Evans (1939), quoting Brash, adds: "This general conclusion, however qualified, is inescapable. It raises resorption to a position of great importance and significance." In 1943 McLean stated: "It thus appears that the decalcification of bone by resorption, involving simultaneous dissolution of both its organic and its inorganic constituents, must be substituted for that of decalcification."

The present work was limited to the isolation in pure culture of one particular organism constantly found in carious material and capable of attack on collagen in cartilage and in bone. Lysis of bone seemed to occur more readily in screw-top phials than in test-tubes plugged with cotton-wool. Lowering of O_2 tension and accumulation of CO_2 occur in cultures in sealed containers.

In 1896 Mall tested the effect of enzymes and of heat (72° and 100° C.) on proteins, finding that exposure to heat followed by exposure to a proteolytic enzyme (e.g., trypsin) produced a greater degree of hydrolysis than either heat alone or the enzyme alone. In the present work there seemed little difference when cartilage was exposed to either 57° C. or 100° C., or autoclaved at about 121° C., though quantitative estimations of hydrolysis were not carried out on cartilage, gross observation appearing adequate. Maximow and Bloom (1942) consider the organic framework of bone to be apparently identical with the collagen of ordinary connective tissue. It is called bone collagen, or ossein. Gelatin is formed from collagen by moist heat. Before they were exposed to proteolytic bacteria, moist heat was applied to both cartilage and bone to sterilize them. The results seen, then, followed exposure to two sets of hydrolytic agents—heat and bacteria. Since Bhagvat and Sreeramamurthy (1944) showed that gelatin (with acid added) was hydrolysed at 120° C. in 45 minutes, it will be clear that sterilization may have caused some degree of hydrolysis.

Some of the above points have been paralleled by other workers. Kowaleski (1940) found collagen to be attacked by mixed cultures from leather works and that Gram-negative bacilli were partly responsible for this attack. Gram-negative bacilli have been shown in the present work to be capable of proteolytic action. The fact that gelatin-peptone bouillon may slowly darken to brown on incubation with bacteria at 37° C. was noted by Drummond (1914). I observed similar appearances with cartilage lysis. Kowaleski (1940) found no bacterial hydrolysis of collagen at pH 5 or 6.5, but maximum action at 7.5. I found the pH value of cultures in which lysis of bone has occurred to vary between 6.5 and 7.5.

These various points bear on relevant aspects of the work, and it will in fact appear that the underlying concept—i.e., that Gram-negative bacilli might attack both the collagen of cartilage and that of bone—existed in full before the present work was started, though it provides evidence bearing out these findings and joining them in one conclusion.

Summary

Tests of the effect on cartilage and bone of bacteria associated with dental caries are described.

Cartilage and bone sterilized by heat are shown to be broken down when incubated at 37° C. in the presence of bacteria taken from carious teeth.

Pure cultures of a bacillus repeatedly isolated from carious teeth are shown to be capable of attacking some proteins.

Following bacterial hydrolysis at 37° C., quantitative estimations of free amino-groups have been made by the use of Sorenson's formol titration method. Bacterial hydrolysis of bone collagen is shown to have occurred in media with pH values close to 7.

Two stages of attack on bone are presented, one more advanced than the other.

Acknowledgments

The encouragement and continued interest of Prof. Margaret Murray, Bedford College, University of London, are gratefully recognized. The possibility of extending work on tooth structure to bone was first brought to notice by Profs. Raper and F. C. Wilkinson, both of the University of Manchester. Laboratory facilities and clinical material have been made available by the University of Manchester and by the Westminster Hospital School of Medicine, the latter through the kindness of Mr. R. S. Taylor. Dr. Fairbrother suggested the use of media containing penicillin. Specimens of bone and cartilage were obtained through the courtesy of the Corporation of Manchester. Miss Dempsey kindly provided microtome preparations and photomicrographs by the courtesy of the British Leather Merchants' Research Association. The Medical Research Council has generously provided financial assistance. For all these facilities I wish to record my sincere thanks.

The research, which is primarily on dental caries, is now, through the kindness of Prof. Samson Wright, being carried on in the Department of Physiology, Middlesex Hospital Medical School.

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THE YEARLY RE-EXAMINATION OF A FACTORY GROUP BY MASS MINIATURE RADIOGRAPHY

BY

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The importance of the periodic re-examination of factory and similar groups by mass miniature radiography after an initial survey is generally recognized, and only the shortage of sets and personnel has prevented its routine application. There has not, however, been the same agreement upon the interval which should elapse between surveys. For instance, a three-monthly check has been advocated in some quarters as necessary if the early case of tuberculosis is not to be missed, while Reid (1940, 1941), in America, has formed the conclusion, after considerable experience of the radiological re-examination of personnel of the Metropolitan Life Insurance Company, New York, that a yearly interval is adequate.

