Examination of converters from negative to high-grade tuberculin sensitivity and their home contacts proved to be a particularly rewarding procedure. During the last three years of the programme a total of 28 new cases out of 194 examinations were discovered in this manner, as opposed to only seven cases from all other examinations. This indicates that about 80% of all new cases of pulmonary tuberculosis that can be discovered by serial tuberculin-testing would be exposed merely by examining the tuberculin converters from Heaf-negative to grade III or IV reactions and their adult home contacts. The number of subjects examined would be small and the yield of new cases high—factors of considerable importance in developing countries where extensive radiography may be impracticable owing to the distances or the costs involved.

Only 358 children with grade I reactions and 1,014 with grade II (including converters) received radiographic examination, partly because the number of children in these categories was so great and partly because the incidence of tuberculous cases did not promise to be high. Only one of those examined was found to have pulmonary tuberculosis. Epidemiological investigations centred around 218 selected tuberculin conversions to grade I or II reactions did not produce results different from those that would have been expected had the children been persistently tuberculin-negative. The results obtained suggest that grade I and possibly grade II reactions in unvaccinated children are of little epidemiological significance in tuberculosis.

This Cardiff programme has shown that the annual tuberculin-testing of an entire school population in a large town is a practical, inexpensive procedure, and that in communities where a definite risk of tuberculous infection from undiagnosed cases exists it can be a useful supplementary case-finding measure. It should, however, be realized that where the prevalence of tuberculosis is low it is of doubtful value in case-finding: it cannot reveal new cases where none exist.

Summary

A serial tuberculin-testing programme whereby tuberculin tests were given annually to 40,000 schoolchildren during four consecutive years was completed in Cardiff during 1962. It yielded 57 new cases of tuberculosis, or 8% of all notifications received in the city during that period. Examination of children found to be high-grade reactors to their first test and of their adult contacts yielded 8 new cases per 1,000 examined in each instance. Re-examination of high-grade reactors yielded 0.9 new cases per 1,000 examinations. The incidence of definite cases of pulmonary tuberculosis among converters from negative to high-grade (Heaf grade III or IV) reactions was 283 per 1,000 for the children and 82 per 1,000 for their adult home contacts (183 contacts with tuberculosis per 1,000 child converters). Examination of children with high-grade tuberculin reactions indicated that if they showed no definite radiographical evidence of pulmonary tuberculosis within a year of developing tuberculin sensitivity they were unlikely to do so during the next few years. Although serial tuberculin-testing of schoolchildren may play an important part in the early diagnosis of tuberculosis during childhood it contributes little to the discovery of new cases in persons over the age of 45.

We are indebted to Dr. W. Powell Phillips, Medical Officer of Health for Cardiff, and Dr. S. H. Graham, consultant chest physician, Cardiff, for their considerable help and interest.

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DECLINING TUBERCULIN SENSITIVITY WITH ADVANCING AGE

BY

R. N. JOHNSTON, M.D., M.R.C.P., M.R.C.P.Ed. **R. T. RITCHIE, M.B., M.R.C.P.Ed.**
I. H. F. MURRAY, M.B., Ch.B.
Dundee Chest Clinic and Department of Tuberculosis, University of St. Andrews

In 1929 Troisier and his colleagues drew attention to "L'anergie tuberculinique sénile," as but little thought had been paid to this until the past decade. A summary of selected papers dealing with large-scale tuberculin surveys concerned especially with the elderly is shown in the accompanying Table. A progressive decline in tuberculin sensitivity with advancing age is the usual finding. Low doses of tuberculin reveal this waning tuberculin allergy in the aged more clearly. Thus Caplin *et al.* (1958) showed this decline best with the Mantoux 1 T.U. test. In the British Tuberculosis Association (1959) report the Mantoux 5 T.U. test revealed declining sensitivity over the age of 45 years, but with the Heaf and Mantoux 100 T.U. test this change was discernible only among those aged 65 and over.

