from coronary heart disease may be explained in the same way and is proportionately larger only because of the greater knowledge about this and because of a shift of diagnosis from other groups to this one. There is direct evidence of this shift having taken place since 1940, for the deaths from other diseases of the myocardium diminished enough to account for much of the increase in 1940-9 and for all of the increase in deaths from coronary disease in 1950-9. The cause of coronary heart disease should therefore be searched for mainly on general pathological and biochemical principles, and not specially on any changes in the environment, though these might be of some lesser importance.

Summary and Conclusions

The death rate from all diseases of the heart started to rise sharply about 1920-4, though before this it had been constant for at least 50 years. By 1959 it was more than two and a half times its earlier level.

The death rate from all causes, after little change for 50 years, decreased to about half its previous level from 1880 to 1920. Since 1926 there has been little change, and further large changes are unlikely until something more can be done to prevent deaths from disease of the heart, vascular lesions of the brain, and cancer.

Assuming (1) that most of the lives saved were young persons who would have died from infectious diseases and tuberculosis, and (2) that one-quarter of them died subsequently from heart disease at the ages when other persons die from this (on the average about 40 years later), a calculation of the expected death rate from all diseases of the heart from 1880 to 1990 has been made. These

expected death rates show close similarities to the death rates observed from 1880 to 1959. This could have been predicted at any time after 1910, though not in such detail until 1926.

It seems that practically all the large increase in deaths from heart disease since 1920, including coronary heart disease, can be explained in this way. This is probably equally true for the deaths from vascular lesions of the central nervous system, though this group has not been discussed in the present paper. No doubt this is the explanation that has been believed by many cardiologists and actuaries: they do not, however, seem to have written much on the subject, though Wood (1956) says that "the increasing age of the population is no doubt partly responsible."

I am grateful to Mr. N. R. Gatenby for reading this and for his suggestions, though he cannot be held responsible for the accuracy of any of the calculations.

REFERENCES

- Campbell, M. (1963). *Brit. med. J.*, **2**, 528.
 Cassidy, M. (1946). *Lancet*, **2**, 587.
 Dublin, L. I., Lotka, A. J., and Spiegelman, M. (1949). *A Study of the Life Table*, 2nd ed. Ronald Press, New York.
 Registrar-General's Annual Report of Births, Deaths, and Marriages in England and Wales (1910). Vol. 73, pp. xxviii and 288. H.M.S.O., London.
 Registrar-General's Statistical Review of England and Wales for 1910. Tables, Part I, Medical. H.M.S.O., London.
 Ibid., 1921. Tables, Part I, Medical.
 Ibid., 1931. Tables, Part I, Medical.
 Ibid., 1938. Tables, Part I, Medical.
 Ibid., 1959. Part I, Tables, Medical.
 Ibid., 1960. Part I, Tables, Medical.
 Ryle, J. A., and Russell, W. T. (1949). *Brit. Heart J.*, **11**, 370.
 Wood, P. H. (1956). *Diseases of the Heart and Circulation*, 2nd ed. Eyre and Spottiswoode, London.

CASE-FINDING BY SERIAL TUBERCULIN-TESTING OF SCHOOLCHILDREN

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The main purpose of a serial tuberculin-testing programme is to detect recently infected persons among those tested and to trace the source of their infection in the population at large. It entails screening a group of individuals with tuberculin tests at regular intervals and selecting subjects for radiographical examination according to the results of those tests. Such a programme requires that the tuberculin test used be safe, cheap, reliable, easily carried out, and readily acceptable to those asked to participate, who, on their part, must be an easily organized accessible group exposed to the risk of tuberculous infection.

These were the main considerations leading to the institution, in 1958, of an annual serial tuberculin-testing programme for 45,000 Cardiff schoolchildren.

Methods

The work of tuberculin-testing the schoolchildren, recording results on individual record cards, carrying out epidemiological investigations, and arranging radiographical examinations was carried out by three full-time junior clerks, two part-time nurses, and two health visitors, who were also engaged on other duties. An account of the organization of the programme and the results of the first

year's work have already been published (Griffith, Bellamy, and MacFarlane, 1960).

