THE ESTIMATION OF PLASMA PHOSPHATASE

as a Test indicative of the

PROGNOSIS OF TUBERCULOUS LESIONS OF BONES AND JOINTS

A Thesis presented for the Degree of M.D., Glas.

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WILLIAM ANDERSON MURRAY, M.B., Ch.B., Glas.

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

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Introduction.

The assessment of activity of tuberculous lesions of bones and joints is at present a matter of combining general impressions with X-ray findings, and the experience of previous similar lesions, as to the time of immobilisation necessary. The red-cell sedimentation rate, which is generally, and very usefully, employed in pulmonary tuberculosis, does not give an equally useful indication as to the activity, or otherwise, of bone or joint lesions. The writer carried out routine blood sedimentation tests in adults and children suffering from bone or joint tuberculosis, who had been under treatment for varying periods. The results were found in many cases to be at complete variance with the clinical signs and, in the few cases which were followed up, sufficient variation was found to indicate that the test was not sufficiently reliable to form an indication as to the degree of healing present.

Temperature records and even fairly free exercise and weight bearing have also proved unreliable, in many cases, and the question of when one may consider that a tuberculous lesion of bone is sufficiently quiescent to allow freedom from immobilisation, or to permit of the operative interference, which is sometimes necessary to obtain a good functional result, is one which is at present extremely difficult to answer with any degree of assurance. A clinical test which would bear a similar relation to bone and joint tuberculosis, as that of red-cell sedimentation to pulmonary tuberculosis, would be invaluable.

The attention of the writer was drawn to the work which had been carried out in the estimation of plasma phosphatase, especially in cases of generalized bone disease (osteitis fibrosa and osteitis deformans). These pathological conditions are accompanied by variations in the amount of enzyme phosphatase in the blood plasma, and the suggestion was made that estimations of plasma phosphatase should be carried out in the case of children suffering from tuberculosis of bones and joints, and under treatment at the Manchester Sanatorium, Abergele, North Wales. It would obviously be of value if any connection could be established between any variations in the plasma phosphatase and the clinical and radiological evidence of activity, extent and duration of disease.

One might reasonably expect that, in cases where destruction of bone had taken place by absorption, an increase in the plasma phosphatase, parallel to that found in the generalized diseases investigated, would be found and, although the variations might be much less with localized lesions, the 400 to 1000% increase found in generalized disease seemed to promise a margin, within the limits of which, sufficient variation might be found to justify investigation.

The following work was therefore undertaken to ascertain whether variations from the normal plasma phosphatase were found in tuberculosis of bone, and whether such variations bore a sufficiently close relation to activity, extent, and duration of disease as to warrant the use of the estimation as a test of quiescence of such lesions.

In the course of the description of the work it will frequently be necessary to refer to the findings of H. D. Kay who did much investigation of the phosphatase content of the plasma, and whose method of estimation has been used in the present series. In a personal communication he states ". . . I am glad to know that you are investigating the plasma phosphatase in tuberculosis. So far as I know, no systematic work has been done on this point up to the present. . ."

Plasma Phosphatase in Tuberculosis of Bone in Children.

The phosphatase of the blood—the enzyme which is found to hydrolyze phosphoric esters such as glycerophosphate, hexophosphate, etc.—has been studied increasingly during the past few years. The earliest work indicated only that plasma had the property of slow hydrolysis of phosphoric esters contained in the red cells (1). Early work had been directed toward the location and estimation of phosphatases in various tissues, and Robison's work (2) as Hunter states (3), seemed to show that osteoblasts and hypertrophic cartilage cells secrete a very active phosphatase which, by hydrolyzing the phosphoric esters of the blood, brings about a local increase in the concentration of phosphate ions, and, the solubility product of tertiary calcium phosphate being exceeded, deposition of this salt takes place in the ossifying zone. This work suggested that the enzyme concerned had a definite role in bone physiology and particularly in the process of ossification, and Hunter (3) summarises the evidence as follows:—

(1) "Phosphatase is present in growing bone in greatest amount in those areas in which deposition of calcium phosphate is taking place most rapidly.

(2) "It can be demonstrated, in vitro, that a growing bone split longitudinally is still capable of the deposition of calcium phosphate from a solution of a soluble calcium phosphoric ester salt, such as calcium hexosemonophosphate or calcium glycerophosphate, and that deposition occurs mainly in the cells in the zone of provisional calcification.

(3) "Phosphatase appears in cartilage simultaneously with the appearance of centres of ossification.

(4) "There is no phosphatase in cartilage which is not ossifying.

(5) "There is a substrate for the enzyme present in the red cells, and also in circulating plasma.

(6) "In certain generalized diseases of bone the plasma phosphatase is high."

This last observation refers to his own work which confirmed and extended the work of H. D. Kay (Department of Biochemistry, Toronto University) (4) who in 1926 evolved a principle for the estimation of tissue phosphatase, and

then turned his attention to the possibility of estimating the amount of phosphatase in the blood plasma (or possibly more correctly the activity of the phosphatase in blood plasma) (5). He found that the quantity of the enzyme in normal plasma was relatively small and that the pH suitable for comparison of the relative activity of two enzymes was not that of normal plasma.

Using a method which, he later confessed, was tedious, involving a pH correction and incubation of tubes for 48 hours, he was able to show that lesions of the bones such as osteitis deformans and osteitis fibrosa, which involved a large portion of the skeleton, were accompanied by a very definite rise in the plasma phosphatase.

This finding, as Kay suggests, tended to confirm Robison's hypothesis that the phosphatase present in bone is one of the essential factors in ossification and in the maintenance of bone, as the diseases named, demonstrating a widespread disturbance of bone metabolism, showed also a marked increase in the phosphatase activity of the blood plasma. Kay originally made no speculation as to the exact significance of his findings with regard to the pathology of bone absorption or overgrowth, but suggested that the work should be extended to examinations of other diseases, in man and animals, associated with bony changes, in an effort to obtain information along these lines.

He later (6) stated, after reviewing the evidence in favour of the importance of phosphatase in bone physiology, in almost exactly the same words as those used by Hunter, and previously quoted, that the result of his work tended to confirm the opinion that, to understand the biochemistry of bone formation, maintenance, and pathology, emphasis should be laid as much on the metabolism of phosphoric acid as on that of calcium.

In the same paper he discussed the question of whether the increased phosphatase in the plasma in bone disease was a cause or an effect. The evidence tended to show that it was an effect, direct or indirect, and he speculated that the enzyme might leak out at more than normal rate on account of a compensatory increase of production, or that a mechanical squeezing out of cell contents might take place in crushed or bent bones.

He gave a few figures showing that it was not possible to prove that the plasma enzyme actually hydrolysed all or part of the circulating substrate for the bone enzyme before it reaches the bone, and that it could not therefore be established as a cause of the disease by virtue of such an action.

I shall refer later to the method and findings described in this work of Kay (1930).

Method of Estimation.

The original method of plasma phosphatase estimation described by Kay (5) in 1929 was, as I have stated, lengthy and required a pH estimation. In this method he expressed the enzyme activity as the number of milligrammes of P liberated as inorganic phosphate from excess of Sodium β glycerophosphate in 48 hours at 38° C. and at pH 7·6 by 1 c.c. of plasma. Under these conditions the normal adult plasma gave a content or activity of 0·124 units (average).

In 1932 (7) Kay published the following method which has various advantages over the older method. Less blood is required (2 c.c. plasma as compared with 5 c.c.), and this naturally an important consideration when it is intended to obtain blood from young children. The time of estimation is considerably decreased as by this method the incubation of the filtrates is cut down to 3 hours, and the total time occupied need not be more than 5—6 hours, during a considerable part of which other work can be undertaken. The omission of a pH estimation does away with the need for a comparator or solutions.

This method has therefore recommended itself to me as being more possible as a routine test, and more feasible in the opportunities available to a Resident in a busy hospital.

(a) **Solutions required.**

(1) Standard substrate.

This comprises (a) 1 part of 2·5% sodium β glycerophosphate with (b) 5 parts of glycine buffer solution.

These solutions were obtained from Messrs. Boots Pure Drug Co. and prescribed as follows :—

(a) Sodium β glycerophosphate 2·5 gm. of pure crystals dissolved in 100 c.c. distilled water.

(b) Glycine pure 6·06 gm. with 4·68 gm. pure sodium chloride dissolved in 328 c.c. of N/10 sodium hydroxide, and the solution made up to 1 litre with distilled water.

(2) Trichloroacetic acid 15%.

(3) Molybdic acid mixture made up as follows :—

1 part 10/N H_2SO_4 is mixed with 2 parts of distilled water, and 1 part 7·5% Na_2MoO_4 is added.

(4) Stannous chloride solution made by diluting ½ c.c. of 40% $SnCl_2$ (concentrated HCl solution) in 100 c.c. distilled water just before using. This solution is not to be relied upon for more than one day.

(5) Standard Phosphate solution, 1 c.c. to contain 0·1 mgm. P. Prescribed thus :—

Pure dry KH_2PO_4, 0·439 gm., dissolved in distilled water and made up to 1 litre.

From this solution further dilutions are made, viz. :—

(a) 1 c.c. standard solution diluted to 50 c.c. :
5 c.c. contain 0·01 mgm. P.

(b) 2 c.c. standard solution diluted to 50 c.c. :
5 c.c. contain 0·02 mgm. P.

(c) 3 c.c. standard solution diluted to 50 c.c. :
5 c.c. contain 0·03 mgm. P.

(6) 15% Potassium Oxalate Solution.

(7) 0·9% Sodium Chloride Solution.

The solutions of β glycerophosphate and the standard substrate were kept in a refrigerator as recommended by Kay. The glycine buffer solution and phosphate standard solution kept well in the laboratory with a little added chloroform. The molybdic acid mixture, and its constituent solutions, kept well at room temperature. The 40% $SnCl_2$ in concentrated HCl kept well.

A supply of small tubes fitting the laboratory centrifuge is necessary, and a plentiful supply of test tubes of more than 10 c.c. capacity is also necessary. For filtration, 7 cm. Whatman No. 30 (phosphate free) filter papers are used. Pipettes of 0·5 c.c., 1 c.c., 2 c.c., and 5 c.c. capacity are necessary, and as accurate measurement is essential, all except the 5 c.c. pipettes should be of the Ostwald pattern.

A water-bath at 38° C. is necessary, and a colorimeter is required for estimation of P in filtrates against the standards of known P content.

(b) **Procedure.**

5 c.c. of blood are withdrawn and put into a centrifuge tube with 2 drops of 15% potassium oxalate solution. The oxalate must be kept at a minimum as the colorimetric estimation is affected by larger quantities of oxalate in solution. The blood is centrifuged at about 3000 r.p.m. for 10 minutes, and the plasma is withdrawn carefully to avoid contamination with white cells. This is necessary as the leucocytes contain phosphatase enzyme, and it may be advisable to filter the plasma withdrawn through a small plug of cotton wool.

Exactly 2 c.c. of plasma is diluted with 2 c.c. of 0·9% NaCl and 0·5 c.c. of this mixture is placed in each of four clean test tubes.

To each of these test tubes 5 c.c. of substrate standard is added (solution (1)) and the contents mixed. Two of these tubes are stoppered, with clean rubber stoppers, and placed in the water-bath at 38° C.

To the other two tubes 2 c.c. of 15% trichloroacetic acid is added at once and the contents mixed. The tubes are allowed to stand for 10 minutes and the contents are then filtered through two filter papers. These filtrates are the "zero filtrates" and are later used to estimate the amount of enzyme activity in the incubated tubes.

After 3 hours the incubated tubes are removed from the water-bath and cooled rapidly under the cold water tap. To each tube trichloroacetic acid is added, as before, and the resulting precipitate filtered.

Four filtrates are thus obtained, two of which have been incubated. From each of these exactly 5 c.c. should be measured into a clean labelled test tube. Two tubes will be labelled "Zero filtrates," and two "Incubation filtrates."

The necessary amount of filtrate is often difficult to obtain and practice will show the necessity for accurate measurement of solutions throughout the estimation.

Two tubes of 5 c.c. standard phosphate dilutions (a) and (b) are made up and the tubes suitably labelled.

To the six tubes 4 c.c. of molybdic acid solution (solution 3) is added and then 1 c.c. $SnCl_2$ solution (solution 4). While this latter is being added it is necessary to stir and, as the final volume in each of the tubes should be kept within the limits of $10 \pm 0{\cdot}1$ c.c., it is necessary to use a clean dry rod to which drops will not adhere.

A deep blue colour develops in all six tubes and, after 3 minutes, the colour in the filtrate tubes should be read against the standard phosphate tube which is nearer in colour to them.

(c) **Colorimeter readings and calculation.**

The amount of P in the unknowns (filtrate) is calculated by the colorimetric formula

$$\frac{\text{Depth of standard in millimetres}}{\text{Depth of unknown in millimetres}} \times \text{concentration of standard in mgm. per c.c.}$$

This represents the amount of P in mgms. in 5 c.c. of the filtrates.

A duplicate result is available for both zero and incubation filtrates. (The duplicate determinations should agree within 3 per cent.).

The average P content of the two " Zero " tubes is subtracted from that of the " Incubation " tubes and the result represents the amount of inorganic phosphate liberated in 5 c.c. filtrate under incubation conditions. Previous to filtration the volume of the solutions was 7·5 c.c. (0·25 c.c. plasma, 0·25 c.c. NaCl, 5 c.c. substrate, and 2 c.c. trichloroacetic acid), so that the amount of P liberated during hydrolysis by 0·25 c.c. of plasma is $(\frac{7 \cdot 5}{5} \times$ the result of the subtraction of the zero tube content from the incubation tube content).

∴ 100 c.c. plasma would liberate 400 times the above subtraction.

The phosphatase content of the plasma is defined as the number of mgm. P which would be liberated by 100 c.c. of the plasma.

The average normal figure found by Kay was 6·06 new units of phosphatase so that comparisons may be made with results obtained by the old method if these results are multiplied by 50. (Old normal average 0·124).

In the method described the use of a strong buffer solution, in the quantity described, should be capable of maintaining the pH of the reaction mixture at 8·8 pH which is found to be close to the optimal pH for the phosphatase enzyme. Kay claims that the glycine-NaCl-NaOH buffer attains this end. Bodansky (8) described a method of the estimation of plasma phosphatase, in guinea pigs with experimentally produced osteitis fibrosa. He states that he found Kay's method unsatisfactory and that he found that an M/10 solution of sodium diethylbarbiturate (veronal) acted as a more efficient buffer. His method is, in other particulars, essentially similar to Kay's but the hydrolysis of the glycerophosphate is more rapid and incubation is carried out for 2 hours at 37° C.

Modification of method of estimation.

H. D. Kay in his paper (7) states that, in the case of generalized bone disease in which high plasma phosphatase is found, the original dilution of the plasma is insufficient and that colours, too deep to read with accuracy, result in the incubation tubes if the plasma is not further diluted.

He recommends that 1 c.c. of plasma diluted 1 : 1 should be further diluted by adding 4 c.c. (or even 9 c.c.) of 0·9 NaCl in such cases and that appropriate allowance for the dilution should, of course, be made in calculation.

He also states, in the same connection, that the standard phosphate solution (c) of which 5 c.c. contain 0·03 mgms. P gives too deep colour for regular accurate use, and that its use should be avoided by suitable dilution of the plasma which should if possible, keep the " hydrolysis " figures between 0·01 and 0·025 mgm. P.

Experimental estimations were carried out before those considered in this work and it was found that " incubation filtrates " were obtained in many cases which necessitated the use of Standard (c). To avoid this, and in case of still

higher figures, a suitable dilution of the plasma was sought. The dilution 1 : 3 was found to be generally useful and to give suitable readings, and this dilution was therefore used, along with the standard dilution, in the preparation of "incubation filtrates." The "incubation filtrate" tubes giving the colour nearest to standard solution (b) were estimated and, if these were the tubes containing plasma 1 : 3, suitable correction was made to allow for the smaller amount of plasma used.

An example of an estimation is given:

S.M. Case No. 36.

(1) Blood 5 c.c. centrifuged with 2 drops Potassium Oxalate Solution for 10 minutes.

(2) Plasma withdrawn carefully and filtered through cotton-wool.

(3) *Exactly* 2 c.c. plasma diluted with 2 c.c. of 0·9% NaCl in test-tube.

(4) To 2 c.c. of this dilution in a test-tube 2 c.c. 0·9% NaCl added (labelled 1 : 3).

(5) To four test-tubes 0·5 c.c. of original dilution pipetted.

(6) To two test-tubes 0·5 c.c. of 1 : 3 dilution pipetted (labelled 1 : 3 dilution).

(7) 5 c.c. Standard Substrate added to all six tubes.

(8) Two unlabelled and two labelled tubes put into water-bath after careful stoppering.

(9) To the other two tubes 2 c.c. 15% trichloroacetic acid added at once—mixed.

(10) In 10 minutes the contents of these tubes filtered carefully and resulting tubes labelled Zero Filtrate (A).

(11) After 3 hours from procedure (8) four tubes removed from water-bath and cooled rapidly under the cold-water tap.

(12) 2 c.c. 15% trichloroacetic acid added to all four tubes.

(13) After 10 minutes the contents of these four tubes filtered.

(14) Filtrates from unlabelled tubes labelled "Incubation Filtrate (A)."

(15) Filtrates from labelled tubes labelled "Incubation Filtrate (A)—1 : 3 dilution."

(16) Two clean test-tubes labelled "Zero Filtrate" and, into these, exactly 5 c.c. pipetted from tubes labelled "Zero Filtrate (A)."

(17) Two clean test-tubes labelled " Incubation Filtrate " and, into these, 5 c.c. pipetted from tubes labelled " Incubation Filtrate (A)."

(18) Two clean test-tubes labelled " Incubation Filtrate 1 : 3 dilution " and, into these, 5 c.c. pipetted from tubes labelled " Incubation Filtrate (A)—1 : 3 dilution."

(19) 5 c.c. of Standard solution (a) and 5 c.c. Standard solution (b) put into appropriately labelled test-tubes.

(20) To eight of the eight tubes, resulting from procedures 16, 17, 18 and 19, 4 c.c. molybdic acid added.

(21) To each of the eight tubes in turn 1 c.c. of Stannous Chloride dilution added, stirring being carried out by using a fresh, dry and clean glass for each tube.

(22) After 3 minutes colour developing in Filtrate tubes compared roughly with standards (a) and (b)

" Zero Filtrates " found to be both nearer to standard (a).

" Incubation Filtrates " (ordinary dilution) very close to standard (b).

" Incubation Filtrates 1 : 3 dilution " therefore discarded.