Apart from the 100 T.U. test there is little information on techniques designed to elucidate the reason and mechanism of this phenomenon. Beresford (1958), using 1,000 T.U. and a depot tuberculin 5 T.U. in 42 negative reactors to 100 T.U., found 25 were tuberculin-positive and considered that these latter had evidence of previous tuberculous infection. The response to B.C.G. vaccination has been examined by Troisier *et al.* (1929), Canetti and Lacaze (1940), Jonsen and Ustvedt (1950), Palitz and Aronsohn (1957), and Prinsley and Droller (1959).

Present Investigation

The present investigation falls into six sections: (1) A survey of males aged 40–70 attending the Dundee Mass Miniature Radiography Unit, 1960–1. (2) A survey of the in-patients of the Dundee Royal Mental Hospital in 1959 and again in 1961. (3) A survey of volunteers in all the old people's clubs in Dundee in 1959. (4) A survey

Selected Tuberculin Surveys Including the Elderly

Author and Place	Age Range	No. Aged 65 and Over or Aged 60 and Over*	Tuberculin Test
Meyer (1951) Oslo	14–60+	6,204*	Pirquet. Danish O.T.
Robins *et al.* (1954 New York City	0–85+	1,764	Mantoux 10 T.U. O.T. (but patch tests for 3,300 children 0–4 years)
Giannini and Sloan (1957) Northern area of Glasgow	15–75+	429	Mantoux 10 and 100 T.U O.T.
Griep and Bleiker (1957) Holland	16–81+	418*	Mantoux 5 T.U. P.P.D.
Beresford (1958) Dorset	65–90+	1,012	Mantoux 10 and 100 T.U. O.T. (1,000 T.U. and Depot 5 T.U.)
Caplin *et al.* (1958) London	45–75+	396+	Mantoux 1, 10, and 100 T.U. and 1,000 T.U. P.P.D.
B.T.A. (1959) England and Scotland	0–65+	433	Mantoux 5 and 100 T.U. and Heaf P.P.D.

of the in-patients in the geriatric units in Dundee and the County of Angus in 1959 and 1961. In all except the last these tuberculin surveys were combined with a miniature radiograph of chest, and those who showed evidence of pulmonary tuberculosis, either active or of doubtful activity, have been excluded in the results of the tuberculin tests. (5) Additional investigations on those initially tuberculin-negative. (6) Studies on B.C.G. vaccination among patients in the Dundee Royal Mental Hospital.

Standards and Definitions

The standard Heaf test has been employed, using the East pattern Heaf gun. Care was taken that the needles were in good condition. Fresh standard P.P.D. tuberculin (Allen and Hanburys) as supplied for the multipuncture test was used. The results of the Heaf tests were recorded grade 0, 0 to 3 papules of induration; grade 1, 4 to 6 papules; grade 2, a ring of induration; grade 3, the centre of the ring has filled in to form a weal of induration; and grade 4, larger reactions with blistering. The tests were read on the seventh day, but in certain of the studies additional readings were made on the third day. The Mantoux 100 T.U. tests were performed with old tuberculin, and this was used within a week of manufacture. These tests were all read at three days. A reaction was recorded as negative where induration measured 5 mm. or less in diameter. Where the diameter of the indurated area exceeded this the test was recorded as positive. The Mantoux 100 T.U. (Allen and Hanburys) and any subsequent tests were applied on the forearm opposite to that of the previous Heaf tests. For the concentrated tuberculins a separate tuberculin syringe was used and kept only for these tests.

Tuberculin surveys in the general population should be related to those performed on tuberculous patients. For the past six years our tuberculous in-patients (predominantly middle-aged and elderly) have received a Heaf test and, if this was negative, a Mantoux 100 T.U. O.T. test: 392 have been positive and only 2 (0.51%) negative. These results approximate to Mascher's (1951) series from Sweden (0.5% of 1,591 patients).

Methods and Results

Survey 1. 1,392 Persons (370 Aged 60+)

The men examined were a random group from all social grades resident in Dundee and were selected only because they had previously been *x*-rayed in the M.M.R. campaign of 1958. They were aged 40–70, and were invited to attend for *x*-ray examination as part of a campaign to eradicate tuberculosis and improve the early diagnosis of bronchial carcinoma. With only a few exceptions these men agreed to a Heaf tuberculin skin test performed by a doctor and returned for reading, usually on the seventh day but in a small group on the fifth or sixth day. Readings were recorded by either the doctor or a trained staff nurse. These tests were spread over a 17-months period; the batch of tuberculin has varied, but has always been in current use in the diagnostic and contact clinics. No additional tests were performed on those who were tuberculin-negative. Negative reactors increased from 3% in the fourth decade to 14% in the seventh decade, while the hypersensitive (Grade 4 reactors) declined from 10% in the fourth decade to 4% in the seventh.