Only the Heaf tuberculin test was used. The tuberculin reactions, seen on the seventh day, were graded as follows:

- Tuberculin-negative
 No reaction or any reaction not amounting to grade I.
 Tuberculin-positive
 Grade I: Four or more palpable indurated areas.
 Grade II: An unbroken ring of induration.
 Grade III: A plateau of induration.
 Grade IV: Any reaction more severe than grade III (blister, ulcer).

Every school in Cardiff was visited during each of the four school years 1958-9 to 1961-2 inclusive, and every child in each school given an opportunity of receiving a tuberculin test each year. The only children not tested during any particular year were those whose parents had withheld consent, persistent absentees, and a small number who were known to have received treatment for tuberculosis.

Results

The results of the radiographical examination of children and their adult home contacts have been grouped according to the grades of the tuberculin reactions of the children and the known results of their previous tuberculin tests.

This gave three main groups of unvaccinated tuberculin-positive children: those who had not been previously tested, those who were tuberculin-positive when previously tested, and those who were tuberculin-negative when previously tested. The adult home contacts of children in the first and last groups were also requested to attend for radiographical examination.

Examination of Tuberculin-positive Schoolchildren

Children Tuberculin-positive at Their First Test.—All the unvaccinated children found to be tuberculin-positive during the initial year of the programme were considered to be in this category, but they were too numerous for all to be visited at home and offered appointments for chest radiography, together with their adult home contacts. Only children with grade III or IV reactions were therefore requested to attend the chest clinic for examination, but 358 out of 1,905 either failed to attend the clinic or were examined in clinics outside the city. A small number (127) of children with grade I or II reactions attended for examination, mainly because their siblings at the same schools, but with larger reactions, had been given appointments. Nearly three-quarters (1,214 out of 1,674) of all examinations of children in this category occurred during the first year of the programme. Only a minority consisting of new school entrants, newcomers to the area, and the previous year's absentees, received their first tuberculin test during the second and subsequent years of the programme. Thirteen children in this category were found to be definite cases of pulmonary tuberculosis, giving an incidence rate of 8 per 1,000 examinations (Table I).

TABLE I.—*Radiographical Examination of Unvaccinated Children, Tuberculin-positive at Their First Test*

Tuberculin Reaction	No. of Children			Incidence Rate per 1,000 Examinations
	Positive at First Test	Examined	Diagnosed as Definite Cases of Pulmonary Tuberculosis	
Grade I ..	1,404	25	0	—
" II ..	751	102	0	—
" III ..	1,160	948	7	7
" IV ..	745	599	6	10
Total ..	4,060	1,674	13	8

Children Known to have been Tuberculin-positive for 12 Months or Longer.—Children with grade III or IV reactions at their second or subsequent tests and who had been tuberculin positive previously were sent appointments by post for radiographical examination at the chest clinic, irrespective of the number of examinations already carried out during previous years. The majority of these children had high-grade tuberculin reactions each time they had been tested and had been examined radiographically. A small minority had been only grade I or II positive previously and were now receiving their initial examination on first showing grade III or IV reaction. A total of 2,379 examinations were carried out, 2,176 involving children who had grade III or IV reactions at their second test. The other 203 were mainly siblings of children given appointments.

TABLE II.—*Examination of Children Who Had Been Tuberculin-positive for 12 Months or Longer*

Tuberculin Reaction at Last Test	No. of Examinations of Children Positive 12 Months or Longer	No. of Children Diagnosed as Definite Cases of Pulmonary Tuberculosis	Incidence Rate per 1,000 Examinations
Grade I ..	18	0	—
" II ..	185	0	—
" III ..	1,423	2	1.4
" IV ..	753	0	—
Total ..	2,379	2	0.8

Two new definite cases of pulmonary tuberculosis were discovered, giving an incidence rate of 0.8 per 1,000 examinations (Table II).

