remaining cases. These results agree with the published observations of other workers and indicate the ineffectiveness of PR8 antigen in stimulating antibody against the influenza-A prime viruses (Sigel et al. 1948, Loosli et al. 1948, Salk and Suriano 1949).

Observations were made with sera from 26 people immunised either intradermally or subcutaneously with the NED virus. PR8 antigen and a red-cell eluate prepared from a recently isolated influenza-A prime virus A/SWE/1950 were used in the tests.

TABLE IV—SERA FROM PEOPLE IMMUNISED WITH NED/1/49 VIRUS

Route	Case no.	NED/1/49		SWE/50		PR8	
		Initial titre	Post-vacc. titre	Initial titre	Post-vacc. titre	Initial titre	Post-vacc. titre
Intradermal	1	20	160	80	160	320	320
	2	30	240	40	160	160	320
	4	20	80	80	160	320	640
	6	15	120	20	160	20	40
	8	20	160	80	320	40	40
	10	25	60	40	160	640	640
	11	20	80	40	160	40	80
	14	40	160	80	320	40	160
	15	20	80	80	160	320	320
	16	37	320	40	160	160	320
	17	20	47	20	80	10	10
	20	40	160	40	320	40	80
Subcutaneous	26	10	240	40	320	160	160
	27	40	320	80	640	160	320
	29	15	1920	20	320	320	2560
	30	20	960	40	640	80	320
	32	15	80	40	160	80	160
	33	30	240	20	160	80	80
	34	60	240	..	...	640	640
	35	20	853	20	1280	80	320
	39	80	640	80	320	40	160
	40	40	160	40	160	80	160
	42	80	320	40	160	80	1280
	43	40	240	40	160	80	320
	44	10	160	10	160	80	320
	45	20	640	10	320	160	320
Geometric mean titre		25·9	216·8	37·8	229·4	91·5	220·3
Antibody rise		× 8·2		× 6		× 2·4	

Table IV shows that, though the titres of antibodies against the PR8 virus underwent a change as a result of the vaccination in some people, the degree of change was quantitatively smaller than with homologous virus. In one person the antibody increase to PR8 was, however, greater than that to the homologous virus (case 42).

The results of tests with the Swedish virus were a little more difficult to interpret, but compared with the results with NED virus the differences were not large and seemed to be due to a high titre in the pre-vaccination serum. As already shown (Stuart-Harris and Miller 1947) the influenza-A prime virus strains are influenced by the exact source of the fowl red cells used in the test. When the same fowl was used as a source of cells in tests made with NED-virus and SWE-virus strains the results were closely similar. But the results with the pre-vaccination sera varied when different fowl cells were used with the different virus-A prime strains.

The results with heterologous viruses did not seem to vary according to the type of vaccination used.

Finally, the sera from people immunised subcutaneously with a vaccine concentrated by centrifugation and prepared from the A/SWE/1950 strain in Copenhagen (personal gift from Dr. von Magnus) were also tested against the SWE and NED viruses. Closely similar antibody titres were obtained with the two viruses, and it seems probable that any difference existing between the virus strains was insufficient to influence immunisation in man.

DISCUSSION

Several prerequisites for a virus vaccine against influenza have become apparent in the past few years. Of these the antigenic constitution of the vaccine has proved to be paramount. Yet from a practical standpoint two other desirable features have emerged: (1) the use of the vaccine should be attended by a low rate of reaction; and (2) the greatest possible economy should be achieved in the use of raw materials, particularly of the egg fluid necessary for each dose of vaccine. The red-cell eluate vaccine suffers from two disadvantages: (1) reactions following its use subcutaneously are significant in number and degree; and (2) a relatively large volume of infected allantoic fluid is necessary to provide the antigen needed for a single inoculum. The incidence of reactions, particularly febrile or systemic ones, was shown by Salk (1948) to depend on the virus content of the vaccine. In the trial carried out in Great Britain in 1945 (Stuart-Harris 1947), 1406 persons received 1 ml. of tenfold concentrated eluate vaccine subcutaneously, and 31 (2·2%) of them had local reactions, 92 (6·57%) had general reactions, and 13 (0·92%) had fever. These figures represent, if anything, a lower incidence of reactions than that recorded by other workers, particularly Sadusk et al. (1949).

The decision in the present study to use virus vaccine adsorbed on to aluminium phosphate arose from previous experience of its low incidence of reaction coupled with satisfactory power to stimulate antibody formation. Since previous workers have compared the antibody-stimulating power of a vaccine given intradermally with that of a tenfold dose of the same vaccine given subcutaneously, the two virus vaccines used by us were brought to similar degrees of concentration. A tenfold concentration compared with the original allantoic fluid was adopted because this was also used in the successful field experiments recorded by the Commission on Influenza (1944) in U.S.A.

The results given above indicate that 1 ml. doses of tenfold concentrated virus vaccine adsorbed on to aluminium phosphate and given subcutaneously are

attended by an insignificant degree of systemic reaction. Nor did significant reactions follow 0·1 ml. doses of eluate vaccine given intradermally, but the antibody response to this amount of vaccine intradermally is clearly inferior to that produced by the 1 ml. dose of adsorbed vaccine subcutaneously. Thus the use of this amount of eluate vaccine intradermally cannot be relied on to produce in adults a maximal antibody response.

The vaccine adsorbed on to aluminium phosphate, which must be given subcutaneously, is unfortunately as extravagant in eggs as the ordinary eluate vaccine given by the same route. It remains to be seen whether a smaller dosage or lesser concentration of adsorbed vaccine would be as effective a stimulant to antibody formation as that used by us.