Survey 2. Dundee Royal Mental Hospital In-patients. 737 Patients (262 Aged 60+)

These tuberculin and M.M.R. surveys were carried out in 1959 and 1961, and 271 patients were common to both years. (The results of the 1961 tests on these 271 patients were not included in the total.) All the available patients were examined, using standard Heaf tuberculin tests, and the results dual-read independently on the seventh day. Those who were then negative were given Mantoux 100 T.U. and those tests likewise read independently on the third day. A few patients were lost to this analysis because for various reasons they were not available at the time of reading.

The 271 patients studied in 1959 and 1961 (dual-read in both years) yielded four readings with a two-year interval between pairs. These results have been analysed as follows:

	Changes of 2° or More Agreed by Both Observers				Agreed Change from Positive to Negative, or Vice Versa		
	Male	Female	Total		Male	Female	Total
Increase ..	3	2	5	Conversion	1	4	5
Decrease ..	4	9	13	Reversion ..	4	9	13

Survey 3. Volunteers in Old People's Clubs. 432 Persons (386 Aged 60+)

These clubs are situated mainly in the industrial centre; the members are drawn from social groups 4 and 5 and are predominantly female. Heaf tests were read on the seventh day.

Survey 4. Geriatric Units in City of Dundee and County of Angus. 431 Patients (417 Aged 60+)

These patients suffered from diverse diseases. No known cases of tuberculosis were included in this survey. Patients who were terminally ill were not examined. The Heaf tuberculin tests were dual-read independently on the third and seventh days, and when negative or the readings disagreed a Mantoux 100 T.U. was done and again dual-read on the third day.

Additional Mantoux 100 T.U. tests were performed on those who were negative to the Heaf test in surveys 2 and 4, and these results showed a similar decline in tuberculin sensitivity.

The results of the Heaf tests of all these surveys are shown in Fig. 1. (An additional 34 patients who were studied later in the geriatric units have been included in this combined analysis.) Our results are further summarized

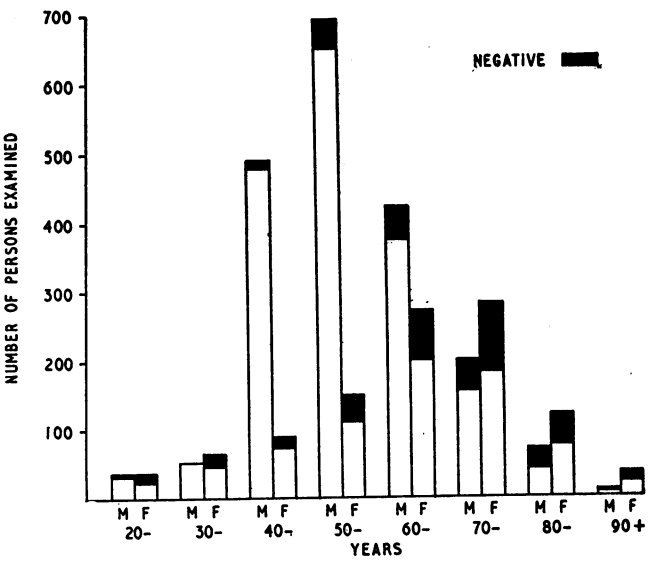

FIG. 1.—Heaf tuberculin results (3,026 persons).

as percentage changes in each sex from the fifth decade onwards (Fig. 2).