(23) " Zero Filtrates " and standard (a) read in colorimeter giving :—

1st tube — Depth of Standard = 40 mm.
Depth of Unknown = 42·4 mm.

$$\therefore \text{ Amount of P in mgm. in 1st Zero tube} = \frac{40}{42{\cdot}4} \times {\cdot}01 = {\cdot}0094$$

2nd tube — Depth of Standard = 40 mm.
Depth of Unknown = 45·4 mm.

$$\therefore \text{ Amount of P in mgm. in 2nd Zero tube} = \frac{40}{45{\cdot}4} \times {\cdot}01 = {\cdot}0088$$

$\therefore$ Average amount of P in 5 c.c. Zero Filtrate = ·0091 mgm.

(24) " Incubation Filtrates " and standard (b) read in colorimeter giving :—

1st tube — Depth of Standard = 20 mm.
Depth of Unknown = 16·8 mm.

$$\therefore \text{ Amount of P in mgm. in 1st Incubation tube} = \frac{20}{16{\cdot}8} \times {\cdot}02 = {\cdot}0238$$

2nd tube Depth of Standard = 20 mm.

Depth of Unknown = 17·3 mm.

$$\therefore \text{Amount of P in mgm. in 2nd Incubation tube} = \frac{20}{17{\cdot}3} \times {\cdot}02 = {\cdot}0231$$

$\therefore$ Average amount of P in 5 c.c. Incubation Filtrate = ·0234 mgm.

(25) Difference between Incubation and Zero Filtrates is therefore ·0234 — ·0091 = ·0143 mgm.

This represents the amount of inorganic phosphate liberated in 5 c.c. filtrate.

But the volume of the solutions before filtering was 7·5 c.c.

Therefore the amount of inorganic phosphate liberated by the plasma used $= \frac{7{\cdot}5}{5} \times {\cdot}0143$ mgm.

The amount of plasma used was 0·25 c.c.

$\therefore$ 100 c.c. plasma would liberate $\frac{7{\cdot}5}{5} \times {\cdot}0143 \times 4 \times 100 = 8{\cdot}58$ mgm.

$\therefore$ Plasma Phosphatase = 8·6 units.

Plan of Investigation.

In his early work Kay found (6) that there was a definite variation in plasma phosphatase according to age, and that the plasma of young normal children contained definitely more phosphatase than the normal adult. He gives the average of 8 normal children as 0·26 as against 0·15 for adults. In very young rabbits (4—10 weeks) he found that the phosphatase content averaged about 0·62 units.

Such being the case, it is obviously necessary to endeavour to establish a normal figure for one or two age-groups among children, and, for this purpose, I have used children under treatment for pulmonary or glandular tuberculosis, carefully selecting such as were free from any stigmata or history of rickets, evidence of hyperthyroidism, or glycosuria, and certainly free from any demonstrable disease of bone.

These are compared with the results of estimations among children suffering from definitely established tuberculosis of bone. These latter findings are classified under age-groups and also with regard to the extent of bone destruction demonstrated radiologically, and as regards activity of disease estimated radiologically and clinically.

Control Estimations.

In order to establish an average figure for the plasma phosphatase in children not suffering from any demonstrable disease of bone, estimations were carried out on 33 children with results as shown in Table I.

TABLE 1.

Case Number.	Tuberculous condition for which child was under treatment.	Age Years.	Sex.	Result of Plasma Phosphatase estimation. (Units).
1	Pulmonary	15 ...	M ...	6·4
2	Abdominal—glandular	11 ...	M ...	5·9
3	Pulmonary	15 ...	M ...	8·4
4	Pulmonary	13 ...	M ...	6·6
5	Abdominal—glandular	9 ...	M ...	8·8
6	Abdominal—intestinal	10 ...	M ...	6·9
7	Pulmonary	12 ...	F ...	7·9
8	Pulmonary and abdominal	5 ...	M ...	10·2
9	Abdominal—glandular	5 ...	M ...	9·0
10	Pulmonary	5 ...	F ...	13·4
11	Pulmonary	5 ...	F ...	9·9
12	Pulmonary	5 ...	F ...	9·2
13	Pulmonary	14 ...	F ...	5·3
14	Pulmonary	9 ...	F ...	10·8
15	Pulmonary	7 ...	M ...	8·5
16	Abdominal—glandular	6 ...	F ...	10·5
17	Pulmonary	7 ...	F ...	9·2
18	Pulmonary	6 ...	M ...	14·2
19	Abdominal—intestinal	6 ...	F ...	7·6
20	Pulmonary	8 ...	M ...	9·5
21	Cervical—glandular	8 ...	M ...	6·6
22	Pulmonary	8 ...	F ...	8·3
23	Pulmonary	9 ...	F ...	9·3
24	Pulmonary	14 ...	M ...	5·0
25	Pulmonary	5 ...	M ...	8·8
26	Cervical—glandular	3 ...	F ...	12·1
27	Pulmonary and abdominal	4 ...	M ...	10·5
28	Abdominal—intestinal	5 ...	F ...	9·8
29	Pulmonary	6 ...	F ...	9·0
30	Abdominal—glandular	2 ...	M ...	9·9
88	Cervical—glandular	10 ...	F ...	8·4
89	Abdominal—glandular	7 ...	M ...	10·0
90	Abdominal—intestinal ..	11 ...	F ...	8·1

The results, given in this table, give an average figure, for the children tested, of 8·9 units. This figure is definitely higher than that given by Kay (7) for normal adults (6·06), but is in keeping with the findings described in his earlier work (6) where he found that the plasma phosphatase in young children was higher than that in adults. This finding was confirmed by Smith and Maizel (9) in 1932.

Few very young children were available for the purpose of this work, but the fact that the children of 7 years and under are in separate wards from those above that age suggested a rough method of analysing the results.

The average figure for those of 7 years and under is 10·1.

The average figure for those over that age is 7·6.

Further analysis according to age groups cannot be made with any degree of certainty on account of the small numbers under review, but it is worth noting that the average result for the six children over 12 years who were tested is 6·6 showing an approach to the normal adult figure.

Sex.

Analysis of the results from the point of view of sex gives the following results :—

Average of all boys tested	= 8·6
Average of all girls tested	= 9·1
Average of boys under 8 years	= 10·2
Average of girls under 8 years	= 10·0
Average of boys over 8 years	= 7·1
Average of girls over 8 years	= 8·3

These figures do not show a variation which would warrant any conclusion as to a difference of plasma phosphatase content in the sexes.

Summary.

This table of results seems therefore to show that in children (free from any demonstrable disease of bone) the plasma phosphatase should be about 8·9 but that in younger children the normal figure will be a little higher.

Plasma Phosphatase Estimation in Children Suffering from Tuberculosis of Bones and Joints.

Figures having been established as normal plasma phosphatase content for children free from any bone or joint lesions, estimations were carried out among 57 children under treatment for tuberculosis of bones and joints.

In view of the findings among normal children the results have been divided into two age groups (a) 7 years and under

(b) over 7 years

and the results are given respectively in Tables 2 and 3.

It will be noticed that, in these tables, duplicate results are given in the great majority of cases, estimations having been done at an interval of a few months in as many cases as possible.

TABLE 2. Children under 7 years.

Case No.	Tuberculous condition under treatment.	Age Years.	Sex.	Result of Plasma Phosphatase estimations. (Units).	
31	Knee joint	6½	M	8·4	6·5
32	Vertebrae	7	F	9·2	12·6
48	Vertebrae	4	F	8·8	20·2
69	Hip joint	6	M	6·2	14·9
66	Hip joint	5	F	13·4	11·6
71	Knee joint	7	M	9·8	—
65	Hip joint	7	M	9·0	14·2
78	Vertebrae	4¾	M	12·6	10·2
72	Vertebrae and wrist.	6	F	11·0	10·8
73	Vertebrae	3	F	10·2	10·2
75	Knee joint	6	F	9·1	8·7
79	Hip joint	4	M	13·6	14·0
53	Hip joint	2	F	12·5	13·7
70	Vertebrae	3	M	9·7	10·2
56	Vertebrae	5	F	9·2	8·8
85	Hip joint	3	F	16·2	24·1
74	Vertebrae	3	M	10·8	11·9
42	Hip joints (bilateral)	4	F	14·8	16·9
82	Hip joint	2	F	10·1	12·6
59	Hip joint & vertebrae	5	M	12·6	19·4

TABLE 3. Children over 7 years.

Case No.	Tuberculous condition under treatment.	Age Years.	Sex.	Result of Plasma estimations.	Phosphatase
33	Hip joint	13 ...	M ...	12·6 ...	14·0
34	Vertebrae	14 ...	M ...	5·0 ...	8·3
35	Vertebrae	15 ...	M ...	12·0 ...	22·8
36	Hip joint	12 ...	M ...	7·0 ...	8·6
37	Hip joint	14 ...	M ...	7·3 ...	8·9
38	Vertebrae	11 ...	M ...	6·8 ...	12·2
39	Hip joint	10 ...	M ...	10·8 ...	13·0
40	Hip joint	11 ...	F ...	11·4 ...	9·2
41	Vertebrae	16 ...	M ...	10·0 ...	8·3
43	Vertebrae	8 ...	M ...	16·0 ...	21·9
44	Hip joint	13 ...	M ...	9·1 ...	8·8
45	Vertebrae	14 ...	F ...	13·6 ...	7·4
46	Vertebrae	10 ...	M ...	12·0 ...	11·4
47	Multiple bones (non-tuberc.)	14 ...	F ...	5·3 ...	—
49	Hip joint	10 ...	M ...	16·3 ...	12·2
50	Vertebrae	10 ...	F ...	7·8 ...	—
51	Vertebrae	12 ...	F ...	12·2 ...	13·9
52	Vertebrae	12 ...	M ...	10·2 ...	10·0
54	Knee joint	10 ...	M ...	8·8 ...	7·3
55	Vertebrae	12 ...	M ...	5·0 ...	7·9
57	Hip joint	9 ...	F ...	9·3 ...	11·6
58	Vertebrae	13 ...	F ...	14·4 ...	8·8
60	Hip joint	7½ ...	F ...	15·4 ...	9·6
61	Vertebrae	13 ...	M ...	9·9 ...	9·1
62	Knee joint	8 ...	M ...	8·1 ...	—
63	Hip joint	10 ...	F ...	7·8 ...	6·4
64	Hip joint	10 ...	M ...	11·6 ...	12·8
67	Hip joint	12 ...	M ...	7·0 ...	—
68	Vertebrae	8 ...	F ...	9·3 ...	8·0
76	Vertebrae & hip joint	11 ...	F ...	8·6 ...	9·0
77	Knee joint	9 ...	F ...	8·1 ...	—
80	Ribs and sternum...	12 ...	M ...	7·9 ...	9·3
81	Knee joint	12 ...	F ...	8·1 ...	—
83	Hip joint	13 ...	F ...	9·1 ...	—
84	Hip joint	9 ...	F ...	6·4 ...	9·2
86	Hip joint	13 ...	F ...	9·9 ...	—
87	Knee joint	12 ...	F ...	6·3 ...	—

From Table 2 it is found that the average figure for all estimations in this group is 12·0.

From Table 3 it is found that the average figure for all estimations in this group is 9·8.

In order to make any assessment of the value of the estimation of Plasma Phosphatase as an indication of the state of a bone lesion, it is obviously necessary to take into account the various factors which might influence the result.

Such factors appear to me to be :—

(a) Age.

(b) Character of lesion as regards decalcification, absorption, or sclerosis as evidenced radiologically.

(c) Activity of lesion as evidenced clinically.

(d) Extent of lesion as evidenced radiologically.

(e) Duration of lesion.

In studying the factors mentioned, the state of the lesion at the time of the first estimation and the result obtained at that time have been considered. The second estimations carried out in many cases will, I think, be more properly investigated later in an effort to discover whether any change of the clinical state has been accompanied by a variation in the plasma phosphatase.

For each factor considered I have used tables giving results, in association with case numbers, subdivided, in each case, in relation to the factor involved. By means of these tables it is possible to arrive at general impressions of variations dependent upon age and other factors and, if necessary, to study individual estimations and cases.

(a) **Age.**

The variation in plasma phosphatase in normal children according to age has already been discussed and, by dividing the results obtained in cases of bone and joint tuberculosis into two age groups, as is done in Tables 2 and 3, a convenient comparison can be made. It will be noticed that an apparently proportionate variation between the age groups is found in the normal and in the bone and joint estimations. The fact of the existence of a bone or joint lesion does not appear to have altered the proportion between the results in the respective groups. This being so, it does not appear to be worth while to analyse further the results in the age groups.

It has already been noted that Hunter (3) concluded that,

(a) There is no phosphatase in cartilage which is not ossifying.

(b) Phosphatase appears in cartilage simultaneously with the centres of ossification.

The finding that the plasma phosphatase is high in normal children in the under 7 years group is interesting, as supporting Kay's hypothesis (6) that the

increased plasma phosphatase noted in generalized bone diseases might be an effect, due to compensatory increase of production, as in such children the centres of ossification, although numerically less than in later childhood or adolescence, are particularly active. This hypothesis is, of course, further supported by the finding that even a comparatively small lesion leads to a further increase in the plasma phosphatase.

It is also interesting to note, in view of the findings in the age group 7—16 years, that, during that period, no new centres of ossification appear in the skeleton apart from four small centres for the xyphoid, olecranon process of ulna, lesser trochanter of femur, and lesser multangular bone of wrist.

As two definite figures have been obtained as normal, according to age, I have, in investigating clinical factors, made separate summaries of the findings in each age group.

(b) **Character of Lesion.**

Subdivisions in this section have been made bearing in mind the role of Phosphatase in the process of deposition of calcium.

(1) In the first group, cases are considered where, radiologically and clinically, it is apparent that disease is actively destructive, and that no evident repair is taking place.

(2) The second group is a small one in which cases have been considered where, in comparison with previous radiograms, there is no progression of destruction, but in which there is also no evidence of repair or sclerosis.

(3) In this group the larger number of cases are included which show varying degrees of recalcification as evidenced by sclerosis and increasing density of the X-ray shadows. One or two cases show very definite and advanced calcification in abscess, with much less sclerosis of bone, and such cases are included in this section but may require to be studied later apart from the other cases in the group.

(4) Cases showing advanced sclerosis with return to normal or exaggerated bone texture are detailed in this group.

(5) The remainder are those in which no alteration of bony texture, sufficiently gross to cause alteration in radiographic shadows, has taken place, e.g., cases of purely synovial tuberculosis showing no radiological evidence of associated bony changes.

TABLE 4. Character of Lesion.

1 Decalcification progressing.		2 Absorption ceased. No recalcification.		3 Recalcification commenced.		4 Scherosis advanced.		5 No gross bony change.	
Case No.	Result (Units).	Case No.	Result (Units).	Case No.	Result (Units).	Case No.	Result (Units).	Case No.	Result (Units).
42	14·8	31	8·4	34	5·0	32	9·2	54	8·8
43	16·0	36	7·0	40	11·4	33	12·6	62	8·1
44	9·1	38	6·8	48	8·8	35	12·0	77	8·1
46	12·0	39	10·8	49	16·3	37	7·3	80	7·9
50	7·8	51	12·2	52	10·2	41	10·0	87	6·3
53	12·5	60	15·4	55	5·0	45	13·6		
59	12·6	64	11·6	56	9·2	47	5·3		
65	9·0	68	9·3	57	9·3	61	9·9		
66	13·4	72	11·0	58	14·4	67	7·0		
69	6·2	75	9·1	63	7·8				
79	13·6	78	12·6	70	9·7				
84	6·4	81	8·1	71	9·8				
		82	10·8	73	10·2				
		85	16·2	74	10·8				
				76	8·6				
				83	9·1				
				86	9·9				
Averages									
11·1		10·6		9·7		9·7		7·8	

Table 4 shows a small increase in the plasma phosphatase in those cases showing decalcification, either in stationary lesions, or those showing advancing destruction. The increase demonstrated by the average figures is further supported by the fact that, of the twelve highest estimations in the series, 5 are in column *1*, 3 in column *2*, 2 in column *3*, and 2 in column *4*. It would therefore seem reasonable to assume that, as five of the twelve cases described as showing progressive decalcification, give the highest results of the series, there is an increase in plasma phosphatase accompanying the actual destruction of bone, even where the lesion is of one bone or joint.

With cessation of the destructive process, but before repair is established, there would appear to be some slight decrease in the average plasma phosphatase and a smaller proportion of high results, viz., 3 in 15 cases. As repair commences, and is established—columns *3* and *4*—a further decrease is apparently shown, and the number of high estimations is small.

In the five cases which showed no bony change there are fairly uniform results, giving an average figure of 7·8. As all these children are over 7 years, the results may be taken as normal in view of the finding in Table 1 that the average plasma phosphatase in those over 7 years was 7·6 units.

In considering the results of the estimations in relation to the character of the lesion as regards decalcification and bone absorption, the following seem to be the points demonstrated :—

(1) There is a definite increase in the plasma phosphatase in those cases described as radiologically progressive, and showing marked and advancing decalcification.

(2) With the cessation of the actual destructive process, there is a tendency to lower plasma phosphatase.

(3) With the establishment of repair, and during the process of repair, the average results tend to fall, but even in cases of advanced healing and apparently complete repair, the phosphatase activity of the plasma is above that of children with no demonstrable lesion of bone.

These findings will be studied in association with those relating to the other factors reviewed, and exceptions to the findings will be discussed later.

(c) **Activity of Lesion.**

For consideration of the findings in relation to the activity of the lesion, I have again arranged five sub-divisions, according to the clinical impression formed by the study of temperature and pulse records, symptoms and signs such as pain and limitation of movement, abscess formation, etc.

(1) The first sub-division, containing those cases showing definite evidence of present activity, is well defined.

(2) This sub-division I have termed "low activity" and, in this, have included the cases showing some fairly well-marked sign of activity of disease, but not giving the clinical impression of progressive destructive lesions.

(3) The third sub-division is of sub-active cases in which there are still factors pointing to incomplete arrest of disease, but which show no very definite evidence of activity.

(4) This sub-division contains the largest number of cases—those in which there is no clinical evidence of activity, but which one would hesitate to call quiescent. It is in this class of case that one would, of course, hope to obtain assistance in clinical assessment.

(5) A small sub-division of definitely quiescent lesions.

Several cases of double or multiple lesions have been estimated, and in such cases, I have taken the most active lesion as that determining the sub-division of the particular case.

TABLE 5. State of Lesion.