Tuberculin Converters.—Children who were tuberculin-negative one year but positive the next were classified as recent tuberculin converters. They had acquired their tuberculin sensitivity as a result of a sensitizing infection during the 12 months preceding the first positive tuberculin reaction. It was intended originally to examine radiographically all tuberculin converters and their home contacts, but the yield from among converters to grade I sensitivity was so low and the amount of work entailed so great that such converters found during the third and fourth years were not offered radiographical examination. The incidence of previously undiagnosed pulmonary tuberculosis was exceptionally high in recent tuberculin converters to grade III or IV reactions, but not among recent converters to grade I or II reactions. A fifth (20%) of those with grade III reactions and nearly half (45%) of those with grade IV reactions were found to be suffering from radiographically demonstrable pulmonary tuberculosis.

TABLE III.—*Tuberculin Converters*

Tuberculin Reaction after Sensitization	No. of Converters	No. Examined	No. of Definite Cases	Incidence Rate per 1,000 Examinations
Grade I ..	1,917	315	0	—
" II ..	94	78	1	13
" III ..	41	40	8	200
" IV ..	20	20	9	450
Total ..	2,072	453	18	

Examination of Adult Home Contacts

Contacts of Children who were Tuberculin-positive at Their First Test.—These adults were examined as household contacts of unvaccinated children found to be tuberculin-positive at their first test at school. There was no indication when these children had been infected, although known tuberculosis cases resided in the homes of some and their contacts had already been examined. Adults in the remaining households had previously no reason for seeking radiographical examination. These adults constituted the majority of those examined in this group. Nearly 90% of adults examined (1,679 out of 1,897) were household contacts of grade III or IV reactors. Thirteen new definite cases of pulmonary tuberculosis were discovered among the 1,679 adult contacts of grades III and IV reactors, giving an incidence rate of 8 per 1,000 examinations (Table IV). This rate is approximately the same as for the corresponding children (Table I). More than half of these examinations (1,011 out of 1,897) occurred during the initial year of the serial testing programme. It should be pointed out that the majority of households had more than one schoolchild and that the grades of tuberculin reaction elicited in these children varied. Under the circumstances Table IV is compiled according to the first child in the family found to be tuberculin-positive to such an extent as to make it necessary to advise the family to attend for examination.

TABLE IV.—*Examination of Adult Home Contacts of Children Tuberculin-positive at Their First Test*

Tuberculin Reaction of Children	No. of Adult Home Contacts		Incidence Rate per 1,000 Examinations
	Examined	With Progressive Lesions	
Grade I ..	59	0	—
" II ..	159	0	—
" III ..	1,045	8	8
" IV ..	634	5	8
Total ..	1,897	13	

Examination of Adult Home Contacts of Converters.—Children from the homes of these adults had become sensitized to tuberculin during the 12 months before the radiographical examinations were carried out. These recent infections usually occurred in households where there had been no previously known cases of tuberculosis and where no previous investigations had been carried out. During the last two years only a few adult contacts of recent converters to grade I were offered radiographical examination for reasons given earlier. The incidence rate among the adult home contacts of converters to high-grade sensitivity was exceptionally high, but no case of pulmonary tuberculosis was found among contacts of converters to low-grade sensitivity (Table V).

TABLE V.—*Examination of Adult Home Contacts of Converters*

Tuberculin Reaction of Converters	No. of Adult Home Contacts		Incidence Rate per 1,000 Examinations
	Examined	With Progressive Lesions	
Grade I	263	0	—
“ II	130	0	—
“ III	85	6	70
“ IV	49	5	100
Total	527	11	

Examination of Child Contacts.—Child contacts of schoolchildren with Heaf grade III or IV reactions had usually been tuberculin tested by the time the adult contacts received radiographical examinations. The majority of these child contacts had already been tested in the same school as the index child, and the results of their examinations are included in Tables I–III. Nevertheless, two cases of pulmonary tuberculosis were discovered among pre-school-age siblings of tuberculin converters; one was a baby aged 10 weeks (contact of a converter to grade III reaction) and the other a boy aged 4 years (contact of a converter to grade IV reaction).

Discussion

An evaluation of serial tuberculin-testing a group of individuals as a means of detecting recent infections and new cases of tuberculosis in a community was studied by Gedde-Dahl (1952) from 1937 to 1944, when he tested annually the population of a town of 6,500 inhabitants. This present survey differs from his work inasmuch as the tuberculin-testing has been confined to the school population of a city of over 250,000 inhabitants and an attempt has been made to relate the results of radiographical examinations with the grade of tuberculin reaction elicited in the children.