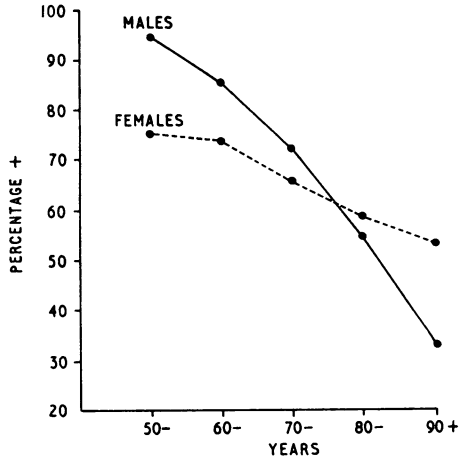

FIG. 2.—Heaf tuberculin sensitivity in old people.

5. Additional Investigations on Geriatric In-patients with Negative Heaf and Mantoux 100 T.U. Tests

Concentrated Tuberculins. — Concentrated (human) P.P.D., Weybridge, Batch 8/59 (2 mg./ml.), was injected intradermally 0.1 ml.=10,000 T.U. into the right forearm and the result dual-read independently at three days. Only 6 (11%) of the 52 persons examined showed a positive reaction

Depot Tuberculin Cream, Batch 3, Glaxo (5 mg. Bovine P.P.D./g.).—This was performed after the method of Pepys, Bruce, and James (1958) using a standard Heaf gun and after we had shown that this produced positive reactions in persons known to be tuberculin-positive. Of 54 persons tested only 2 (4%) showed a positive reaction. These two techniques have therefore failed to reveal any notable degree of latent tuberculin allergy.

Effect of Local Cortisone Combined with P.P.D. on the Mantoux 100 T.U.—Pyke and Scadding (1952) and Citron and Scadding (1957) found that 50% of patients with sarcoidosis who were insensitive to tuberculin became tuberculin-positive after the addition of local cortisone. We have repeated their experiments in 25 geriatric patients. A Mantoux 100 T.U. P.P.D. (Allen and Hanburys) was performed on the right forearm while at the same time a Mantoux 100 T.U. P.P.D. with the addition of cortisone acetate 1.25 mg. was applied to the left forearm. These reactions were dual-read independently on the third day. Fifteen of these patients were negative to the Mantoux 100 T.U. test, and in none of these did the addition of cortisone yield a positive reaction. Of the 10 Mantoux-positive patients, three remained positive with cortisone while seven reverted to negative. This technique, which in some tuberculin-negative sarcoid patients has revealed latent senstivity to tuberculin, failed to do so in our patients.

Response to a Skin Irritant.—Pilcher (1930) found in patients with advanced tuberculosis a decrease in sensitivity to tuberculin and to a non-specific skin irritant. For the latter he used 0.1 ml. of a 1 in 1,000 solution of codeine phosphate, which in " several hundred " normals produced a weal reaching a maximum size of 11 to 13 mm. in 5 to 10 minutes, and this gradually disappeared in the course of an hour or more. On the basis of the depression of both types of skin reaction he concluded that there was a lessened circulation in the skin and subcutaneous tissue. We have studied Pilcher's codeine skin test in a group of 28 geriatric patients, none of whom were acutely or terminally ill, and related this to their tuberculin sensitivity. There was no difference in this immediate-type skin reaction between the tuberculin-positive and the tuberculin-negative.

Response to Candida albicans Antigen.—In a search for an alternative antigen capable of producing a delayed tuberculin-type response, we considered both tricophytin and *Candida albicans* antigens. The former was reported to yield only 35% positive reactions in normal individuals (R. W. Riddell, personal communication, 1962), and was therefore unsatisfactory for our purpose. Citron (1957) has reported a delayed tuberculin-type response using a *Candida albicans* antigen (0.25% suspension) and found that 90% of his normal controls gave a positive reaction (5 mm. or more induration at 48 hours) compared with only 40% in patients with sarcoidosis. Before using this antigen on our patients one of us tested his own response with 0.5% suspension and was impressed by the acute-and-immediate-type response obtained. For this reason we measured the size of the lesion in our patients at 6, 24, 48, and 72 hours, using a 0.25% suspension. We have found not a tuberculin-type reaction but an immediate-type response which shows a progressive decline from 6 to 72 hours (Fig. 3). We concluded that this particular antigen was not relevant to the further study of the delayed-type skin response. Nevertheless a comparison of those who received both Heaf and candida tests showed that among 46 who were Heaf-negative 28 showed a positive response to candida, confirming the capacity of the elderly who are tuberculin-negative to react to other stimuli.