1 Acute and definitely active.		2 Low activity.		3 Sub-active.		4 Apparently inactive.		5 Quiescent.	
Case No.	Result (Units).	Case No.	Result (Units).	Case No.	Result (Units).	Case No.	Result (Units).	Case No.	Result (Units).
42	14·8	39	10·8	31	8·4	32	9·2	45	13·6
44	9·1	43	16·0	36	7·0	33	12·6	47	5·3
46	12·0	51	12·2	57	9·3	34	5·0	61	9·9
50	7·8	54	8·8	58	14·4	35	12·0	62	8·1
53	12·5	56	9·2	71	9·8	37	7·3		
59	12·6	60	15·4	74	10·8	38	6·8		
64	11·6	63	7·8	83	9·1	40	11·4		
65	9·0	68	9·3	87	6·3	41	10·0		
66	13·4	70	9·7			48	8·8		
69	6·2	72	11·0			49	16·3		
75	9·1	73	10·2			52	10·2		
79	13·6	78	12·6			55	5·0		
82	10·1	81	8·1			67	7·0		
84	6·4	85	16·2			76	8·6		
						77	8·1		
						80	7·9		
						86	9·9		
Averages									
	10·6		12·0		9·4		9·2		9·2

Table 5 shows result of estimations divided into sub-divisions according to the activity or quiescence of the lesions.

From the table it would appear that the highest phosphatase activity is found in those lesions which, having passed the first stage of acuteness, are still active. Acute cases give a high average, but those which are apparently, or definitely, inactive, show a return to normal levels.

The quiescent lesions are too few in number to place reliance on an average result, and, with one exception (case No. 45), the results are in the normal range.

The findings arrived at as a result of a study of the estimations in relation to activity of the tuberculous lesion appear therefore to be:—

(1) In definitely, acutely active lesions the phosphatase activity is increased, but the figure is not so high as in less acute cases.

(2) Where the acuteness of the lesion has subsided, the plasma phosphatase is at its highest.

(3) With subsidence of activity there is some decrease in the average plasma phosphatase but, in a relatively large number of cases, the phosphatase activity does not decrease in proportion to the lessening activity of disease.

(4) Even in definitely quiescent cases a high phosphatase activity may be found.

(d) **Extent of Lesion.**

The extent of bone destruction, absorption, and the accompanying osteoporosis is of course estimable only by a study of radiograms taken at or near the time of phosphatase estimation. In order to be able to study, both any variations of plasma phosphatase found with varying degrees of destruction of similar bones or joints and also, any variations found in relation to the actual amount of bone involved, I have endeavoured to divide this section to show the comparative results from both points of view.

(1) **Hip joint disease.**

These cases I have divided into those showing gross destruction of head and neck of the femur or with acetabular erosion, and those showing only partial destruction of head or acetabulum. No case of purely synovial disease of the hip joint was available for estimation.

(2) **Spinal disease.**

These cases are divided firstly, into those showing only localized disease, e.g., a single body with little or no loss of bone, secondly, those showing destructive disease of one or at most two vertebral bodies, and thirdly, those showing more extensive disease with absorbtion, or comparitively localized lesions with absorption of more than two vertebral bodies.

(3) **Knee joint disease.**

These cases fall naturally into two groups according as to whether the disease is confined to synovia and cartilage, or has caused erosion of bone. Cases with extensive osteoporosis have been included among those showing bony changes.

(4) **Other bones and joints.**

Only two cases fall into this section, one of multiple bone abscesses of a doubtfully tuberculous nature, and one of rib and sternal abscesses in which no bone destruction could be shown radiologically.

TABLE 6.

Hip Joint.					Vertebrae.				Knee Joint.					Other bones and joints.			
Head and neck of femur or head and acetabulary.		Head only or acetabulary only.			Small localized lesion, little absorption.		Destruction of one or two bodies.		More extensive disease and destruction.			With bony change.		No bony change.			With bone destruction.		No bone destruction.	
Case No.	Result.	Case No.	Result.		Case No.	Result.	Case No.	Result.	Case No.	Result.		Case No.	Result.	Case No.	Result.		Case No.	Result	Case No.	Result.
33	12·6	40	11·4	...	32	9·2	45	13·6	35	12·0	...	31	8·4	54	8·8	...	47	5·3	80	7·9
36	7·0	60	15·4	...	34	5·0	55	5·0	36	9·2	...	75	9·1	62	8·1	...				
37	7·3	66	13·4	...	38	6·8	61	9·9			...	71	9·8	77	8·1	...				
39	10·8	82	10·1	...	41	10·0	68	9·3			...			81	8·1	...				
42	14·8	85	16·2	...	43	16·0	70	9·7			...			87	6·3	...				
44	9·1			...	46	12·0	74	10·8			...					...				
49	16·3			...	48	8·8					...					...				
53	12·5			...	50	7·8					...					...				
57	9·3			...	51	12·2					...					...				
59	12·6			...	52	10·2					...					...				
63	7·8			...	58	14·4					...					...				
64	11·6			...	72	11·0					...					...				
65	9·0			...	73	10·2					...					...				
67	7·0			...	78	12·6					...					...				
69	6·2			...							...					...				
76	8·6			...							...					...				
79	13·6			...							...					...				
83	9·1			...							...					...				
84	6·4			...							...					...				
86	9·9			...							...					...				
Averages																				
	10·1		13·3			10·5		9·7		10·6			9·1		7·9			5·3		7·9

Studying Table 6 one finds that the highest average figures are obtained in the case of extensive hip and spinal lesions, whilst those cases of knee joint disease show normal results. An analysis, however, of the results in the hip and spinal columns, gives rather conflicting results.

In the 20 cases of fairly extensive disease of the hip joint 13 give results above normal, but the average finding is less than that of 5 cases which showed less absorption or osteoporosis radiologically.

The spinal lesions show little difference between the average figure for extensive and localized lesions, and, to arrive at any conclusion regarding the results in the more extensive spinal lesions, it will be necessary to study the lesions as regards number of vertebrae affected. The cases described as most extensive in this series are numbers 41, 50 and 52, and these give results respectively, 10·0, 7·8 and 10·2. On the other hand, the cases in which disease appears radiologically to be confined to four vertebral bodies or less are numbers 43, 46, 48, 58, 72, 73 and 78 and the results are respectively, 16·0, 16·0, 8·8, 14·4, 11·0, 10·2 and 12·6.

One is therefore forced to the conclusion that, in the case both of hip joint and spinal disease, the extent of infection, and the extent of destruction, as shown radiologically, do not, of themselves, bear a direct ratio to the phosphatase activity of the blood plasma. They do in fact appear to bear a definitely inverse ratio.

The conclusion from this section would therefore appear to be, provided the bony lesion is more extensive than that found in the cases of knee joint tuberculosis under review, that high phosphatase activity is found in comparatively localized lesions, and that a lesser plasma phosphatase, still however above the normal figure, accompanies extension of bone destruction.

(e) **Duration of disease.**

The great majority of the cases available for the purpose of this work are of considerable standing, and the sub-division of these is necessarily arbitrary. Where double or multiple lesions are present, the oldest lesion has been taken as the basis of classification.

(1) Less than 1 year.

(2) 1 year to 3 years.

(3) 3 years to 5 years.

(4) Over 5 years.

TABLE 7.

6 months to 1 year.		1 year to 3 years.		3 years to 5 years.		Over 5 years.	
Case No.	Result.	Case No.	Result.	Case No.	Result.	Case No.	Result.
42	14·8	31	8·4	32	9·2	33	12·6
80	7·9	35	12·0	37	7·3	34	5·0
		40	11·4	46	12·0	36	7·0
		43	16·0	52	10·2	38	6·8
		48	8·8	55	5·0	39	10·8
		53	12·5	57	9·3	41	10·0
		54	8·8	61	9·9	44	9·1
		56	9·2	67	7·0	45	13·6
		59	12·6	69	6·2	47	5·3
		60	15·4	78	12·6	49	16·3
		62	8·1	84	6·4	50	7·8
		65	9·0			51	12·2
		66	13·4			58	14·4
		68	9·3			63	7·8
		70	9·7			64	11·6
		72	11·0			71	9·8
		73	10·2			76	8·6
		74	10·8			77	8·1
		75	9·1			81	8·1
		79	13·6			83	9·1
		82	10·1			86	9·9
		85	16·2				
		87	6·3				
Average	11·4		10·9		8·6		9·9

Table 7 contains a division of cases, and results of plasma phosphatase estimation, having regard only to the duration of the lesion, as obtained from the case history.

There is no very definite conclusion to be arrived at from a preliminary study of this table. The average figures in the four sub-divisions are not widely separated, and there is not a disproportionate number of high or low estimations in any one of the sub-divisions.

The number of early cases is too small for useful comparison or study but, even if cases of duration up to 1½ years are included with those of 1 year and less, it will be found that no definite finding can be made.

The analysis of this table seems therefore to show that the duration of the lesion does not, of itself, influence the phosphatase activity of the blood plasma.

Summary of Findings in Relation to Factors Examined

Investigation so far has seemed to establish by the use of controls, apparently free from disturbance of bone metabolism, that the normal plasma phosphatase is slightly higher in younger children, and that an approach to the normal takes place towards puberty.

It is interesting to note, in view of the average of 10·1 units established for children under 7 years, that Dr. Jean Smith, in an investigation (10) of Plasma Phosphatase in Rickets and other disorders of growth, found the average plasma phosphatase of normal, breast-fed, healthy infants to be 0·2—0·3 units. Multiplying by 50, in accordance with Kay's finding, previously discussed, this gives an average of 10—15 new units.

The investigation of cases of bone and joint tuberculosis has not shown any disturbance of the proportion between the results in the younger and older children, nor has it appeared to show any new factor which would require to be investigated as regards the age of the patient. It may be worth while, at this stage, to study the few cases among the control estimations which show an appreciable increase in Plasma Phosphatase. These are numbers 10, 14, 18 and 26. The first of these is a child of apparently normal skeletal development and in good general condition, but suffering from a definite epituberculosis of the right lung.

The second is a small child, in fairly good general condition, with healing adult type of tuberculosis in both lungs. Recovery has been extremely slow with long-continued temperature irregularity.

The third is a very poorly-developed, and very small, child (age 7 years, height 3ft. 4in., weight 2st. 9lb.) suffering from tuberculosis of hilar glands with no temperature irregularity or symptoms.

The fourth is a child of apparently normal development and general condition suffering from moderately acute cervical glandular tuberculosis. The only point of note about this child is extreme nervous instability and a tendency to chilblains.

In the light of the present knowledge of the plasma phosphatase, the only one of the above cases which seems to offer interest is the third where development is obviously poor.

Study of the phosphatase activity in relation to the decalcification present seemed to demonstrate that there was a progressive fall, but not a return to normal,

with increasing recalcification, and that decalcification was accompanied by high plasma phosphatase. In several cases of apparently advanced sclerosis high figures were obtained, and these are difficult to understand if one accepts the first finding as being the result of increased secretion, this last being a reaction to the stimulus of the disease process.

One would expect that, as decalcification and recalcification move roughly parallel to activity and inactivity of disease, the findings in relation to activity of disease would be similar to those already described, and this is true, with the additional indication that the peak of phosphatase activity is reached with subsidence of the first acuteness of the lesion. These findings are, I think, in keeping with the present conception of the role of plasma phosphatase in bone production and metabolism, and strongly support the evidence that the increased plasma phosphatase is an effect of the disturbance of bone metabolism locally at the site of the lesion. The delayed development of increased plasma phosphatase might also, I think, be considered as supporting these hypotheses if one conceives of it as a reaction, analogous to any other reaction to a stimulus, after a period of shock. The findings in relation to activity of a lesion have been found, however, to be less constant of fulfilment than those in relation to decalcification and exceptions are numerous.

The study of the results in relation to the extent of the lesion has indicated that the highest plasma phosphatase is found in the more localized lesions. Such a finding seems reasonable if one visualises the hypertrophic cartilage cells and osteoblasts as stimulated to a hyper-secretion of phosphatase, and later overcome by the destructive process, in a fashion analogous to the stimulation and later destruction of the leucocytes in inflammation and suppuration. At first sight, it seems contradictory that a more extensive lesion should not give a higher plasma phosphatase in view of the very high figures obtained in generalized bone diseases, but caseation and complete absorption of bone are processes practically limited to tuberculosis, and involve very extensive destruction of the phosphatase-secreting cells.

It has not been possible to demonstrate any relevant relationship between the duration of a lesion, considered apart from its activity or extent, and the degree of the rise in plasma phosphatase. This is not surprising, in view of the findings described in the examination of the character, extent and activity of lesions. In view of the role of phosphatase in growth and maintenance of bone, these other factors would presumably influence the secretion much more than mere duration of a lesion, and, in the case of tuberculosis, where one may have long-continued activity or repeated reactivation, it is obviously not possible to expect findings proportionate as between activity of disease and duration of lesion.

Having reviewed the findings, it may be useful to study a few of the cases which appear to contradict these findings, and to determine whether any supplementary indications are obtained thereby.

In the grouping of cases under "Character of Lesion" the following, although definitely decalcifying, give low estimations :—
No. 50. Extensive, active lesion of dorsal spine, abscess formation, temperature irregularity, pressure symptoms. General condition poor. Development normal.

This child died of Tuberculous Meningitis a few weeks after estimation, and her increasing lack of resistance to the tuberculous infection may have determined a low phosphatase secretion.

No. 69. Rapid absorption of head of femur in progress at time of estimation with spreading decalcification. General condition poor. Development normal. Difficulty in obtaining the requisite amount of Zero Filtrate during estimation is the only point of note in relation to this case.

No. 84. A case of apparently progressive and active disease. General condition good. Very fat but rather flabby. Jewess. Present acute lesion is a relapse after apparent arrest. No special point of interest appears to arise in this case.

In the grouping of cases as regards activity, the most contradictory cases are those showing high phosphatase with definitely quiescent or apparently well-sclerosed lesions.

No. 45. Extensive destructive disease of lumbar vertebrae. Child ambulant over a period of one year without reaction of any kind. General condition and development excellent.

No. 49. Apparently quiescent lesion of hip joint. Child ambulant for a few months before estimation, without reaction. General condition good. Development normal. This joint was considered unstable and a grafting operation was carried out recently (May, 1934). At operation much softening of bone was found. It is also interesting to note the remark in the X-ray report, " marked osteoporosis."

This latter case is one in which the need for a helpful prognostic test is demonstrated, and the high plasma phosphatase might have been taken as an indication that firm repair would not be found at operation.

Case No. 45 however seems to contradict this entirely.

In the grouping of cases according to extent of disease, the finding arrived at by the study of averages and cases, is apparently contradicted by several of the particular estimations, e.g.,

No. 42. Bilateral acute disease of hip joint. Extensive spreading erosion and abscess formation. Plasma Phosphatase 14·8 units.

No. 49. This case has already been discussed as an exception to the finding re

activity of the lesion. The lesion is undoubtedly an extensive one. Plasma Phosphatase 16·3 units.

No. 79. Rapidly advancing destruction of head and neck of femur. Marked osteoporosis. Plasma Phosphatase 13·6 units.

No. 43. Extensive destructive disease of dorsal vertebrae with abscess formation. 3 vertebral bodies destroyed. Plasma Phosphatase 16·0 units.

No. 58. Destructive collapse of four lumbar vertebrae. Disease of old standing, recently reactivated with abscess formation. Plasma Phosphatase 14·4 units.

These are a few of the typical exceptions which would tend to demonstrate that the extent of the lesion is of less importance than its character and activity. One interesting point, arising out of a study of these cases, is that all show abscesses of fairly recent date, not extensively calcified. Cases Nos. 53 and 59, plasma phosphatase 12·5 and 12·6, are further instances of this co-existence of uncalcified abscess and high plasma phosphatase.

Having summarised the findings so far, it will be of interest to note whether the second estimations, carried out in many of the cases, conform to the general impressions. A table has been prepared showing the results of both estimations and, between them, in the form of columns, an assessment of the change, if any, which took place in the clinical and radiological appearances during the interval between the estimations.

Case No.	1st estimation.	State i.s.q.	Activity increased.	Activity less.	Decalcification increased.	Decalcification less.	Extent increased.	Interval mins.	2nd estimation.
31	8·4			+		+		6	6·5
32	9·2	+						5	12·6
33	12·6					+		2	14·0
34	5·0	+						1	8·3
35	12·0			+		+		2	22·8
36	7·0	+						4	8·6
37	7·3	+						5	8·9
38	6·8			+		+		3	12·2
39	10·8			+				3	13·0
40	11·4			+		+		4	9·2
41	10·0	+						4	8·3
42	14·8	+			+			4	16·9
43	16·0	+					?+	3	21·9
44	9·1	+						5	8·8
45	13·6					+		2	7·4
46	12·0		+		+		+	1	11·4
48	8·8	+					+	3	20·2
49	16·3	+			+			2	12·2
51	12·2	+			+			6	13·9
52	10·2	+						1	10·0
53	12·5	+		+				3	13·7
54	8·8	+						2	7·3
55	5·0	+						4	7·9
56	9·2	+						2	8·8
57	9·3	+						2	11·6
58	14·4	+						2	8·8
59	12·6		+		+		+	4	19·4
60	15·4	+						4	9·6
61	9·9	+						2	9·1
63	7·8			+				3	6·4
64	11·6			+				4	12·8
65	9·0		+		+		+	4	14·2
66	13.4		+		+		+	4	11·6
68	9·3			+				3	8·0
69	6·2			+		+		3	14·9
70	9·7			+		+		3	10·2
72	11·0	+		+				1	10·8
73	10·2	+						1	10·2
74	10·8			+		+		3	11·9
75	9·1			+		+		3	8·1
76	8·6	+						3	9·0
78	12·6	+						2	10·2
79	13·6	+						1	14·0
80	7·9	+						2	9·8
82	10·1			+		+		2	12·6
84	6·4			+		+		2	9·2
85	16·2			+		+		2	24·1

A study of this table should be made in the light of the findings previously examined.

Firstly, decalcification was found to be accompanied by increasing phosphatase, and one would expect that the seven cases, noted as showing increased decalcification, would not show any decrease in plasma phosphase as compared with the first estimation. In cases Nos. 42, 51, 59 and 65, the finding is one of increased phosphatase. In case No. 46, a very small decrease is found (0·8 units). Case No. 49 shows a very definite decrease (4·1 units) and has already been discussed, as an exceptional case, in respect of the first estimation. Case No. 66, despite a definite increase in decalcification and a persistent activity, shows a definite decrease (1·8 units).