The present paper gives the results of the yearly re-examination for four years of personnel of Factory A of the Medical Research Council's Report on Mass Miniature Radiography of Civilians (1945). The findings of the initial re-examination have been published previously as a supplement to the above report.

The surveys under review differ from those reported by Reid in two important particulars—namely, no pre-employment radiography was undertaken, and the annual fluorographic examinations were entirely voluntary and in no way part of a yearly medical check-up. Nevertheless, as is shown below, there has been a marked diminution in the number of significant lesions found in the factory.

It will be realized that the personnel of a factory is constantly changing, and that at each re-examination there is a proportion of persons who have not previously been employed. The following two factors relating to Factory A will help to give an indication of the changing structure of the group. First, the labour turnover in the factory averaged about 24% annually; and, secondly, during the period of the survey the number of employees contracted by approximately 20% each year until the final twelve months, when it expanded by about 10%.

For the purposes of the survey the examinees were placed in one of the following three categories: (1) those who were employed at the factory during the survey of the previous year and who were fluorographed at that time, hereafter designated "EX"; (2) those employed but not examined during the previous survey, "EO"; and (3) those newly employed, "OO." The number of persons in each of these groups together with the volunteer response is given in Table I.

TABLE I

Year	No. of Volunteers	Response	EX Group	EO Group	OO Group
1944	3,539	83%	2,912 (82%)	148 (4%)	479 (14%)
1945	2,649	81%	2,218 (84%)	214 (8%)	217 (8%)
1946	1,987	74%	1,300 (65%)	107 (5%)	580 (29%)
1947	1,843	61%	1,254 (68%)	282 (15%)	307 (17%)

It will be seen that there has been a steady fall in the volunteer response. That this is not due to any waning of enthusiasm as the result of previous visits is suggested by the fact that a similar drop in response, when compared with the war years, is a common finding in surveys to-day. Fear of loss of employment following the discovery of disease (a much more definite possibility now), or the rather general ennui which has been prevalent, may account for the fall. Adequate education of the public in the importance of repeated fluorographic examination is the true answer to this problem of response.

As it was not the policy of the factory management to dismiss from their employ workers who were found to have a significant lesion, it was to be expected that there would be a considerable increase in the number of persons with known lesions who presented themselves for examination. That this was so is shown in the last column of Table II. In this group were cases being kept under observation whilst remaining at work and those who had returned to work after successful treatment at hospital or sanatorium. Ten cases in this group showed evidence of hitherto unsuspected relapse.

An analysis of the findings in the factory as a whole and irrespective of whether or not the individual examinee had been fluorographed a year previously is shown in Table II.

TABLE II.—Analysis of Total Fluorographed

Year	No. Examined	Observation Cases	Treatment Cases	Total (O. + T.)	Known Cases
1943 (M.R.C.)*	4,720	51 (1.1%)	15 (0.3%)	66 (1.4%)	24 (0.4%)
1944	3,539	23 (0.6%)	7 (0.2%)	30 (0.8%)	37 (1.0%)
1945	2,649	6 (0.2%)	2 (0.1%)	8 (0.3%)	34 (1.3%)
1946	1,987	8 (0.4%)	2 (0.1%)	10 (0.5%)	26 (1.3%)
1947	1,843	8 (0.4%)	2 (0.1%)	10 (0.5%)	22 (1.2%)

* A larger survey by the Middlesex Unit in 1944 of some 34,000 factory employees produced a very similar proportion of cases—i.e., observation 1%, treatment 0.3%, and known 0.4% (Dick, 1945).

The figures for the original M.R.C. survey in 1943 are included for comparison. It will be seen that at the initial re-examination of the factory after one year the percentage of newly discovered significant lesions fell to approximately one-half of the M.R.C. findings. All three subsequent

surveys showed a further fall, giving a percentage of cases equivalent to about one-third of the 1943 figures.

A comparison of the findings in Groups OO and EX is shown in Table III. The proportion of significant lesions among the new employees is similar to that found in the general population. The fall noted in Table II is seen to have its origin in Group EX. That the rate of declension is very similar in Tables II and III is due to the relatively small number of new employees examined each year. The proportion of observation to treatment cases in the EX group is higher than in the OO group or in the original M.R.C. survey, in spite of the fact that one would expect a tendency to place in the treatment class cases having had a negative film at the previous survey. This can be accounted for by the minimal extent of the lesions found.