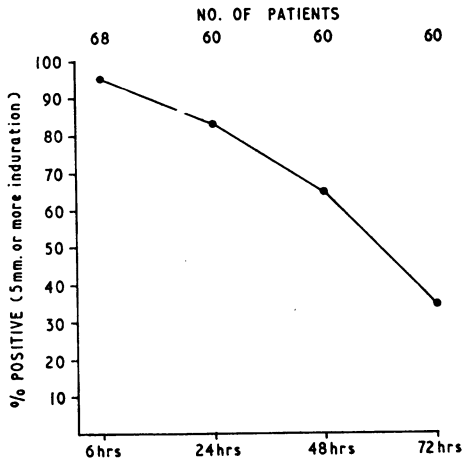

FIG. 3.—Response to intradermal *Candida albicans* (0.1 ml. of 0.25% suspension).

Blood Lymphocyte Counts.—Pepys (1955) has postulated that tuberculin antibodies are produced and transported by cells of the reticulo-endothelial system and that the antibody is brought to the site of challenge in the skin by cells, probably lymphocytes, which migrate into the site. Of 30 of our tuberculin-negative geriatric patients only two showed a significant lymphopenia (absolute lymphocyte counts 494 and 330 ; the remainder 1,140–3,700).

Studies on B.C.G. Vaccination

B.C.G. vaccination serves a twofold purpose in this problem of waning tuberculin allergy—first as a potent " tuberculin " test (Koch phenomenon), and, secondly, to examine the tuberculin-negative patients' capacity to undergo tuberculin conversion. To detect differing degrees of the Koch phenomenon it was necessary to examine the evolution of the B.C.G. lesion at various stages and necessary to know the " normal " evolution of this lesion

using current vaccines. The evolution of the B.C.G. lesion has been studied in 180 Heaf-tuberculin-negative adolescents.

B.C.G. vaccination was offered and given to 128 patients in the Dundee Royal Mental Hospital; four were discharged within two months, leaving 124 patients—80 in 1959 and 44 in 1961: 71 were aged 60 or over. B.C.G. (Danish liquid vaccine—batch numbers 1380, 1382, and 1476) was administered within five days of the date of preparation. Patients were initially given a Heaf tuberculin test and, if negative, a Mantoux 100 T.U. Both of these tests were dual-read independently, and when there was disagreement the Mantoux test was given in addition. B.C.G. vaccine was offered to those who were Mantoux-negative and also those in whom there was disagreement on the Mantoux reading. The B.C.G. sites were inspected 3, 14, and 56 days after vaccination, and at the last the Heaf test was repeated and, if negative, a Mantoux 100 T.U. given.

The evolution of the B.C.G. lesion in patients aged 70 or over has been examined. At the third-day reading large reactions were no more prevalent than in the adolescent group and the incidence of immediate Koch phenomena remained the same at 2–3%. The interesting findings are those at 14 days, and here there is evidence of a *delayed*-type reaction. There were five times as many large reactions (15 mm. or more) as were found among the adolescents. By the 56-day reading the results approximated to those in the young. B.C.G. vaccine therefore demonstrated a tissue change and evidence of previous tuberculous infection more clearly than our special tuberculins.

Tuberculin Conversion Following B.C.G. Vaccination

Of the total 124 patients vaccinated and available for study in both years, 31 failed to convert on the Heaf test (conversion 75%) and 10 to the subsequent Mantoux 100 T.U. (conversion 92%). These failures to convert were found from among those exhibiting both the smallest and the largest reactions to B.C.G., but all had a B.C.G. lesion. Fourteen patients received B.C.G. in 1959 and again in 1961. Six converted and four failed to convert in both years, while the remaining four showed conversion one year but not the other. Subsequent Heaf tests of those vaccinated in 1959 showed a declining conversion—58% at 12 months and only 34% positive at 21 months.