Where decalcification has lessened during the interval, the finding that decreasing decalcification is accompanied by lower phosphatase activity is supported by cases No. 31, 40, 45, and 75, but cases No. 33, 35, 38, 69, 74, 82, 84, and 85, show varying degrees of increasing phosphatase. Of these, cases No. 69 and 84 have already been considered as exceptional in respect of their first estimations, and the second estimations may be more correct indications of the clinical state. The very high figures found at second estimation in cases No. 35 and 85 are very difficult to understand, the former being a localised spinal lesion definitely quiescent at the time of the sound estimation, the patient being ambulant. The latter case is one of extensive and rapid absorption of the femoral head and acetabulum in which, at the second estimation, repair, although not advanced, appeared to have commenced.

In considering the table with regard to any change in activity one finds, as might be expected, that the cases, apparently contradictory to previous findings, include those already discussed as unusual in respect of the decalcification. In three of the cases it may be possible to believe that the peak of phosphatase activity found with lessening acuteness of disease was being reached at the time of the second estimation. The following are the particulars of these cases :—

No. 53. Lesion of 1½ years duration. Very acute at first estimation.

No. 64. Recrudescence of disease 1 month before first estimation.

No. 82. Lesion of 1½ years duration. Very acute at first estimation.

Two cases which were clinically more active show some decrease in plasma phosphatase. These are Nos. 46 and 66, and in neither case is it possible to demonstrate any obvious explanation of the seeming contradiction.

In three cases considered as clinically unchanged between estimations very definite increase in plasma phosphatase is shown, and in two cases a marked fall has taken place. These are Nos. 32, 43 and 48, and Nos. 58 and 60 respectively, and they are considered in the following table.

Case No.	Remarks.
32.	A child with an apparently inactive lesion who remained ambulant without evidence of reaction, during the interval between estimations.
	No explanation of high phosphatase possible.
43.	The maintenance of *status quo* is less definite in this case, the child having remained immobilised in bed, but no increased activity or extent of disease was noted.
	Development good.
48.	This child had an extensive lesion and appeared, clinically, to be slowly consolidating repair with a little increase in the collapse and kyphosis of the spinal column. No evidence of reactivation.
	The only complication was the co-existence of paralysis due to anterior poliomyelitis at 4/12 years.
58.	Extensive spinal lesion with large abscess. Disease recenty active. It is worthy of note that this abscess was incised and expressed in March, 1934, and showed fairly advanced inspissation.
60.	A case of active disease of the hip joint showed no marked evidence of arrest. The clinical picture was, however, complicated by the co-existence of a urinary B. Coli infection.

Marked rise.

Marked fall.

Conclusion.

In 57 cases of bone and joint tuberculosis in children, the plasma phosphatase has been estimated, and in 33 children, not suffering from demonstrable disturbance of bone metabolism, estimations have been carried out in order to control results, and in an effort to establish a normal figure for plasma phosphatase in children. The purpose of the investigation has been to discover whether a tuberculosis lesion of bone is accompanied by an increase in plasma phosphatase, and whether any variations which may take place in the plasma phosphatase, during the existence of such disease, bear a sufficient relationship to the stage of the disease to justify the use of the plasma phosphatase estimation as a test, which would be of assistance in the assessment of the state of the lesion.

The method of estimation has been described and results tabulated. These results have been analysed in relation to various factors which might be expected to exercise an influence on the plasma phosphatase, and conclusions have been arrived at in respect of each of the factors concerned. These conclusions have been summarized, and apparently contradictory findings have been investigated.

Finally, estimations of plasma phosphatase carried out at varying periods after the first estimations have been examined, in the light of the conclusions arrived at, and in relation to any clinical change noted in the interval.

A case sheet has been prepared in respect of each patient concerned, and these are bound with this thesis along with reduced photographs of radiograms, the latter being contemporary with the phosphatase estimations.

For the employment of the estimation as a test I feel that the following are the essential conditions, and it will be necessary to find in how far these have been satisfied.

(1). A definite increase in plasma phosphatase must be shown to accompany tuberculosis of bone.

(2). Such increase must be of sufficient magnitude to eliminate the possibility of false conclusions through unavoidable variations in the absolute accuracy of estimation.

(3). Any increase must be comparable in lesions which are clinically and radiologically comparable.

(4). Variation in the plasma phosphatase must accompany a change in the state of the lesion.

(5). For the test to be usefully employed in assessment of quiescence, a constant difference must be established between the plasma phosphatase with quiescent and non-quiescent lesions.

(6). Any factors, apart from the state of the lesion, which might influence the plasma phosphatase, must be recognised, and the degree of their influence known in order that allowance may be made for them.

It now remains to discuss in how far the results of this investigation satisfy the above conditions.

No. 1. Tables 2 and 3 of the main part of this thesis showed that an average increase in plasma phosphatase was found in the cases under review which would satisfy the primary essential condition. A study of the individual results shows, however, that 26 of the 104 estimations carried out do not satisfy the condition, the phosphatase being at, or below, the figure established as normal for children of the age group concerned. The age groups being, however, arbitrarly determined and the normal figure being the average of 33 estimations, many of which were necessarily below that figure, one is, I think, justified in concluding that the first condition has been satisfied.

No. 2. The extremely small amount of hydrolysis obtained in the estimations make it seem likely that even small errors in pipetting or colorimetry will cause a considerable variation in the final result, and examination of the figures obtained shows that this is so. Where one is endeavouring to compare cases in which the estimation is only increased by 50% to 100% it would seem necessary to be able to rely exactly upon the volume of solutions and especially of filtrates. Accurate measurement of solutions and checking of final solutions to within 0·1c.c. before colorimetry should, however, eliminate very largely the possibility of such error. It is difficult to eliminate the personal factor and the factor of external lighting in colorimetry; but repeated observations and the striking of average results make for exact colour matching. With careful working and good laboratory equipment this condition is, I think, fairy well satisfied.

No. 3. This condition really means that there should not be exceptions to the rules established in order that, all known factors having been allowed for, it should be possible to estimate an unknown factor. In the course of the analysis of results, and the study of conclusions in this investigation, a number of apparently exceptional results was noted, and in many of these, one was forced to leave the contradiction unexplained. It must therefore be said that in this series the third condition is only partially fulfilled.

No. 4. Variations in the plasma phosphatase have been found to accompany a change in the state of the lesions as regards decalcification and activity, and, as these are the important clinical factors in the assessment of which help is desired, one can say that this condition is fulfilled. Exceptions have been

found and examined, but are not sufficiently numerous or striking to upset the conclusion arrived at above.

No. 5. The following statements have been made in relation to activity of a lesion :—

(a). "In a relatively large number of cases the phosphatase activity does not decrease in proportion to the lessening activity."

(b). "Even in definitely quiescent cases a high plasma phosphatase may be found."

These statements show that no constant and definite variation as between quiescent and non-quiescent cases has been established, and this condition is, therefore, not satisfied.

No. 6. In the course of the investigation several factors which might be labelled "extraneous" have been noted and their effect, if any, on the plasma phosphatase has been noted. Examples of such factors are: (a) Age of patient, (b) Sex, (c) Co-existence of non-calcified abscess, (d) Poor skeletal development. The rise in plasma phosphatase met with in generalized diseases of bone has been noted. The number of unexplained exceptions to the general rules established make it appear possible, however, that factors, still unrecognised, exert an influence on the plasma phosphatase, and it is possible that this last condition is in our present state of knowledge incompletely satisfied.

The plasma phosphatase estimations examined do not, therefore, satisfy all the conditions laid down and, in view of the non-fulfilment of the important conditions regarding comparable and quiescent lesions, I feel that it is not possible to put forward the estimation of plasma phosphatase as a reliable test of the state of a tuberculous lesion of bone. As previously stated, however, amplification of our present knowledge of the factors influencing the phosphatase content of the plasma might well explain much that seems contradictory, and this research has, I consider, shown that the subject is worthy of further investigation, and that although it is not at present possible to advocate the establishment of the plasma phosphatase estimation as a test, as was desired, it may yet prove possible to do so.

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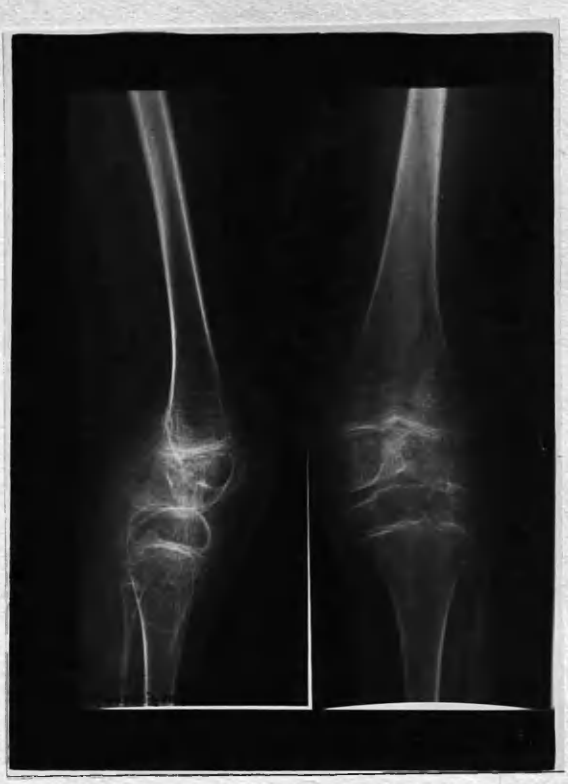
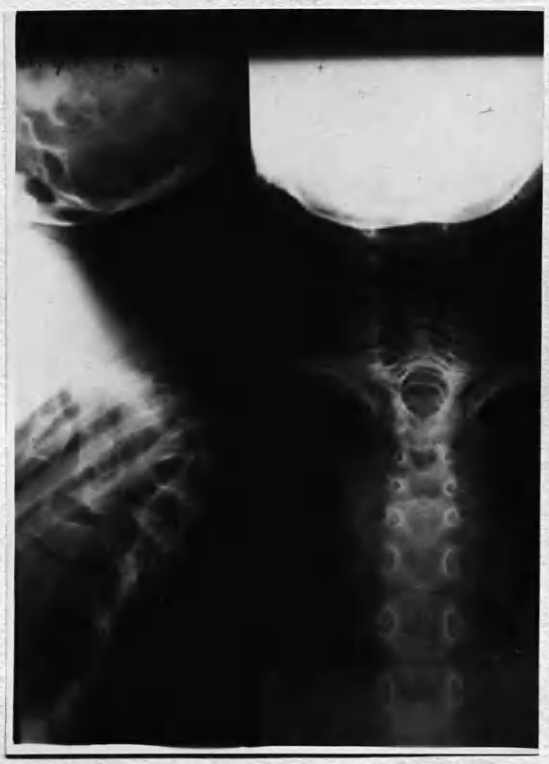


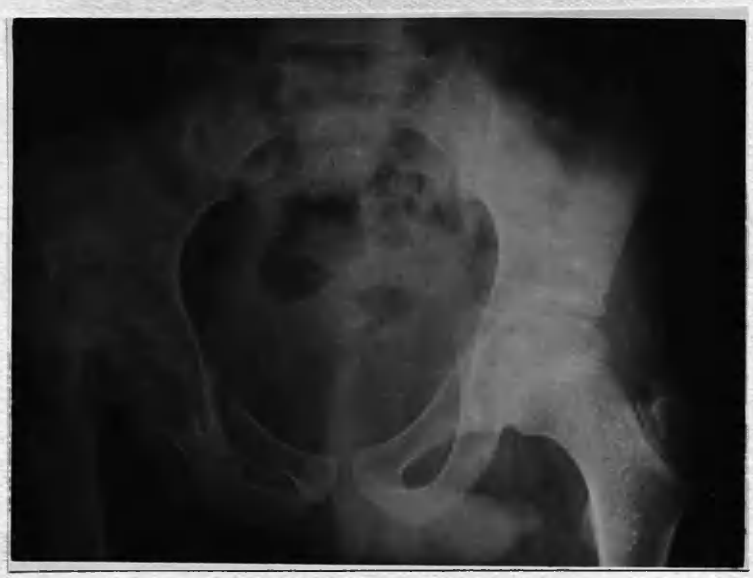


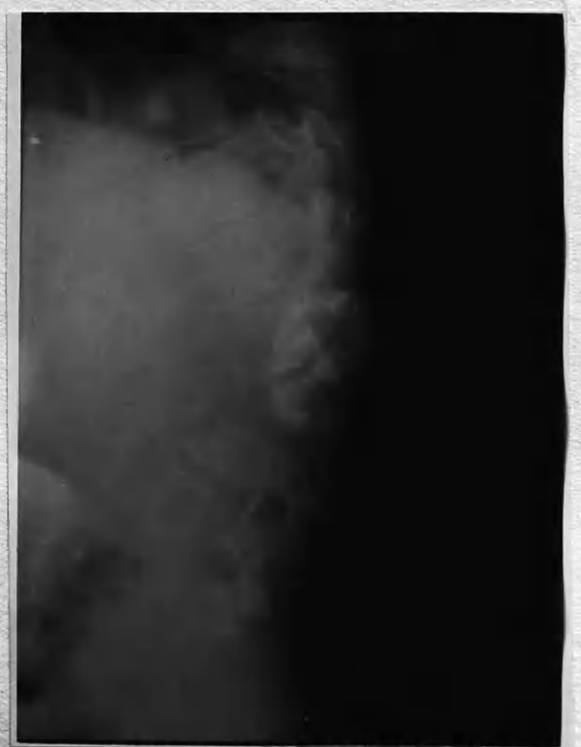
CASE NO. 31. E.F. Age 6½ years.

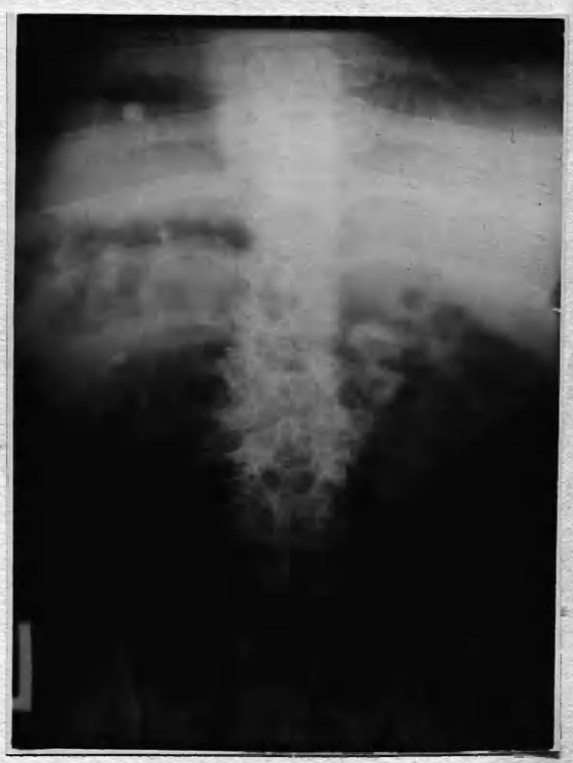
Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Right knee joint.	3 years.	Injury in 1930—Thomas splint and plaster fixation. Sinus developed June, 1930, and slight discharge was still present in June, 1931.	Erosion (not extensive) of lateral half of femoral epiphysis. Osteoporosis of femur and tibia. Subluxation.	(a) Occasional temperature irregularity. (b) Nil. (c) Very slight flexion only possible. (d) Nil at time of recording.	Sub-active lesion. Poor general condition and development.

CASE NO. 32. I.G. Age 7 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Dorsal Vertebrae	4 years	No accurate history obtained, but child was ambulant wearing spinal brace for some months prior to June, 1932, when she had symptoms—anorexia, listlessness, and loss of weight.	Gross destruction of dorsal vertebral bodies. ? 4th to 9th. Old calcified abscess shadow.	(a) Nil. (b) Nil. (c) Large kyphosis. Lumbar movements free. (d) Residual abscess.	Apparently inactive lesion.





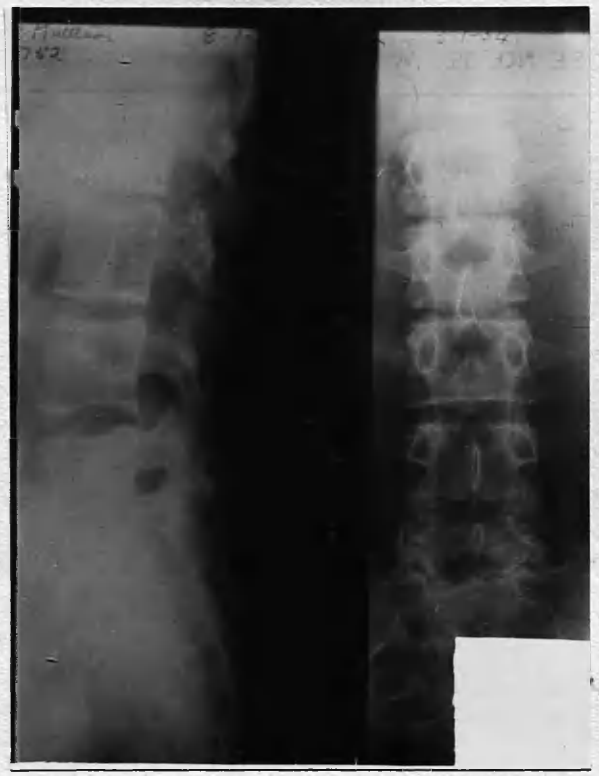


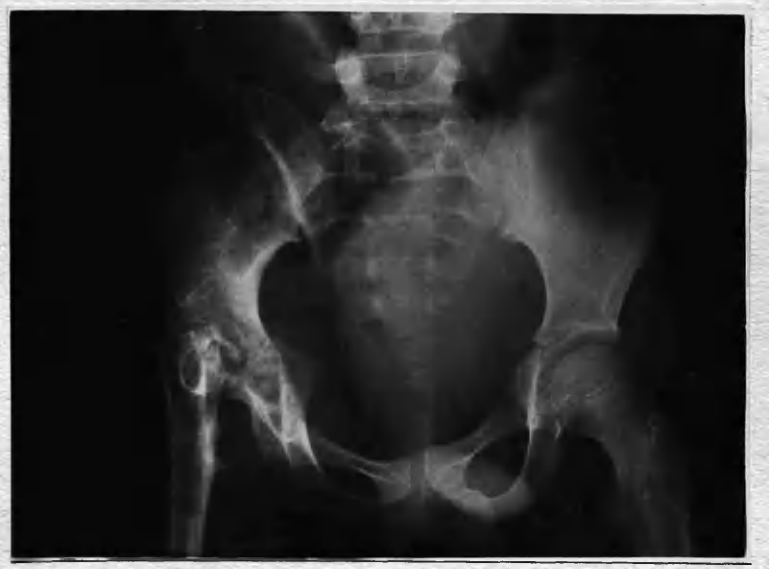
CASE NO. 33. J.C. Age 13 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Left hip joint.	6 years.	None obtained. Abscess aspirated in 1930 — sinus formed and healed in 1931.	Destruction of head and neck of femur. Erosion of acetabulum, Ankylosed.	(a) Nil. (b) Nil. (c) Ankylosed. (d) Nil at present.	An old lesion but note abscess history.