Vaccine adsorbed on to calcium phosphate was considered by Salk (1947) to exert an antigenic effect as great as that of a larger amount of unadsorbed vaccine given by the same route. Similar observations were made by one of us (F. H.) with vaccines adsorbed on to aluminium phosphate given to mice. This superior antigenic effect was attributed by Salk in his investigations to a relatively slow release of antigen. Such an effect might be responsible for the good results obtained by us with the vaccines adsorbed on to aluminium phosphate. However, if a really longer antigenic effect was produced by adsorbed vaccine in our case, it seems likely that a divergence between the antibody levels at the interval of two months after inoculation in the subcutaneous and the intradermal groups would have been apparent.

When the antibody response induced by vaccination is determined for heterologous viruses as well as the homologous strain, the results are complex. It has been shown conclusively by other workers and confirmed by us that the standard PR8-virus strain does not stimulate antibodies against the A prime group of strains. However, the A prime antigen does stimulate some antibody formation against the PR8 virus, but the response to inactivated virus is much less robust and more irregular than that produced by infection. In infection (Stuart-Harris and Miller 1947, Stuart-Harris et al. 1949) the antibody response may be demonstrable more readily and more often by using the PR8 antigen in the in-vitro tests with human sera than by using the homologous A prime antigen. Further work is desirable with different strains of the A prime group not only from the standpoint of breadth of antibody response but also because these strains seem to be relatively poor antigens (Salk et al. 1949). The selection of an A prime antigen which is highly antigenic is of great importance for the future use of influenza vaccine.

SUMMARY

Volunteers were inoculated subcutaneously with 1 ml. doses of influenza-virus vaccines adsorbed on to aluminium phosphate, or intradermally with 0·1 ml. amounts of virus vaccines prepared by red-cell adsorption and elution. All the vaccines were concentrated tenfold in terms of the original allantoic fluids. The vaccines were prepared either from influenza-A virus (PR8) or an A prime strain (NED/1/1949).

General reactions were insignificant, and local reactions, though frequent after subcutaneous immunisation, were trifling.

The antibody response to the strain of virus incorporated in the vaccine was determined by comparing serum titres before and two weeks after vaccination by the agglutination-inhibition test. Significantly higher antibody levels were present after immunisation in the subcutaneously inoculated volunteers compared with those in the volunteers inoculated intradermally.

The enhancement of antibody levels induced by the PR8 vaccines seemed to be greater than that following the A prime virus, irrespective of the route of immunisation.

The antibody titres attained two weeks after immunisation were maintained in more than half the volunteers, as shown by serum samples collected two months after vaccination.

Though the PR8 vaccines did not stimulate antibodies against the 1949 A prime virus, the vaccines made from the latter occasionally induced alterations in titre of antibodies to PR8 virus, and regularly produced a rise in antibodies to a second A prime virus (A/SWE/1950).

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REFERENCES

Bruyn, H. B., Meiklejohn, G., Brainerd, H. D. (1949) *Amer. J. Dis. Child.* **77**, 149.
Commission on Influenza (1944) *J. Amer. med. Ass.* **124**, 982.
Eaton, M. D., Martin, W. P. (1942) *Amer. J. Hyg.* **36**, 255.
Henle, W., Henle, G., Hampil, B., Maris, E. P., Stokes, J. jun. (1946) *J. Immunol.* **53**, 75.
Hirst, G. K., Rickard, E. R., Whitman, L., Horsfall, F. L. jun. (1942) *J. exp. Med.* **75**, 495.
Loosli, C. G., Schoenberger, J., Barnett, G. (1948) *J. Lab. clin. Med.* **33**, 789.
Rantz, L. A., Randall, E. (1949) *Stanford med. Bull.* **7**, 25.
Sadusk, J. F. jun., Bassett, P. C., Meddaugh, J. S. (1949) *Amer. J. Hyg.* **49**, 148.
Salk, J. E. (1947) *J. Immunol.* **57**, 301.
— (1948) *Ibid*, **58**, 369.
— Suriano, P. C. (1949) *Amer. J. publ. Hlth*, **39**, 345.
— — Laurent, A. M., McGinnis, R. C. (1949) *Fed. Proc.* **8**, 410.
Sigel, M. M., Shaffer, F. W., Kirber, M. W., Light, A. B., Henle, W. (1948) *J. Amer. med. Ass.* **136**, 437.
Stuart-Harris, C. H. (1947) *Lancet*, i, 201.
— Miller, M. H. (1947) *Brit. J. exp. Path.* **28**, 394.
— Laird, J., Tyrrell, D. A., Kelsall, M. H., Franks, Z. C., Pownall, M. (1949) *J. Hyg., Camb.* **47**, 434.
Van Gelder, D. W., Greenspan, F. S., Dufresne, N. E. (1947) *Nav. med. Bull., Wash.* **47**, 197.
Weller, T. H., Cheever, F. S., Enders, J. F. (1948) *Proc. Soc. exp. Biol., N.Y.* **67**, 96.

"MYOCARDITIS" AND AORTIC HYPOPLASIA IN ARACHNODACTYLY

REPORT OF A CASE

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ARACHNODACTYLY was first described by Marfan (1896) under the name of dolichostenomelia and is consequently often called Marfan's syndrome. Méry and Babonneix (1902), who described Marfan's original case some six years later, called it hyperchondroplasia. Poynton (1903) was the first in this country to refer to it and called it atavism, but Achard (1902), in France, suggested arachnodactyly, and this name has come into common use.

Well over 200 cases have been recorded, and the abnormalities that characterise the condition are now well known. Briefly, they comprise abnormal height, poorly developed musculature, absence of subcutaneous fat, long slender extremities, particularly the fingers and toes, abnormal extensibility of joints, with a tendency to contractures, a funnel-shaped chest or pigeon breast with kyphosis, scoliosis, and often winging of the scapulæ, a dolichocephalic skull with prominent supraorbital