An additional examination was made of the 1961 group six months after B.C.G. vaccination. The B.C.G. lesion was inspected and Mantoux 10 T.U. P.P.D. (human, Lot CT/14, Glaxo) applied to the left forearm, while a Mantoux 10 T.U. B.C.G. tuberculin (Lot B.C.G./3, Glaxo) was applied at the same time to the right forearm. Both results were dual-read on the third day. Thirty-four persons received human-type tuberculin (one refused) and 16 (47%) were positive. Thirty-five received the B.C.G. tuberculin and 19 (54%) were positive. Apart from these three patients positive only to the B.C.G. tuberculin, three showed larger reactions to this B.C.G. tuberculin, while one showed the reverse. Twenty-four persons had identical reactions (either positive or negative) to both tuberculins. Inspection of the B.C.G. site showed varying lesions in all, though the mildest was only a minute 3-mm. white scar. The tuberculin tests again showed no clear relation to the size of the B.C.G. lesion. B.C.G. tuberculin, though slightly more sensitive, had failed to show any significant advantage.

We conclude, therefore, that there is a diminished capacity to achieve *and maintain* tuberculin conversion in the elderly after B.C.G. vaccination. Since these results were obtained on patients in hospital suffering from varying mental disorders we have examined the tuberculin reactions of tuberculous psychotic patients over the past five years. Heaf tuberculin tests were performed on 23 patients, and all of these were tuberculin-positive. The possibility of a drug effect was considered. None of these patients were receiving A.C.T.H., or corticosteroids, antihistamines, or regular acetylsalicylic acid. We considered this last drug because it is known to suppress immediate-type cutaneous responses (Truelove and Duthie, 1959), but in doses of 30–40 gr. (2–2.6 g.) daily we have found no significant effect on the Heaf tuberculin test in 10 patients. Certain of these patients were on chlorpromazine. We have examined the Heaf tuberculin tests of a further eight patients receiving chlorpromazine (300–400 mg. daily) and observed that all were positive. We have therefore no evidence of any drug action to explain our findings.

Discussion

Instability of the Tuberculin Reaction.—Dahlstrom (1940) drew attention to the instability of the tuberculin reaction in a study of 3,919 members of 513 families observed for 5–15 years. During this period 11.1% (276) of the 2,490 tuberculin-positives reverted to negative. These reversions were more likely among children where there was no history of tuberculous contact and the initial tuberculin reactions were weak. Reversion to negative reactions proved rare in adult life, but these were all grouped together as "20 or over" and no observations were made specifically on the middle-aged or elderly.

Latent Tuberculin Allergy and B.C.G. Vaccination

Pollock *et al.* (1959) pointed out that even with the 1,000 T.U. Mantoux test the limit of detecting tuberculin sensitivity had not been reached in young Service recruits. Our investigations with concentrated tuberculins and depot-tuberculin cream have yielded so few positives that these techniques are of little value in the aged. On the other hand, B.C.G. vaccine by revealing a delayed-type Koch phenomenon has proved more successful as a test for latent tuberculin allergy, and is probably the most potent "tuberculin" at present available.

The previous authors already mentioned who have studied B.C.G. vaccination in the elderly have altogether examined 176 persons. At least 12 of these failed to show tuberculin conversion. In our own group of 124 patients, 10 failed to convert with the additional 100 T.U. test, while 31 failed to convert with the Heaf test. It is well known that rates for tuberculin conversion vary with vaccines produced in different laboratories and at least some of the failures in earlier studies may be due to a particular vaccine. Throughout we have adhered to the Danish liquid vaccine, since conversion rates for this vaccine have been uniformly high. Irvine and Barr (1960) reported 99.6% conversion with the Heaf test in 3,497 adolescents who had a B.C.G. lesion, however small (40 different batches of Danish liquid vaccine). The Medical Research Council (1956) noted 99.6% conversion with 100 T.U. in 7,300 children, again using the Danish liquid vaccine. We have used three different batches of this vaccine, and from inspection of the vaccination site know that B.C.G. lesions were present in all our patients. We were satisfied that both the vaccine and our technique could not account for these failures and considered there must be some other reason in these elderly people for their failure to undergo tuberculin conversion. None were acutely ill. Tuberculin sensitivity is depressed in sarcoidosis. The previous

occurrence of this condition might explain some, though probably not all, examples of this phenomenon in the elderly. The mechanism of tuberculin insensitivity in sarcoidosis differs from the usual pattern in old age; thus Israel *et al.* (1950), Forgacs *et al.* (1957), and Scadding (1960) have all reported a common failure of tuberculin conversion after B.C.G. vaccination.