CASE NO. 34. H.S. Age 14 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Dorso-lumbar vertebrae.	11 years.	Immobilisation on frames. Aspiration of abscesses 1928 and 1930—(recurrence). Abscess broke down and healed 1931.	Destructive disease of 12th dorsal and upper four lumbar vertebrae (3 bodies absorbed). Bilateral abscess formation. Recalcification in progress.	(a) Nil. (b) Nil. (c) Free above and below lesion. (d) Bilateral.	Apparently inactive lesion but note fairly recent abscess activity.



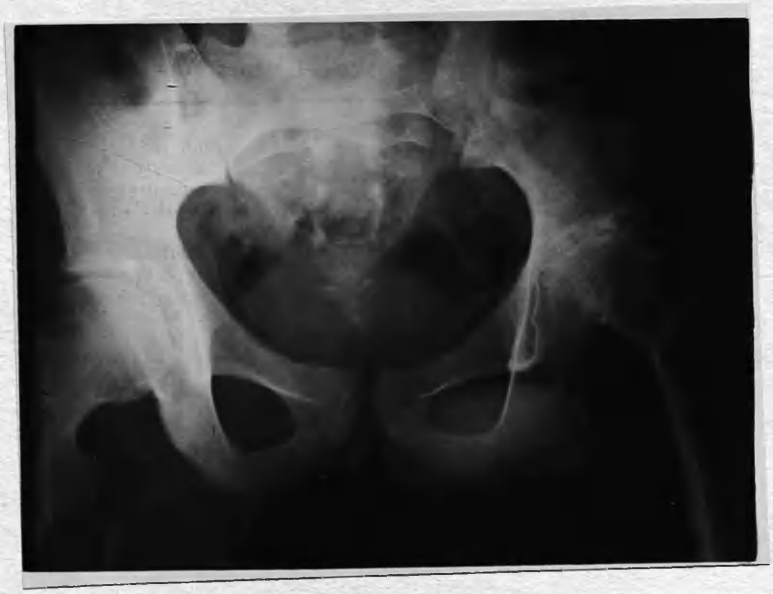


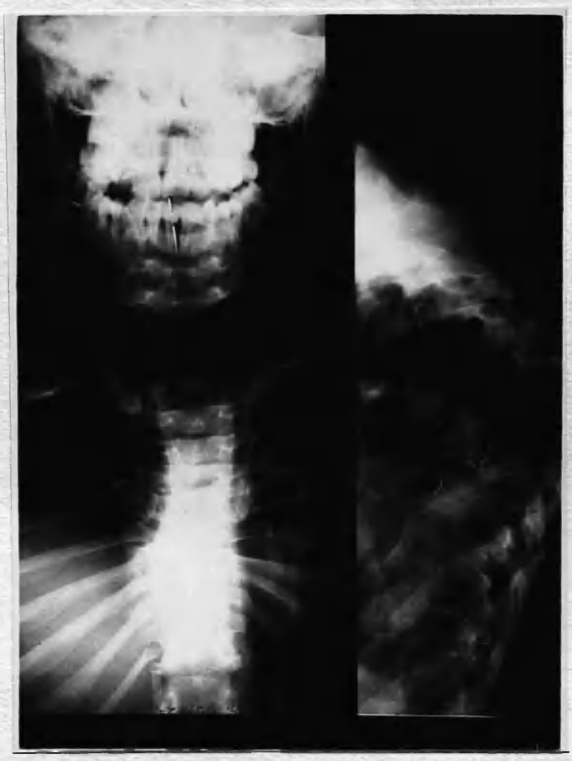
CASE NO. 35. W.M. Age 16 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
5th lumbar vertebral body.	3 years.	Immobilisation on frame. Aspiration of lumbar abscess 1931. Immobilisation in plaster spinal jacket.	5th lumbar body and lumbo-sacral articulation eroded.	(a) Nil. (b) Nil. (c) Lumbar movements poor. (d) Definite evidence of posterior lumbar abscess — absorbing rapidly.	An apparently inactive lesion.

CASE NO. 36. S.M. Age 12 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Right hip joint.	8 years.	1924 immobilisation on frame. 1927 noted as "ankylosed — inactive." 1928 lumbar abscess —sinuses formed. 1931 persistent sinuses.	Head, neck and part of shaft of femur absorbed. Extensive erosion of acetabulum. Extensive osteoporosis.	(a) Occasional temperature irregularity. (b) Nil. (c) Ankylosed. (d) Persistent discharging sinuses.	Sub-active lesion of old standing. General condition poor but no evidence of lardaceous disease.



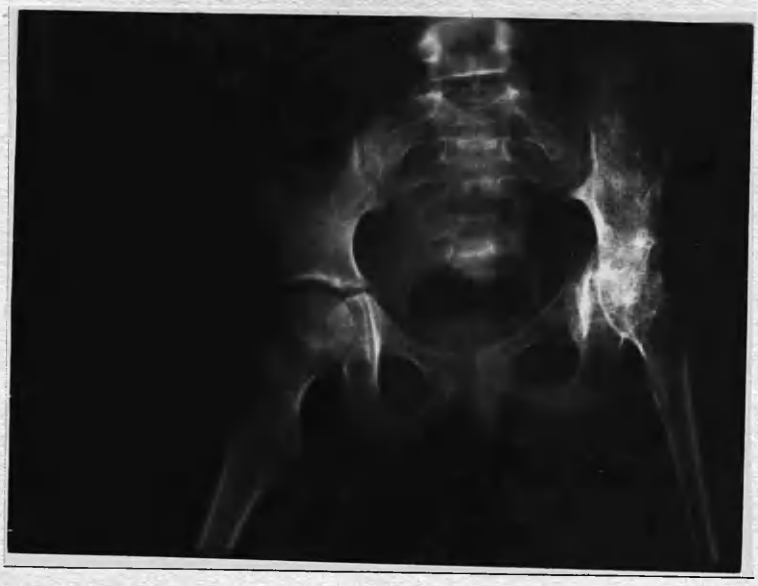


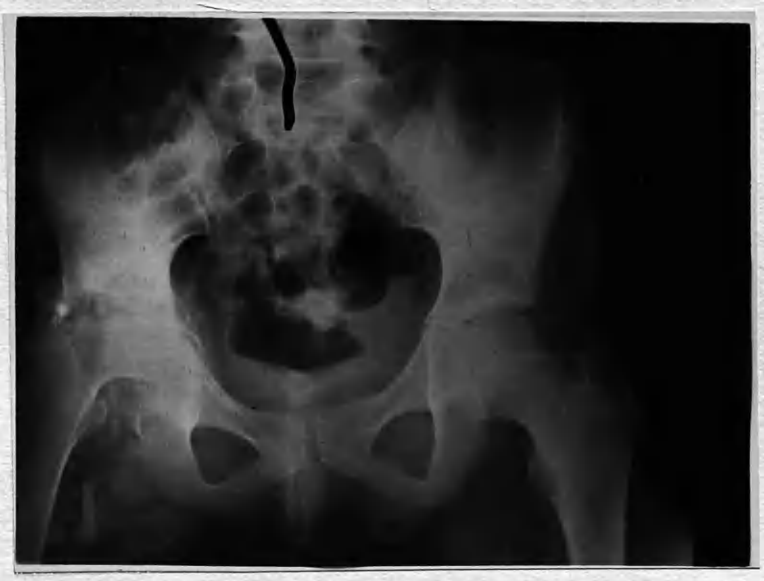
CASE NO. 37. J.L. Age 14 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Right hip joint.	4 years.	Plaster of Paris splints for long periods. Aspiration of abscesses 1929 and 1930, when lesion noted as "very active."	Head of femur and small area of neck absorbed. Advancing ankylosis. Acetabulum not extensively eroded. Sclerosis advanced.	(a) Nil. (b) Nil. (c) Fixed joint. (d) Scars of old sinuses but no clinical or radiological evidence of present abscess.	Apparently inactive. General condition only moderately good.

CASE NO. 38. N.V. Age 11 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Dorsal vertebrae.	9 years.	No early history available. Immobilisation and hyperextension from 1930 to date—treated as "subactive."	Disease of 4th to 9th dorsal vertebrae. Complete absorption of two bodies. Little or no evidence of sclerosis in affected vertebrae. No abscess shadow.	(a) Nil. (b) Nil. (c) Movements limited but no spasm—large kyphosis. (d) Nil.	Apparently inactive. General condition poor and not improving.



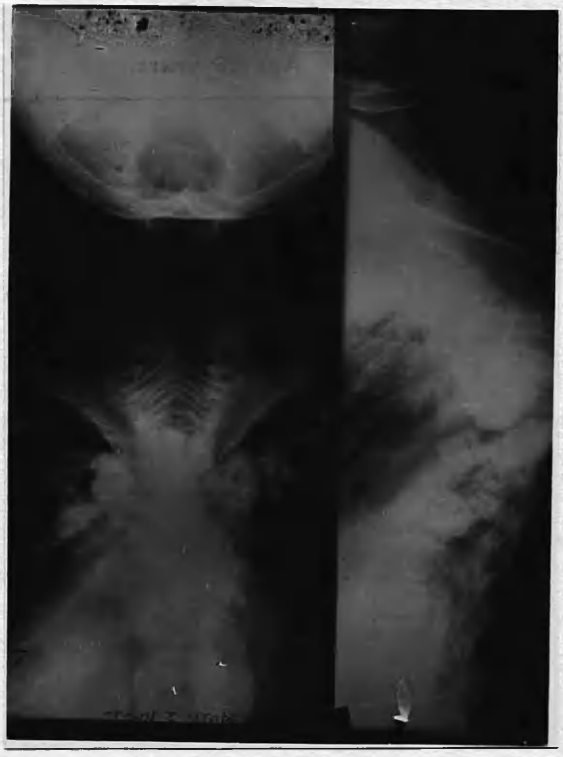


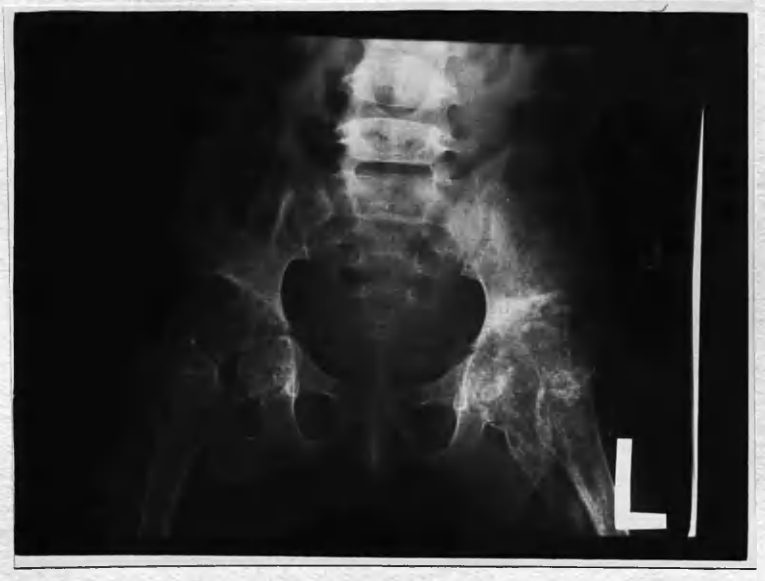
CASE NO. 39. J.S. Age 10 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Right hip joint and right ilium.	9 years.	1923 — 1930 treated by immobilisation for varying periods in different hospitals. 1930 discharging sinus over right hip joint. "Firm ankylosis" noted in 1931. Albumen found in urine June, 1931.	Very extensive absorption — head, neck and part of shaft of femur. Extensive erosion of blade of ilium. Much osteoporosis.	(a) Occasional slight evening rise of temperature to 99·8 or 100°. (b) Nil. (c) Ankylosed. (d) Abscess cleared at operation—sinus persists.	Low activity. Much soft bone found at operation.

CASE NO. 40. M.S. Age 11 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Left hip joint.	1 6/12 years.	Immobilisation in plaster of paris splints since early stage. No history of abscess.	Absorption of about two-thirds of epiphyseal head. Erosion of base of acetabulum — not widespread. Recalcification in progress.	(a) Temperature range to 99·4° at night. Pulse 92—100. (b) Nil. (c) Very slight flexion possible. No spasm. (d) Nil.	A rapidly healing lesion.

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CASE NO. 41. W.H. Age 16 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Dorsal vertebrae.	12 years.	On spinal frame for two years. Convalescent for a time. At special school for several years. Recurrence 1930—immobilisation and extension.	All dorsal vertebral bodies small and irregular — several bodies (?4) destroyed. Bone detail good but masked by widespread shadowing of calcified abscesses.	(a) Nil. (b) Nil. (c) Large kyphosis—dorsal spine fixed. Lumbar movements free. (d) Large residual abscesses.	Apparently inactive. General development poor.

CASE NO. 42. M.C. Age 4 years.

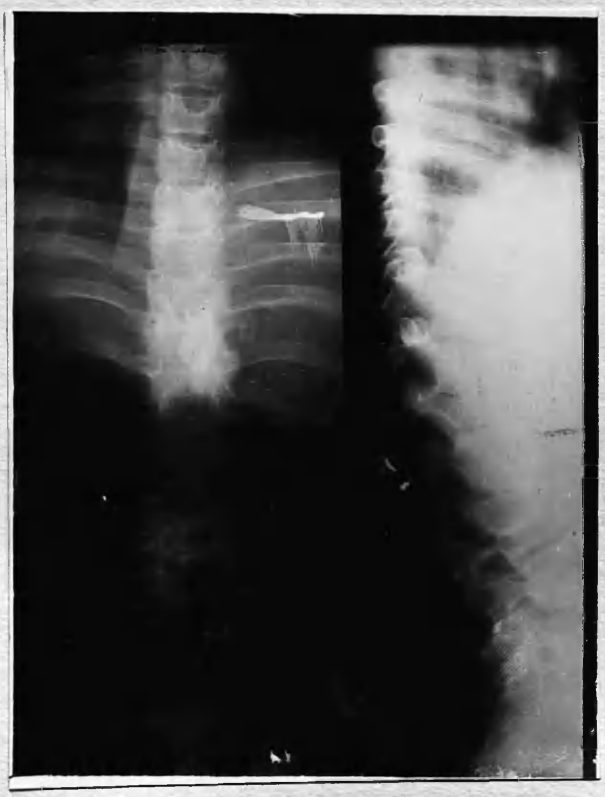
Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Both Hip Joints.	10/12 year.	Immobilisation and extension on Pyrford frame. Bilateral abscess formation requiring aspiration.	Gross bilateral erosion of acetabulum with absorption of part of head of each femur. Subluxation. Destruction apparently still progressive.	(a) 98° to 101°F. Pulse 110—120. (b) Yes +. (c) Yes—bilateral with spasm. (d) Yes—bilateral	An acute lesion still progressive.

CASE NO. 43. A.J. Age 7½ years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Dorsal vertebrae.	2 years.	1930. Result of a fall. Immobilisation on frame. 1932 Immobilisation in plaster bed.	Partial destruction of 10th, 11th and 12th dorsal vertebral bodies. ? extension of erosion in recent radiogram. Posterior mediastinal abscess —not increasing. Gibbosity increased lately.	(a) Slight temperature irregularity to 99·6°F. Pulse 92—112. (b) Nil. (c) No movement in dorsal area. No spasm. (d) No abscess palpable but seen on radiogram.	Activity of lesion has subsided to some extent.. General condition very poor.

CASE NO. 44. C.B. Age 13 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Left Hip Joint.	6 years.	Opening of abscesses. Extension on abduction frame. Immobilisation in plaster splints. Sinuses scraped July 1932.	Loss of femoral head and part of neck of femur. Extensive acetabular erosion. Bone detail poor.	(a) Irregular to 101°F. Pulse 100—120. (b) Nil. (c) Partial ankylosis. (d) Multiple infected sinuses with profuse discharge.	Lardaceous disease. Active lesion. (This patient died in January, 1934).

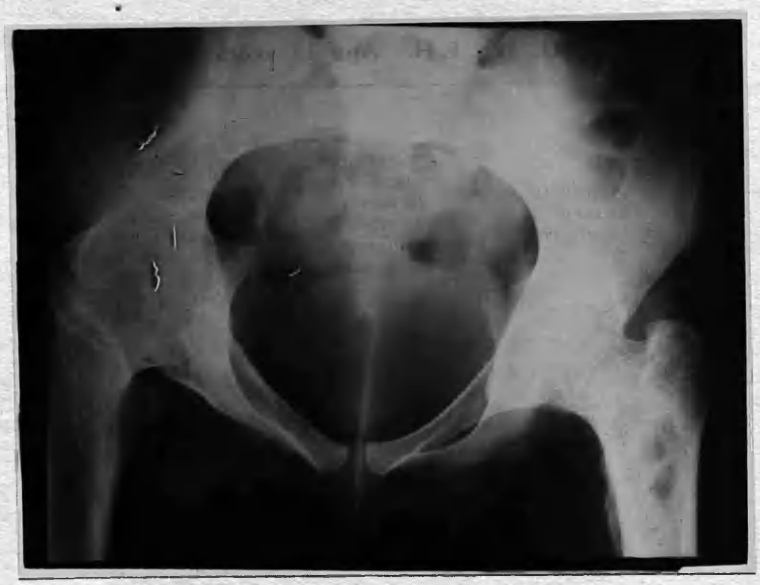


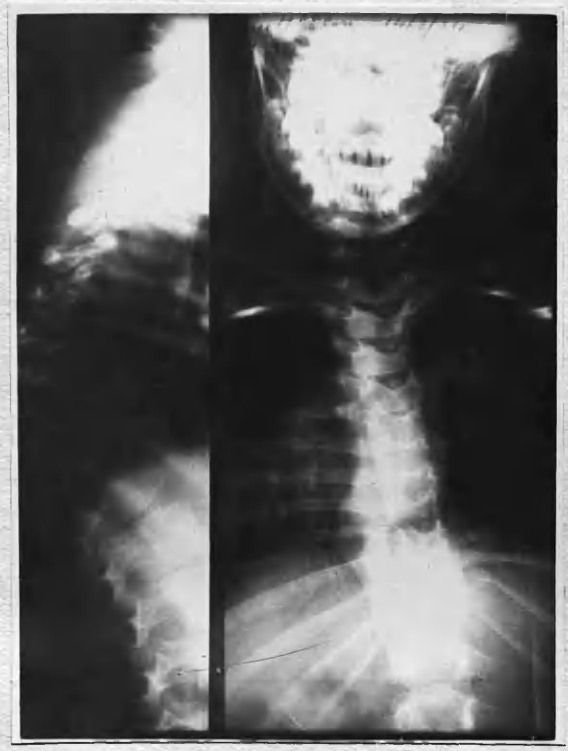
CASE NO. 45. E.C. Age 14 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Lumbar vertebrae.	9 years.	Immobilisation on frames and in plaster splints in various institutions. Aspiration of psoas abscess in 1930—sinus formed and healed rapidly.	1st to 3rd lumbar vertebral bodies eroded. Complete destruction of 2nd body. Sclerosis advanced. No abscess shadow.	(a) Nil. (b) Nil. (c) Lumbar spine rigid. No spasm. (d) No evidence of abscess.	Child ambulant. Lesion apparently quiescent. General condition good.