TABLE III.—Analysis of EX and OO Groups

Group	Year	No. Examined	Observation Cases	Treatment Cases	Total (O. + T.)
OO	1944-7	1,583	14 (0.9%)	5 (0.3%)	19 (1.2%)
EX	1944	2,912	18 (0.6%)	4 (0.1%)	22 (0.8%)
EX	1945	2,218	4 (0.2%)	2 (0.1%)	6 (0.3%)
EX	1946	1,300	4 (0.3%)	1 (0.1%)	5 (0.4%)
EX	1947	1,254	4 (0.3%)	0	4 (0.3%)

Of the 37 cases with significant lesions in Group EX 36 were minimal in extent using the diagnostic standards of the National Tuberculosis Association of America (1940). The remaining case was that of a woman aged 29 who was found to have far-advanced disease with excavation and who subsequently died. She gave a history of having had a productive cough, with pains in the chest, and severe headaches for three months. She was losing weight. She well illustrated the fulminating type of phthisis with little or no resistance. Since the introduction of mass radiography it is often possible to show that this type of case has had a negative film only a few months before being diagnosed, thus confirming the rapid onset of this malignant form of the disease.

A follow-up after one year of the 26 observation cases found in Group EX in 1944-6 showed that 5 (1 man and 4 women) had relapsed. All were under 30 years of age. In addition 5 (2 men and 3 women) of the 7 original treatment cases in this group were under 30.

During 1944-7 there were examined 751 persons who, though employed at the factory at the time of the immediately previous survey, had not then been x-rayed. Only two cases with significant lesions were found, both in 1947. One, a man aged 30, was kept under observation while remaining at work; the other, a girl aged 18, required sanatorium treatment.

In addition to those cases of pulmonary tuberculosis found by mass radiography there were others diagnosed between surveys, in persons with a previously negative fluorograph, as the result of the development of symptoms. The type of disease, the duration of symptoms, and the time interval between fluorography and diagnosis are shown in Table IV.

TABLE IV.—Analysis of Cases found Between Surveys Following a Negative Fluorograph

Year	Sex	Age	Type of Disease	Interval between Fluorography and Diagnosis	Duration of Symptoms before Diagnosis
1943-4	F	20	Post-primary, minimal	8 months	1 month
"	F	21	Plural effusion	9 "	1 "
"	F	21	Post-primary, far advanced	11 "	4 months
1946-7	M	33	Post-primary, moderately advanced	17 "	4 "

Comments

It would appear from these results that a year is a suitable interval between surveys, thus supporting Reid's findings in America. However, the public must be educated in the advantage to be obtained from a periodic x-ray examination of the chest, as only by an adequate response can the scheme become fully effective. The fact must be stressed that a negative fluorograph is no guarantee that an abnormality will not develop at some future date.

The considerable fall in the number of cases of pulmonary tuberculosis found seems to be due to at least two factors; (1) the discovery of the early observation lesion with the chances of its subsequent control; and (2) the diminution of the infector pool. The early removal of the infective case must greatly lessen the incidence of disease among its contacts of all ages is generally admitted, and has been demonstrated in contact work at the Ealing Chest Clinic (Dick and Thompson, 1946). This preventive aspect of mass radiography is probably not fully appreciated.

Also, by finding cases *before* they have become sources of infection to their fellows and not, as is more usual if diagnosis has to wait on symptoms, after they have broadcast bacilli for many months or even years, the infector pool is prevented from being restocked. In this light the importance of mass radiography as a preventive measure is truly seen.

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Medical Memoranda

Transmission of Syphilis

In a previous communication it was shown that the transmission of syphilis was possible during the incubation stage in the male (Ross, 1939). It was suggested that the semen was infectious and that seminal transmission of the disease had occurred in the case quoted. A case has recently occurred in which the male was suffering from sero-negative primary syphilis and according to some standards was adequately treated. It is again suggested that the method of transmission was by the seminal fluid.

CASE RECORD

On April 1, 1947, a married woman aged 31 reported at a clinic complaining of discomfort in the genital area. She stated that her husband was home on leave in July, 1946, and led a normal married life. In November he was demobilized, but did not resume marital relations. She was of the opinion that her husband realized that she was fatigued by the attention she had to give to a child of the marriage 18 months old who was in indifferent health. However, during the New Year celebrations, while he was partially intoxicated, intercourse occurred on two occasions, and thereafter was discontinued. At the end of January she experienced some discomfort in the genitals, but as this passed off in a few days she did not seek advice. Towards the end of March the discomfort returned and she reported at the clinic. No extramarital intercourse was admitted.