Declining Contact with Tuberculous Infection

Among those who showed tuberculin conversion after B.C.G. vaccination, and in whom the host response was therefore intact, it was most probable that this decline of tuberculin allergy with advancing age was the result of declining contact with *Mycobacterium tuberculosis*. This hypothesis fits well with the fact that tuberculin sensitivity in each age-group is weaker among women, who, for the most part, are less likely to be exposed to chance infection in the community. Moreover, as this phenomenon is observed well beyond the menopause it is difficult to explain this on an endocrine basis. In the minority who failed to show tuberculin conversion there must be some other factor. Our experience indicates that this is not in the skin, and we therefore assume a failure in the reticuloendothelial system to produce adequately sensitized lymphocytes.

Summary

Using the Heaf multipuncture test in 3,026 persons (1,469 aged 60 or over) we have confirmed declining sensitivity with advancing age, and this trend becomes discernible from the fifth decade onwards.

There was also a qualitative change in that those who were most sensitive (Grade 4 reactors) showed a progressive decline between the fourth and seventh decades.

When serial tuberculin tests in the *same* individual after a lapse of two years showed a change, tuberculin sensitivity was more likely to wane.

Those who were tuberculin-negative still showed normal immediate-type skin reactions when codeine phosphate and *Candida albicans* antigen were used.

Using special tuberculins, we failed to elicit any appreciable number showing latent tuberculin allergy. The delayed-type Koch phenomenon seen after B.C.G. vaccination is possibly a more critical test of latent tuberculin allergy.

There was a diminished capacity to achieve and maintain tuberculin conversion after B.C.G. vaccination in 124 persons, most of whom were elderly.

We gratefully acknowledge the co-operation of many patients and volunteers, the help of our medical and nursing colleagues in the Chest Service, in the Dundee Royal Mental Hospital, in the Geriatric Service, and in the Department of Dermatology, Dundee Royal Infirmary. Dr. R. W. Riddell, Brompton Hospital, kindly provided the special candida antigen. We are indebted to Dr. I. W. Lesslie, Central Veterinary Laboratory, Weybridge, and Drs. J. Ungar and P. W. Muggleton, of Glaxo Laboratories Limited, for special tuberculins. We wish to record our thanks to Mrs. P. Brough for considerable secretarial help.

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TYPE-SPECIFIC IMMUNITY AGAINST WHOOPING-COUGH

BY

NOEL W. PRESTON, M.D., Dp.Bact.

Senior Lecturer, Department of Bacteriology, University of Manchester

Although whooping-cough in this country is less prevalent and usually less severe than it was before the introduction of pertussis vaccine, it still occurs, sometimes with fatal results, and moreover it occurs in children who have been vaccinated (Galbraith and Cockburn, 1963). One possible explanation of the occurrence of whooping-cough in vaccinated children is that the infecting bacterium may be different serologically from the organism with which the child has been immunized.

It was Andersen (1953) who first described the serological typing of freshly isolated strains of *Bordetella pertussis*, and her findings have been confirmed by Eldering *et al.* (1957), Preston and Te Punga (1959), and Lacey (1960). All strains possess a common antigen (antigen 1), but they may also possess one or more of a series of type-specific antigens (antigens 2, 3, and 4).

It has recently been shown (Preston and Evans, 1963) that these type-specific antigens play a part in immunity to experimental pertussis infection in mice, and the present communication presents evidence which suggests that they may also play a part in immunity to pertussis infection in children.

Materials and Methods

Strains.—Strains of *Bord. pertussis* were obtained from the Public Health Laboratories in Brighton, Bristol, Leeds, and Manchester; Hope Hospital, Salford; Royal Manchester Children's Hospital; Fazackerley Hospital, Liverpool; and from home cases in Manchester and Salford.

Typing Sera.—Antisera to four different serotypes of *Bord. pertussis* were produced in rabbits. These sera were freed from antibody to heat-stable antigens by absorption with heated suspensions of the homologous strains. They