CASE NO. 46. J.C. Age 10 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Dorso-lumbar vertebrae.	4 years.	Immobilisation & hyperextension on various frames. Iliac abscess incised in 1929—persistent sinus.	Destructive disease of 2nd and 3rd lumbar vertebrae and of 11th and 12th dorsal vertebrae. Progressive erosion and collapse. Abscess bilateral.	(a) Temperature irregular, 100° to 101°F. Pulse 92—112. (b) On movement or flexion of spine. (c) Movement of spine limited—some spasm. (d) Left iliac abscess and sinus. Two lumbar sinuses.	An active progressive lesion with no repair. Lardaceous disease.



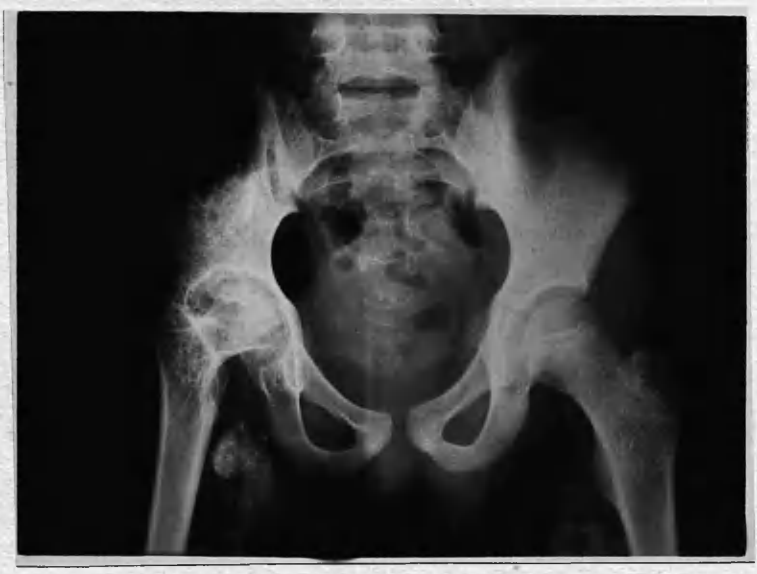


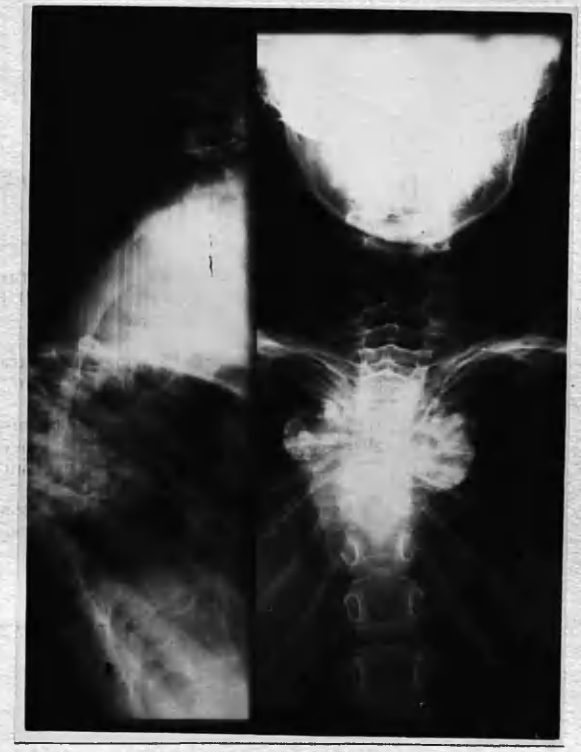
CASE NO. 47. E.H. Age 14 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Multiple lesions. Left hip, left tibia, right scapula, left elbow, sub-cutaneous abscesses (multiple).	9 years.	Several operations. Left hip firmly ankylosed. Sequestrum removed from tibia 1932 — wound healed well.	Fusiform swelling of left tibia in middle third of shaft with cavity —sclerosing. Bony ankylosis of left hip joint. Periosteal proliferation on shaft of left femur. No other bone changes observed.	(a) Nil. (b) Nil. (c) Ankylosis left hip. Other movements free. (d) Multiple old abscesses but none at present.	Non - tuberculous streptococcal infection. All lesions quiet.

CASE NO. 48. A.McE. Age 4 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Dorsal vertebrae.	2 years.	1930 — "advancing disease" treated on frame. Lumbar abscess—sinus formed and healed.	Absorption of 9th and 10th dorsal vertebral bodies and erosion of 8th and 11th vertebral bodies. Efficient collapse with some recalcification.	(a) Nil. (b) Nil. (c) Movements limited. No spasm. (d) No abscess now present.	Apparently inactive lesion. No weight bearing allowed so far. Right anterior poliomyelitis — infection at 9/12 years.



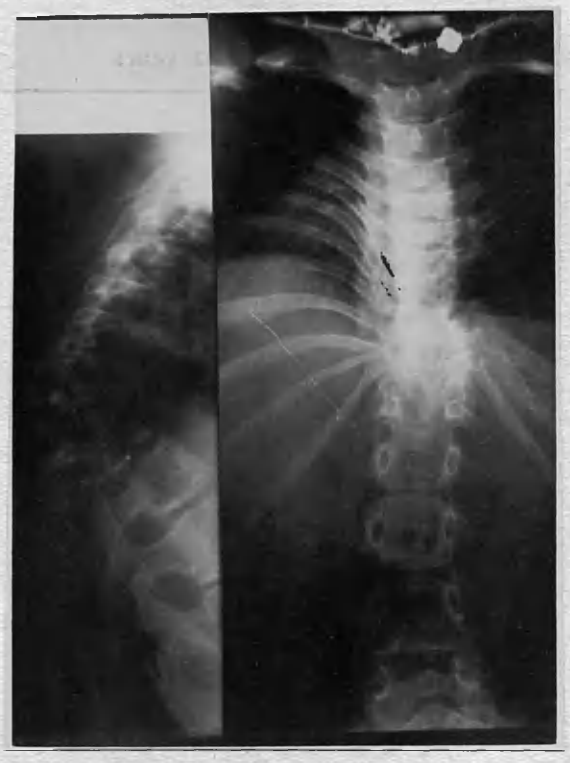


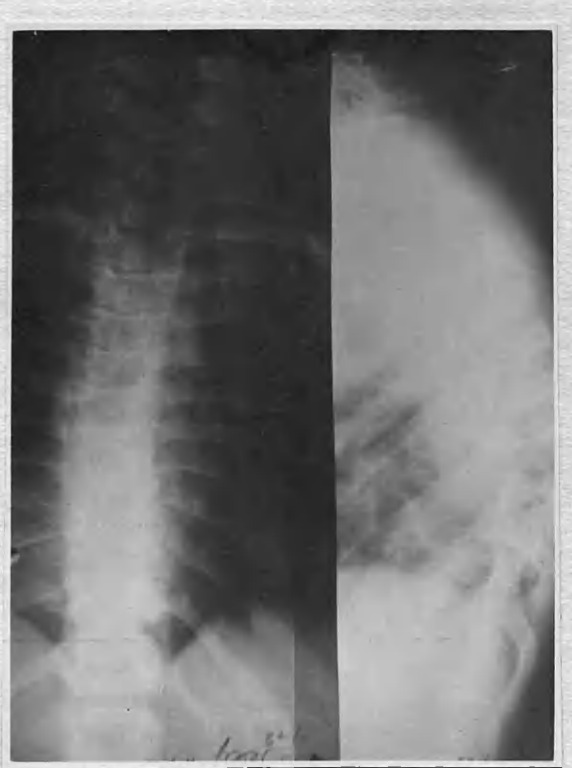
CASE NO. 49. W.B. Age 10 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Left hip joint.	8 years.	1924 to 1928—various periods of immobilisation. Hip abscess aspirated in 1929. Immobilisation in plaster splint since 1931.	Head and part of neck of femur absorbed. Some erosion of acetabulum. Widespread osteoporosis showing some evidence of recalcification in areas. Calcified abscess in angle between femur & ischium.	(a) Nil. (b) Nil. (c) Partial ankylosis. No spasm. (d) As noted—not acute.	Apparently inactive lesion. (Extra — articular graft May, 1934—"much soft bone found").

CASE NO. 50. D.S. Age 10 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Dorsal vertebrae.	7 years. Apparent inactivity 1929 — 1930. Recurrence of activity in 1930.	No reliable history, apart from long periods of fixation in various splints.	Extensive erosion of almost all vertebral bodies. Disease appears active. Bilateral psoas abscess.	(a) Temperature irregular to 100°F. Pulse 90—120. (b) Spastic paraplegia with pain. (c) Much spasm—very little movement of any kind. (d) Bilateral psoas—fluid abscesses.	Lesion remains acute. Spastic paraplegia with cystitis. Child died of tuberculous meningitis 25/12/32.



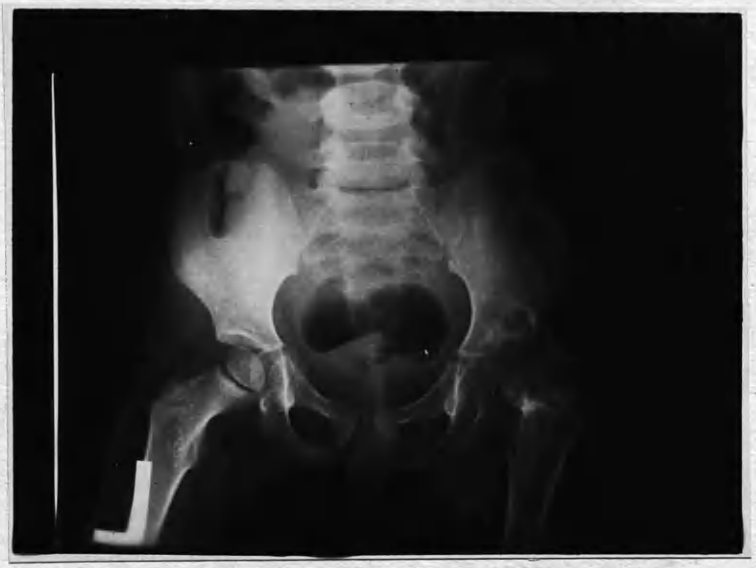


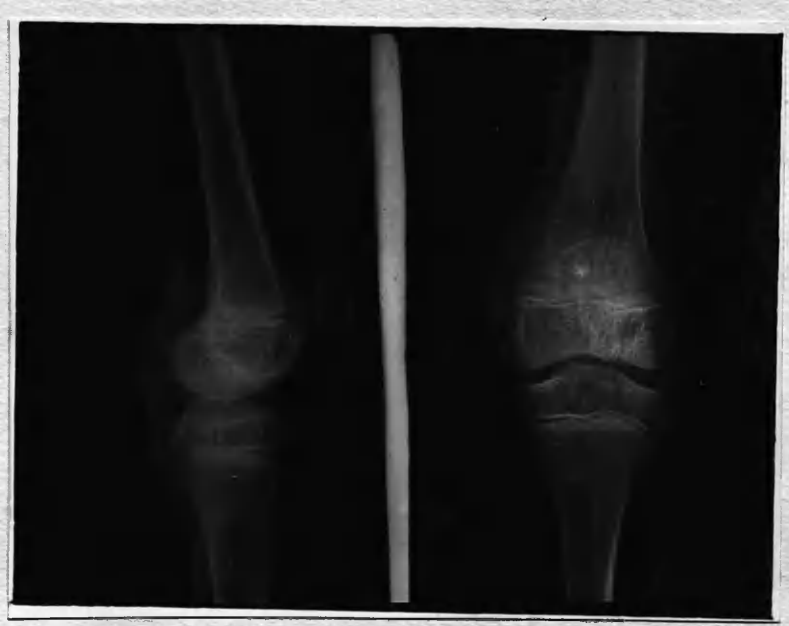
CASE NO. 51. M.R. Age 12 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Dorsal vertebrae.	9 years.	No history of particulars of treatment. Old lumbar abscess.	Erosion or destruction of dorsal vertebrae 4th—9th, absorption of three dorsal bodies. No apparent extension of lesion since admission.	(a) Occasional irregularity of temperature to 100°F. (b) Nil. (c) Mechanical impairment. No spasm. (d) Lumbar abscess reformed and incised May, 1932—sinus formed.	An active lesion. General condition very poor.

CASE NO. 52. W.K. Age 12 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Dorsal vertebrae.	3½ years.	Immobilisation on frames and in plaster splints in several institutions.	Extensive infection of dorsal vertebral bodies. 4th to 11th bodies small, and showing mottled shadowing. No gross absorption of vertebral bodies. Very small abscess shadow.	(a) Temperature irregular to 99.2° F. Pulse 80—90. (b) Nil. (c) Spinal movements very limited. No spasm. (d) No clinical evidence of abscess.	Apparently inactive. General condition poor.



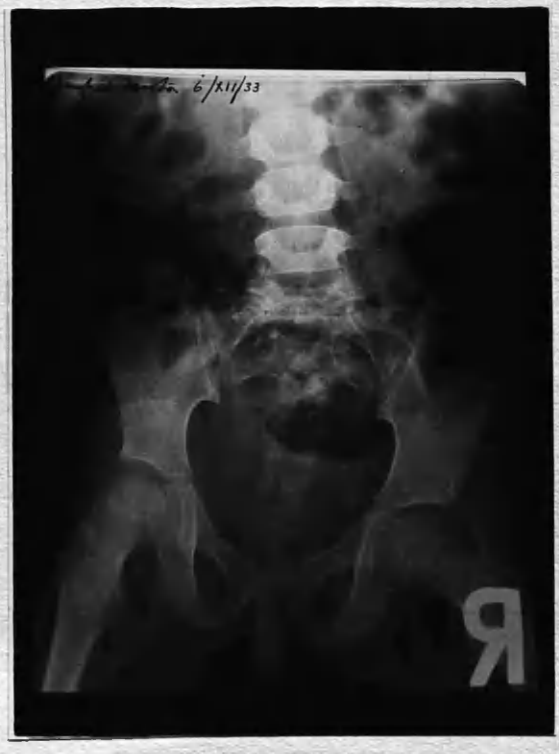


CASE NO. 53. S.H. Age 2 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Right hip joint.	1½ years.	Immobilisation and extension on Pyrford frame. Aspiration of hip abscess — sinus on on right thigh.	Progressive destruction of head and neck of femur with some acetabular erosion and subluxation. Excavation of trochanteric area.	(a) Occasional temperature irregularity to 99.6°F. (b) Pain on movement. (c) Limitation of movements with considerable spasm. (d) Abscess present with sinus.	Lesion still active and destructive process acute. General condition reasonably good.

CASE NO. 54. R.F. Age 10 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movemcnt.* *d Abscess formation.*	*Remarks.*
Left knee joint.	3 years.	Repeated periods of immobilisation in plaster splints. Apparent quiescent periods with recurrence of activity	No bony change observable. Slight loss of joint space.	(a) Temperature irregular to 100°F. Pulse 84—100. (b) By passive movements. (c) Flexion very limited. (d) Nil.	A synovial lesion apparently remaining active.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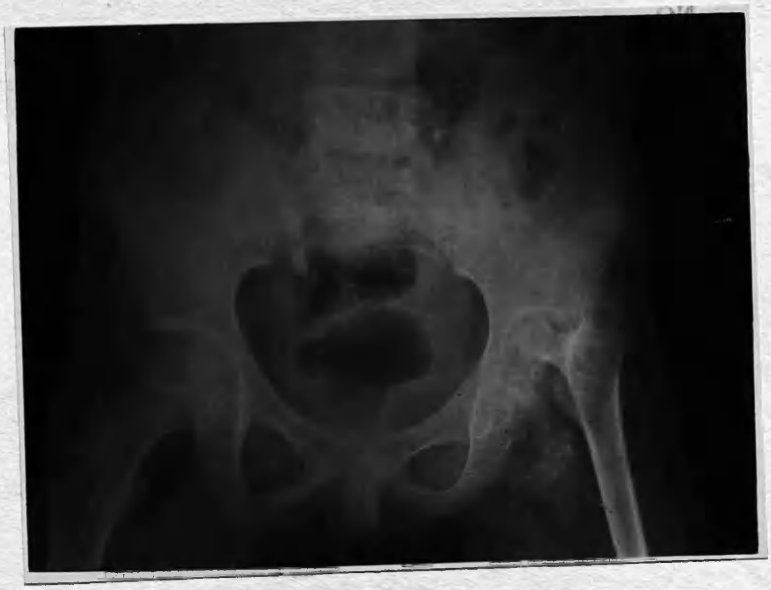
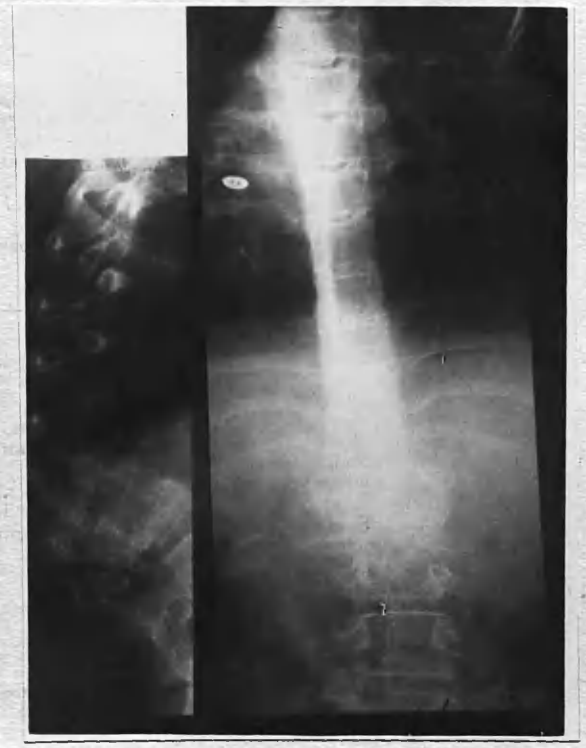
CASE NO. 55. E.A. Age 12 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Cervical vertebrae.	4 years.	Treated at home and dispensary 1928—1930. Immobilisation and extension on frame.	Partial destruction and absorption of 5th, 6th and 7th cervical vertebral bodies. Very small abscess shadow in front of affected bodies, partly calcified.	(a) Nil. (b) Nil. (c) Limitation of flexion and hyperextension of neck. (d) No clinical evidence of abscess.	Apparently inactive lesion.