A total of 57 previously undetected new definite cases of pulmonary tuberculosis were discovered in Cardiff over a period of four years as a result of examinations carried out under this serial tuberculin-testing programme. They amounted to 8% of all the notifications received during those four years and accounted for half the notifications of persons under 15 years of age. On the other hand, the

TABLE VI.—*Notifications of New Cases of Pulmonary Tuberculosis in Cardiff 1958–9 to 1961–2*

School Year	No. of New Notifications of Pulmonary Tuberculosis in Age-groups							
	From All Sources				Resulting from Serial Tuberculin-testing			
	0–14	15–44	45+	Total	0–14	15–44	45+	Total
1958–9	23	115	99	237	9	10	3	22
1959–60	17	91	74	182	11	4	0	15
1960–1	13	72	67	152	7	2	1	10
1961–2	13	52	70	135	6	2	2	10
Total	66	330	310	706	33	18	6	57

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serial tuberculin-testing programme accounted for less than 2% of notifications of persons aged 45 years or over during that period (Table VI). This suggests that there may be little contact between elderly undiagnosed tuberculous persons and children.

Table VI also reveals that the yield obtained from the serial tuberculin-testing programme decreased from year to year as, presumably, the prevalence of infection decreased. The initial year's work yielded 22 new cases of tuberculosis, which was nearly 40% of the total yield for the four years and two more than the entire yield from the work of the last two years.

The group of children found with grade III or IV reactions to their first tuberculin test had been infected at some unknown period during their lifetime. Some had been infected during the previous 12 months, but others had been infected more than a year previously. It was not possible to distinguish one set of children from the other. The second set consisted of some who had already been examined under some other arrangements and had been found fit after infection had occurred (contacts from known tuberculous homes) and some from homes where there were no known cases of tuberculosis and who had not developed symptoms or signs of ill-health to warrant medical investigations during the years after infection had occurred. Sufficient time had elapsed since infection had occurred for the disease to have become manifest clinically in some children with the result that if they had been diagnosed they would have already been removed from this group. The children undergoing radiographical examination therefore consisted of those who had survived for 12 months or more after infection without showing signs and symptoms of disease and those infected during the last 12 months. This also applied to the adult contacts of these children.

It is not surprising, therefore, that the yield of new cases obtained by the examination of these children and their adult contacts was not particularly high—8 per 1,000 examinations of children and of adult contacts. It is probable that most of the cases discovered were in households where the children had become tuberculin-positive only during the preceding 12 months. If that were so, radiographical examination of strong positive reactors found by tuberculin surveys and their adult contacts would give a disappointing yield in a community where the prevalence of tuberculous infection was decreasing rapidly. Conversely, in communities where its prevalence was increasing a radiographical examination of strong reactors would give a high yield of new cases.

Re-examination of children with high-grade reactions known to have been tuberculin-positive 12 months previously revealed only two new cases of pulmonary tuberculosis from over 2,000 examinations, an incidence rate somewhat lower than that obtained by the Medical Research Council (1956), who reported an incidence rate of 3.5 per 1,000 per annum among adolescents with reactions of 15 mm. or more to an initial 3 T.U. O.T. Mantoux test. The subjects and the follow-up are not completely comparable, for the Medical Research Council's follow-up occurred almost a decade earlier and the subjects were adolescents, but these factors are insufficient to explain the difference in the findings. The results obtained in Cardiff would indicate that annual re-examination of initially radiographically clear high-grade reactors gives only a low yield of new cases. No case of pulmonary tuberculosis was found among those children who had low-grade reactions one year but high-grade reactions the next.

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.

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REFERENCES

- Gedde-Dahl, T. (1952). *Amer. J. Hyg.*, **56**, 139.
Griffith, A. H., Bellamy, M. J., and MacFarlane, J. K. (1960). *Tubercle (Lond.)*, **41**, 233.
Medical Research Council (1956). *Brit. med. J.*, **1**, 413.

DECLINING TUBERCULIN SENSITIVITY WITH ADVANCING AGE

BY

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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 <i>et al.</i> (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 <i>et al.</i> (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.