On examination numerous small superficial circular ulcers were found on the labia minora and perineum. Inguinal lymphadenopathy was marked but no other signs were present. Dark-ground examination showed *Treponema pallidum* in serum from the ulcerated areas and the blood Wassermann reaction was strongly positive. A diagnosis of early syphilis was therefore proved, but it was difficult to decide whether it was a case of early secondary syphilis or of

sero-positive primary syphilis with multiple lesions. The date of infection must have been about Jan. 2.

The husband was found to be attending a male clinic, and his history was of illicit intercourse in August, 1946, followed three weeks later by a primary lesion of the penis. *T. pallidum* was found in the lesion, but the blood Wassermann reaction and Kahn tests were negative. He was treated in a military hospital for ten days and received 30,000 units of penicillin in aqueous solution every three hours to a total of 2.4 mega units. Thereafter weekly injections of neoarsphenamine and bismuth were continued till Oct. 31, when the total dosage was 2.85 g. of neoarsphenamine and 1.2 g. of bismuth.

He came under the care of the civilian clinic on Dec. 18 and presented no signs of syphilis. The blood Wassermann and Kahn tests were negative. On that day and on Jan. 2 and 8, 1947, he was given 0.6 g. of neoarsphenamine and 0.12 g. of bismuth. He defaulted from treatment, and except for one visit on Feb. 21 was not seen till April 8, when he was clinically and serologically negative.

Thus it would appear that the male patient, infected in August, whose treatment was begun during the sero-negative primary stage in September and continued until Oct. 31 and whose blood Wassermann and Kahn reactions were negative on Dec. 18, was still capable of transmitting the disease during sexual intercourse on Jan. 1 or 2. Further, in spite of the lack of treatment between Jan. 8 and April 8, he was clinically and serologically negative on the latter date.

Therefore the question arises, When is a male who has suffered from syphilis non-infectious? From occasional cases seen in the past twenty years one is confirmed in the belief that the time factor is of more value than the serological test for syphilis. In support of this belief another conjugal case is quoted.

In March, 1936, a woman aged 32, married some eight months, reported with periostitis of both tibiae of the type associated with early syphilis. She gave no history of extramarital intercourse. Her blood Wassermann was strongly positive, and it was thought advisable to ask for the attendance of the husband. He proved to be a defaulter from treatment, but all tests of blood and cerebrospinal fluid were normal.

He was first treated in London in February, 1932, for secondary syphilis. In July of that year his blood Wassermann was negative and a second course of treatment was begun, but he defaulted and received only 2.25 g. of neoarsphenamine and 1.2 g. of bismuth. In August, 1934, he returned with acute gonorrhoea, and, since there were no signs of syphilis and his blood Wassermann was negative, no treatment for syphilis was given.

If the facts and implication of this case are accepted then a three-years history of negativity is not sufficient to exclude the possibility of the infectivity of the semen in a syphilitic. On the other hand, it is a matter of everyday experience that a male whose infection is of more than five years' duration, whether his serological tests are negative or positive, is extremely unlikely to infect his wife.

The advice, therefore, that should be given to an adequately treated male is that he should not attempt to procreate children until five years after the date of his infection.

Since this paper was written Leeming (1947), quoting a personal communication from D. A. Erskine, gives reasons for the belief that men treated for gonorrhoea by adequate doses of penicillin may, in a prolonged sero-negative syphilis d'émblée, infect their wives.

My thanks are due to Dr. R. B. Nelson, whose notes on one of the cases have been quoted.

July, 1947.

A. O. F. ROSS.

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The Minister of Health has received letters of thanks from the French Minister of Industrial Production and the Minister of Public Health for medical help given after the Lorraine mining disaster in January. The Ministry granted facilities for Sir Archibald McIndoe, the plastic surgeon, of Queen Victoria Hospital, East Grinstead, and Squadron-Leader F. T. Moore, R.A.F. Medical Service, who is working with him, to fly to the scene of the disaster. The Ministry also arranged for large supplies of plasma from the National Blood Transfusion Service to be flown across for use in treating casualties. The French Minister of Production in his letter to Mr. Bevan wrote: "This outstanding assistance, so spontaneously extended, has been appreciated in all its value, and both the Government and the nation feel it to be yet another sign of the friendship which binds our two countries."