CASE NO. 56. W.N. Age 5 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Lumbo-sacral articulation.	3 years.	Immobilisation on plaster bed. Aspiration of abscess of right thigh. Incision and removal of sequestrum required in 1931. Sinuses with secondary infection.	Gross destruction of 5th lumbar vertebral body and loss of lumbo-sacral articulation. Some evidence of sclerosis in area of erosion and of calcification in abscess.	(a) 99° to 101°F. Pulse 100 to 120. (b) Nil. (c) Spinal movements very limited as a result of fixation. (d) Copious purulent discharge from sinuses.	Condition very poor and bones generally osteoporotic. Doubtful if tuberculous lesion of bone is in itself very active.



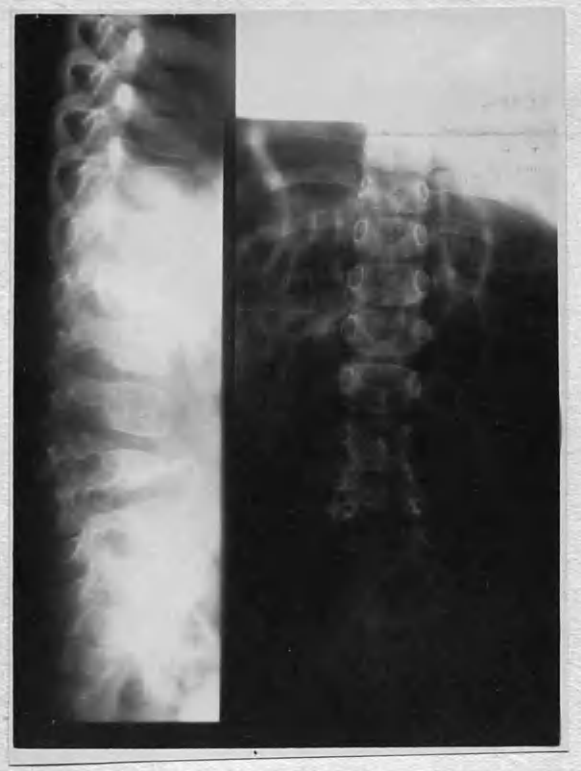


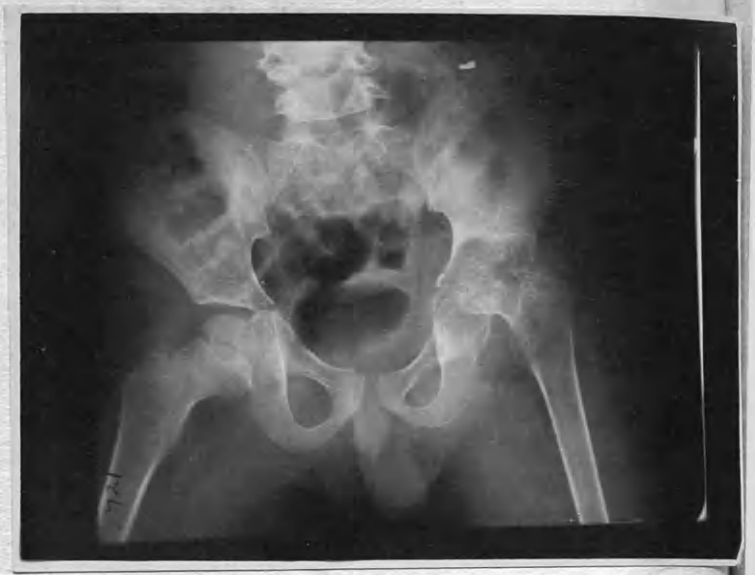
CASE NO. 57. F.B. Age 9 years.

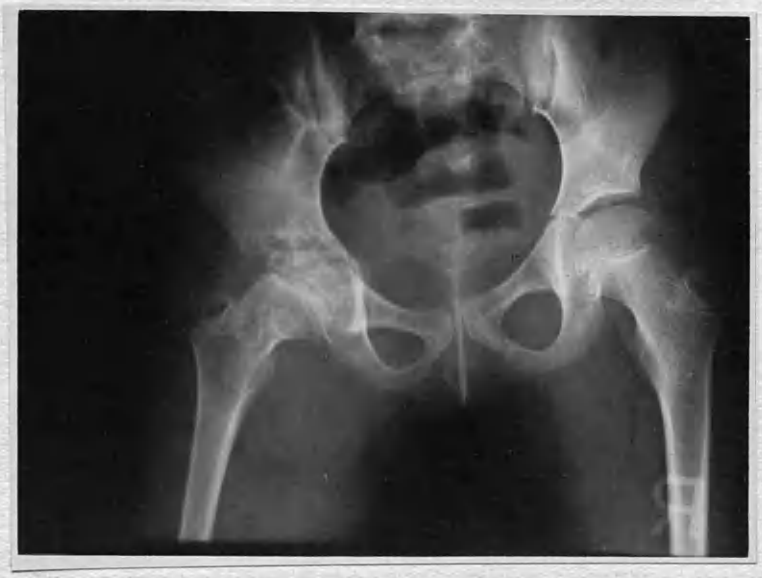
Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Right hip joint.	4 years.	Immobilisation in plaster splints. Old healed sinus on right thigh.	Head and neck of femur largely destroyed. Remains of neck forming new head in widely eroded acetabulum. Evidence of sclerosis in diseased area. Some calcification in abscess.	(a) Temperature swinging to 100·4° F. Pulse 94 to 104. (Probably due to chronic otitis). (b) Nil. (c) Limitation of flexion. Nil spasm. (d) Partially calcified abscess.	Lesion not definitely quiescent but activity probably very low.

CASE NO. 58. J.C. Age 13 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Lumbar vertebrae.	10 years.	1922 onset followed a fall. Immobilised with apparent healing. 1927 to 1930 attended special school. 1930 abscess formed. Immobilised again. 1932 large thick psoas abscess.	Disease of upper four lumbar vertebrae. Almost complete absorption of 2nd and 3rd bodies with collapse. Some evidence of sclerosis at margins of area of erosion. Left psoas abscess—showing some calcification.	(a) Nil. (b) Nil. (c) Spinal movements very limited. (d) Left psoas abscess palpable. Too thick for aspiration.	Disease apparently quiet at present but note reactivation in 1930. General condition good & improving.





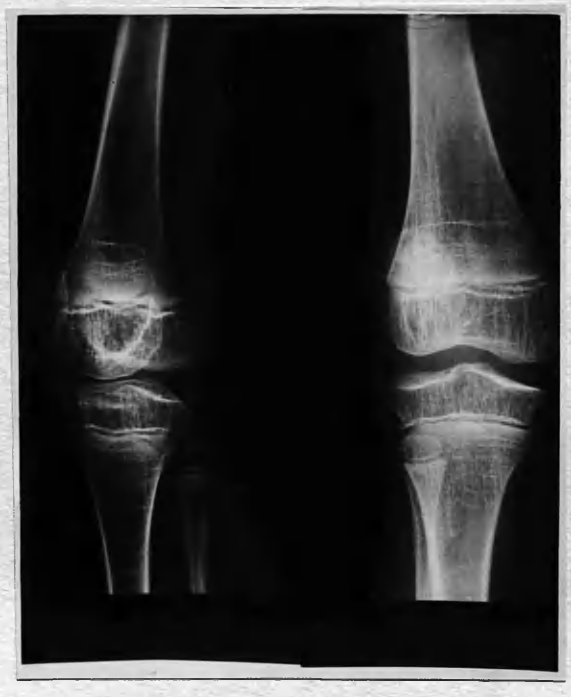


CASE NO. 59. W.D. Age 5 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Right hip joint. Lumbar vertebrae.	Hip-2 years. Spine - 6/12 years.	Immobilisation and extension on Pyrford frame.	Head of right femur absorbed and acetabulum eroding. Marked osteoporosis. Partial erosion and absorption of 3rd and 4th lumbar vertebral bodies. Left psoas abscess.	(a) Temperature swinging to 100° F. Pulse 96 to 112. (b) Pain on movement of hip or pressure on lumbar spine. (c) All hip movements very limited—spasm. Spinal movements also small and painful. (d) Psoas abscess —palpable.	Active lesion. Acute destructive process.

CASE NO. 60. L.S. Age 7½ years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movemcnt.* *d Abscess formation.*	*Remarks.*
Left hip joint.	2½ years (doubtful).	No very accurate history obtained but in Aug., 1930, "marked rarefaction of head of femur" was reported. Treated by extension and immobilisation on various frames and splints.	Epiphyseal head of left femur partly absorbed but destruction of bone not extensive. Remains of head well impacted in acetabulum and position good.	(a) Temperature very irregular. Ordinary range 98° to 100°F. but occasional periods of irregularity to 103°F. (b) Nil. (c) Very slight flexion only possible at hip joint. (d) No clinical evidence of abscess.	A B-Coli infection of the urinary track explains periods of high swinging temperature. The bone lesion gives the impression of remaining activity. Note: Hip abscess formed and discharged during the latter part of 1933.

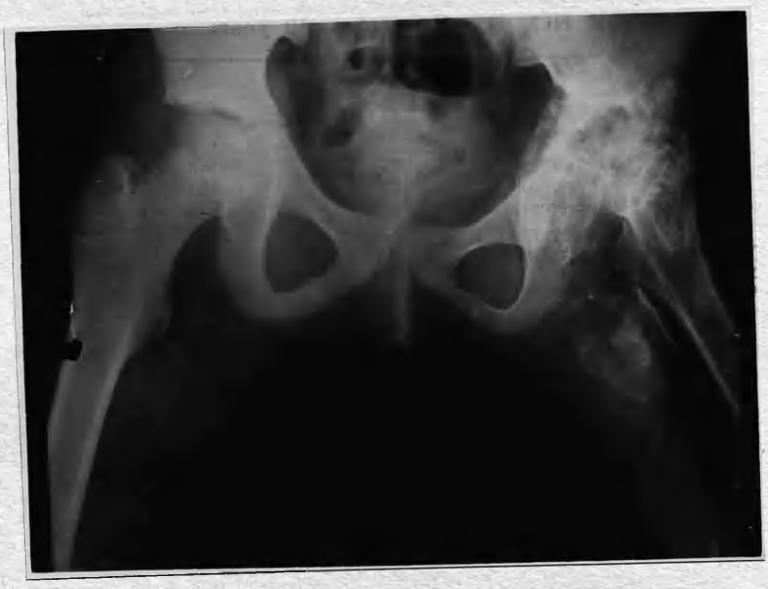


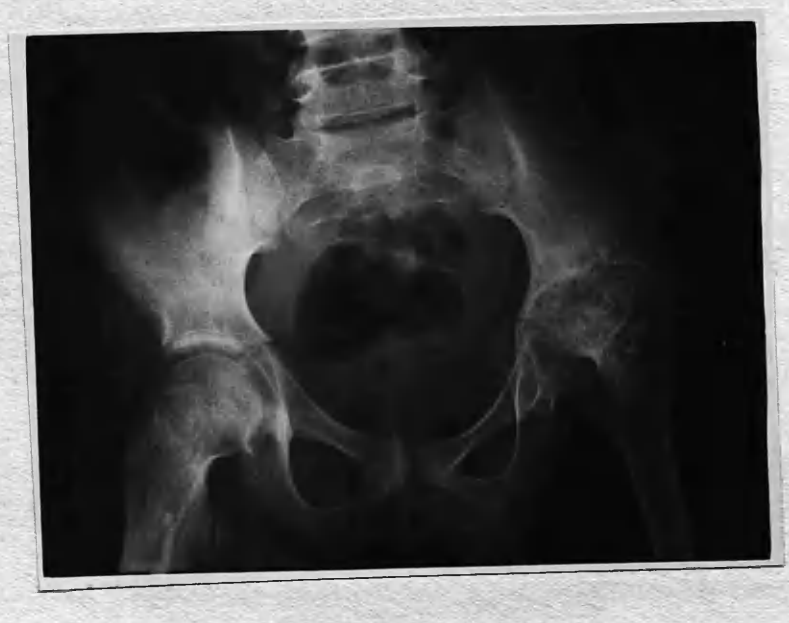
CASE NO. 61. A.T. Age 13 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Dorso-lumbar vertebrae.	4 years.	No history of early treatment available. Long periods of immobilisation and hyperextension. No history of abscess formation.	Partial destruction of 2nd and 3rd lumbar vertebral bodies. Good fusion of fragments and marked sclerosis at fusion.	(a) Nil. (b) Nil. (c) Good movements above and below lesion. (d) Nil. Lesion obviously inactive.	Child ambulant, in good general condition, and with high exercise tolerance.

CASE NO. 62. T.B. Age 8 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Right knee joint.	3 years.	Plaster fixation for two years. Gradually increased exercise & weight-bearing.	No erosion of bone. Decreasing osteoporosis of femoral epiphysis.	(a) Nil. (b) Nil. (c) Slight limitation of flexion. (d) Nil. A definitely quiescent lesion.	Child ambulant for 4 months before estimation wearing caliper splint. Tuberculin sensitivity was ++



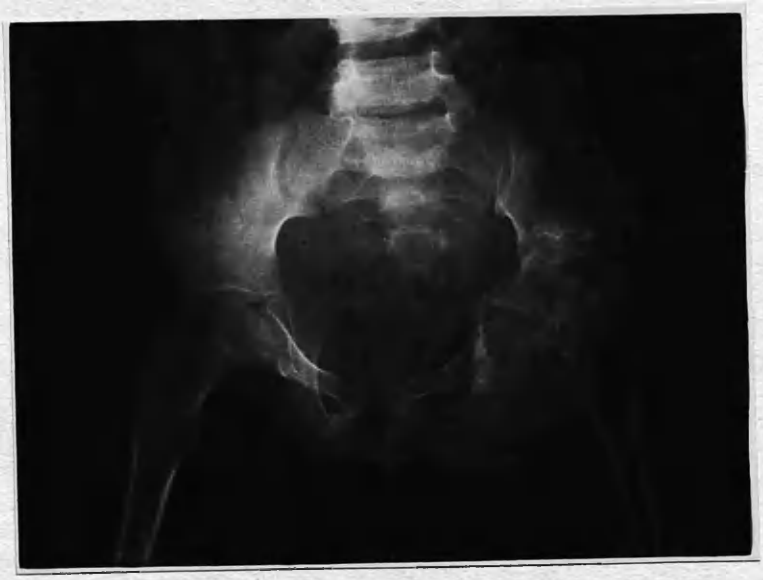


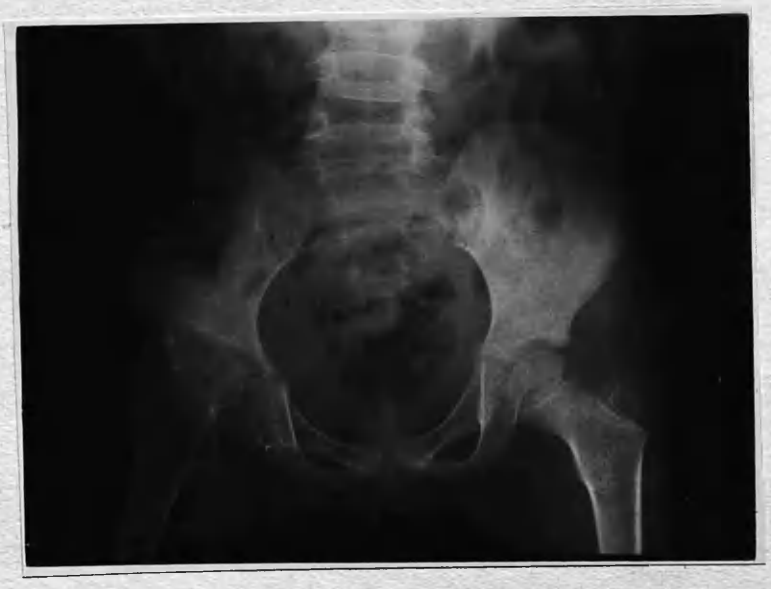
CASE NO. 63. E.B. Age 10 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Left hip joint and right ankle joint.	7 years.	No history of treatment obtained. Old healed sinus on left thigh. Recent immobilisation in plaster splints.	Destruction and absorption of head of femur. Erosion of acetabulum and subluxation. Large calcified abscess. Ankle: Irregularity of articular surfaces of tibia & astragalus. Loss of joint space. Bone detail good.	(a) Nil. (b) Nil. (c) Partial ankylosis of hip joint. Movements of ankle joint limited. (d) No clinical evidence of abscess formation.	Ankle lesion inactive. Hip lesion probably still mildly active. General condition very good.

CASE NO. 64. C.L. Age 10 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Right hip joint.	8 years (total). Reactivation with abscess 4 months before estimation.	1924—onset. Immobilisation and extension in various splints. Apparently quiescent in 1931 and sent to special school. Re-admitted to Abergele October 1932, with abscess in front of hip joint.	Extensive absorption of head and neck of femur and erosion of acetabulum. Good impaction & partial ankylosis with good bone detail except along line of ankylosis.	(a) Temperature irregular to 99.4°F. Pulse 90 to 100. (b) Nil. (c) Very slight flexion movement of hip possible. (d) Palpable fluctuant abscess in front of hip.	General condition very poor. Reactivation of lesion at line of attempted ankylosis.



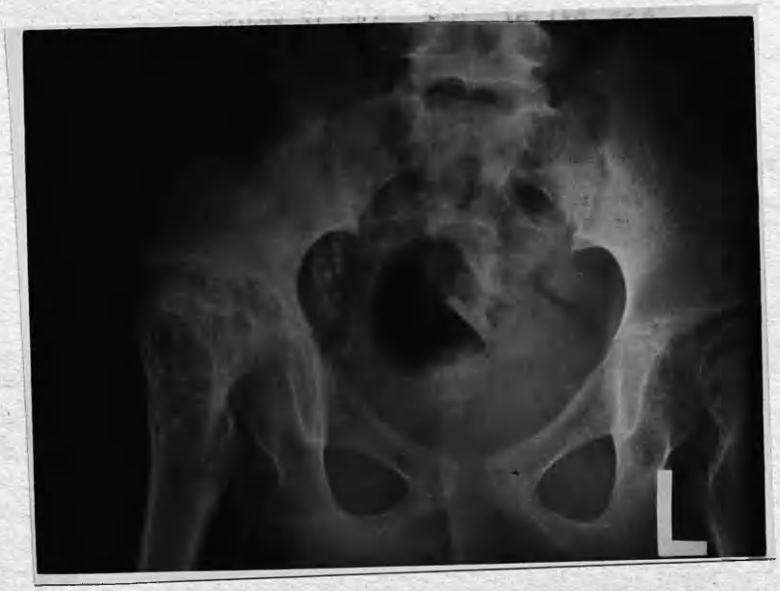


CASE NO. 65. D.McH. Age 7 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Right hip joint.	2 years.	1930—onset. Immobilisation in plaster splints. Admitted to Abergele in January, 1932.	Advancing destruction of head and neck of femur. Increasing erosion of acetabulum. Marked osteoporosis.	(a) Temperature to 100°F. Pulse 80—112. (b) Pain on movement. (c) Movements very limited and painful. (d) No evidence of abscess.	An advancing lesion. General condition very poor. All bones thin and osteoporotic. Note: Hip abscess formed and discharged in January, 1934.

CASE NO. 66. D.N. Age 5 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Left Hip Joint.	1½ years.	July, 1931 — onset. Admitted to Abergele, December, 1931. Treated on Pyrford frame.	Advancing absorption of head of femur and erosion of neck of femur. No abscess shadow.	(a) Temperature irregular to 99.8°F. (occasional rise to 101°F). (b) Pain on movement. (c) Marked spasin. (d) No clinical evidence of abscess.	Acute lesion. General condition miserable. Phlyctenular conjunctivitis. Septic sores on knees resulting from extension.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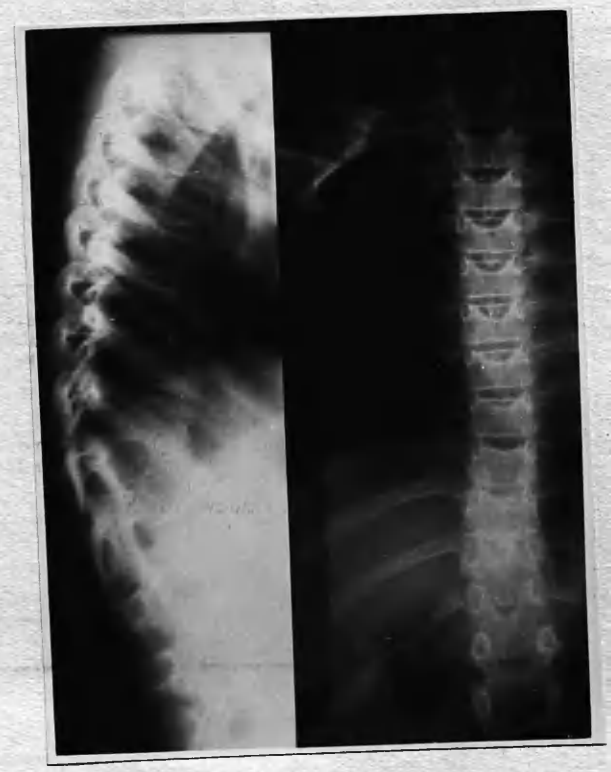
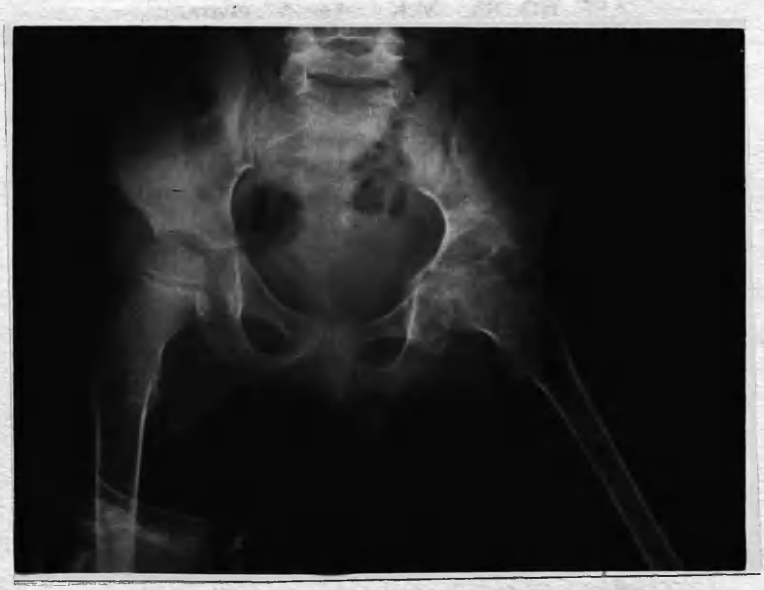


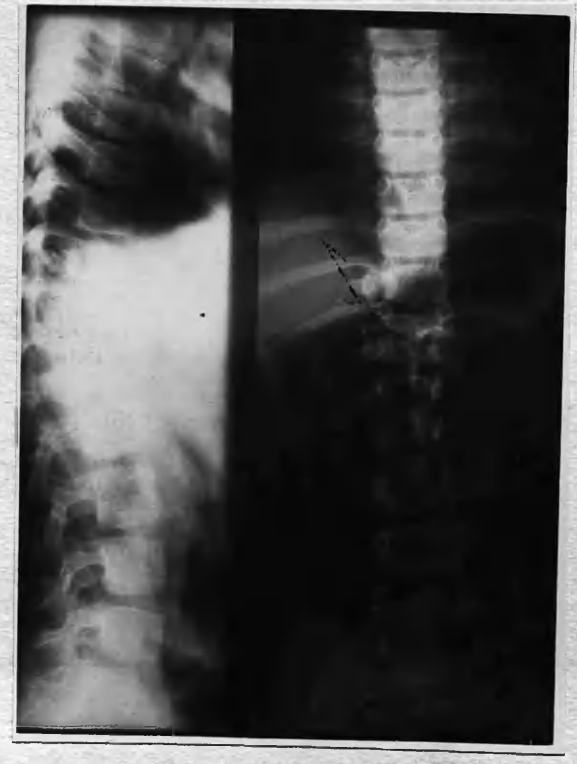
CASE NO. 67. B.R. Age 12 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Right Hip Joint.	4 years.	1928—onset. Ambulatory for a time. 1929, Aspiration of large abscess which absorbed later. Immobilised in plaster splints. January, 1932—admitted to Abergele.	Absorption of head and neck of femur and upward erosion of acetabulum. Moderately good ankylosis. Calcified iliac glands.	(a) Temperature 97·4° to 99·4°F. Pulse 88 to 100. (b) Nil. (c) Ankylosed. (d) No evidence of abscess.	General condition fairly good. Limited movements at knees and ankles. Bilateral talipes equino varus. Hip lesion apparently inactive.

CASE NO. 68. C.B. Age 8 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Dorsal vertebrae.	2 years.	No history of early treatment. Immobilised in plaster bed since admission to Abergele — January, 1932.	Erosion of 10th and 12th dorsal vertebral bodies. 11th body absorbed. Efficient collapse in progress but bone detail poor. No abscess shadow.	(a) Temperature 99·4°F. at night. Pulse 84 to 100. (b) Nil. (c) Spinal movements very limited. (d) Nil.	A moderately active lesion at time of estimation. General condition fairly good.



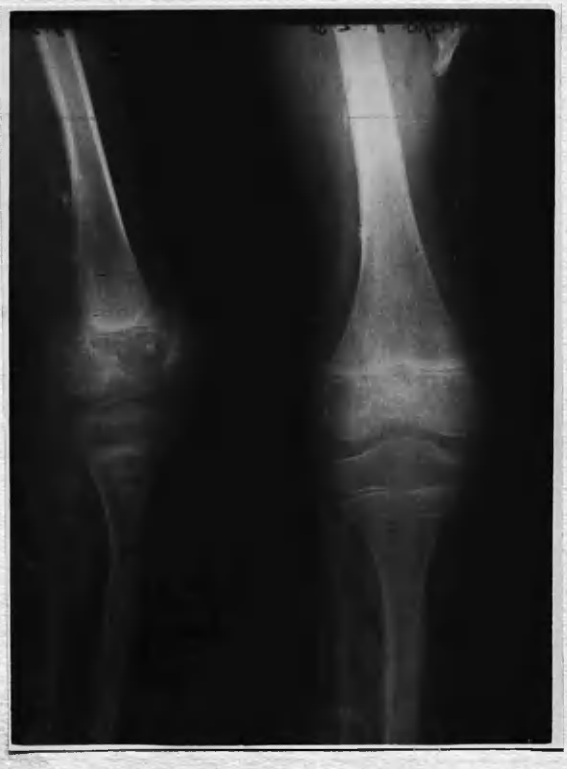


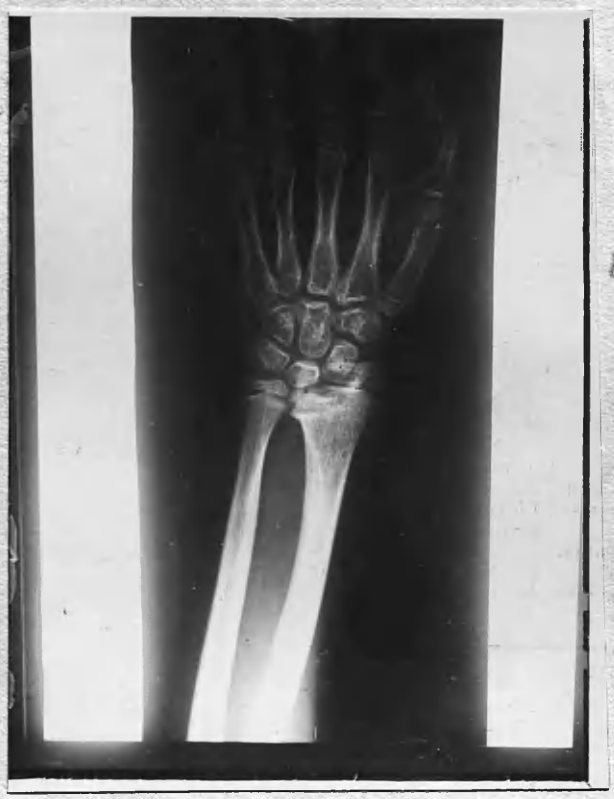
CASE NO. 69. M.K. Age 5¾ years.

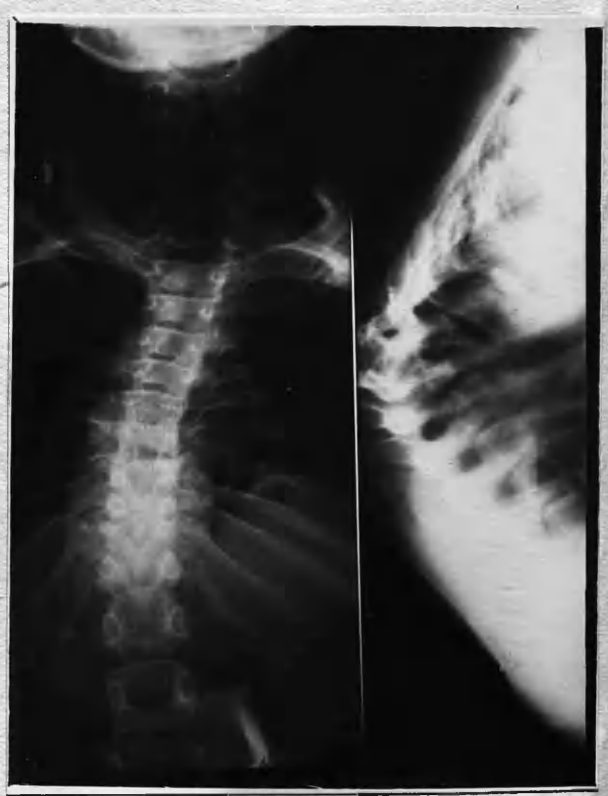
Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Right Hip Joint.	3¼ years.	1929 onset after fall. Immobilisation and extension on frame. Admitted to Abergele in November, 1931.	Advancing destruction of head of femur. Erosion of acetabulum.	(a) Occasional irregularity of temperature to 99·8°F. Pulse 80—108. (b) Pain on movement of joint. (c) Movements limited by spasm. (d) Nil.	An active progressive lesion. General condition poor.

CASE NO. 70. K.T. Age 3 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Dorso-lumbar vertebrae.	2½ years.	Immobilised on frame at home. Admitted to Abergele, November, 1931. Immobilised in plaster bed.	No abscess. Disease of 11th and 12th dorsal vertebral bodies and of 1st lumbar body. Bodies of 11th and 12th dorsal largely absorbed. Efficient collapse in progress. Some evidence of sclerosis.	(a) Temperature reaching 99·8°F. at night. Pulse 90 to 100. (b) Nil. (c) Lumbar movements limited. No spasm. (d) Nil.	Apparently a healing lesion but questionable if activity has ceased.





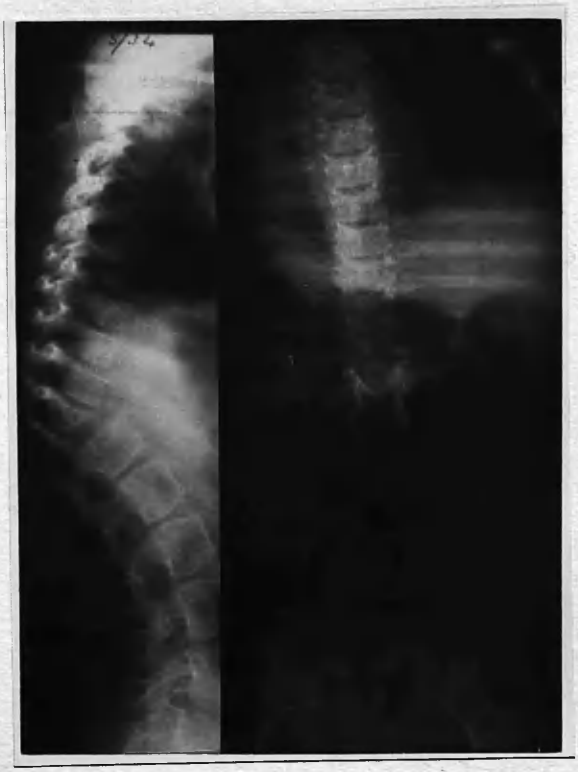


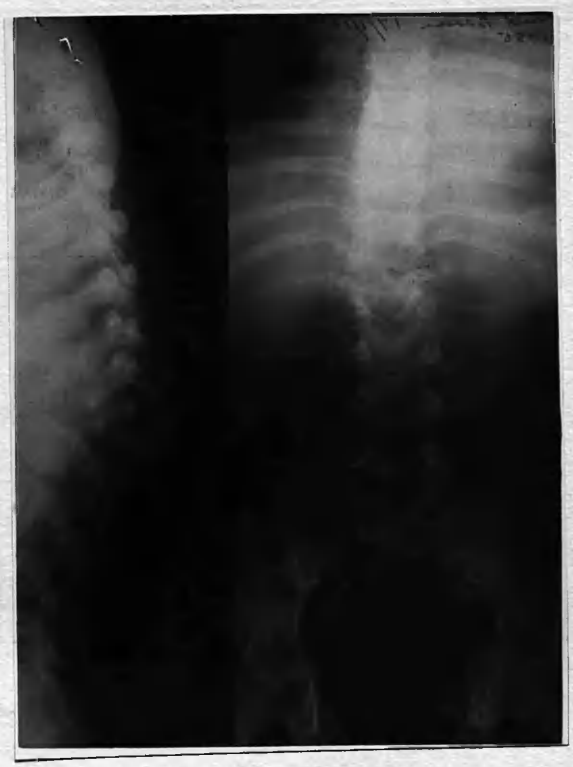
CASE NO. 71. G.P. Age 7 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Right Knee Joint.	6 years.	1926, onset after a fall. Long treatment in various institutions. Periods of apparent quiescence. No accurate history of treatment. Admitted to Abergele in December, 1931—scar of sinus present over lateral epicondyle of femur.	General osteoporosis of femur and tibia. Very fine irregularity of articular surface of femur. Small calcified shadows lateral to lower third of shaft of femur with periosteal irregularity.	(a) Nil. (b) Pain on passive movement. (c) Flexion very limited. (d) No present evidence of abscess.	Disease appears quiet at present, but, three months ago the lesion seemed active, flexion taking place as soon as splint was removed.

CASE NO. 72. C.L. Age 6 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Dorsal vertebrae. Right Wrist Joint.	Wrist — 3 years. Spine — 2 years.	Immobilised on spinal frame since 1929 in various institutions. Wrist immobilised in plaster splint.	Four dorsal vertebral bodies eroded —two bodies absorbed. Large fusiform abscess. Collapse with large rounded kyphosis. Wrist: Excavation of epiphysis of radius — sclerosis advanced.	(a) Temperature irregular to 100°F. Pulse 94 to 110. (b) Nil. (c) Spinal movements in abeyance. No spasm. Flexion of wrist limited. (d) No clinical evidence of abscess.	Lesion of spine is probably still mildly active but the wrist lesion appears to be quiescent.



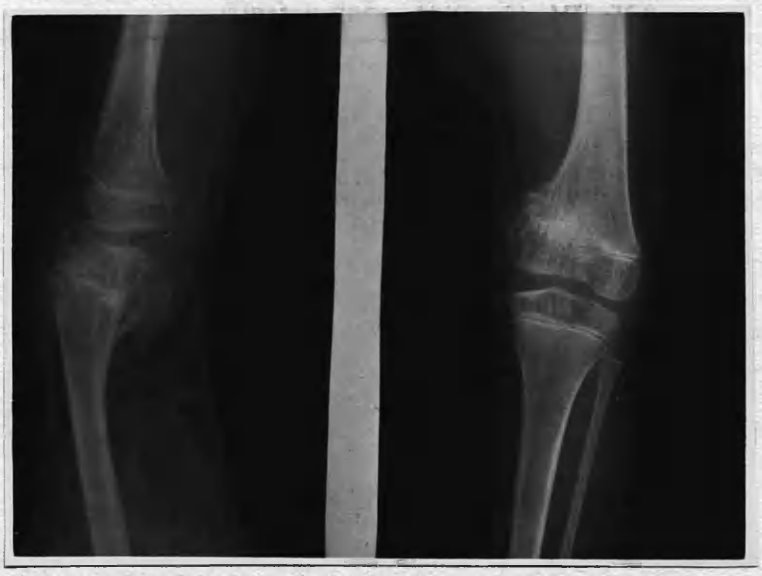


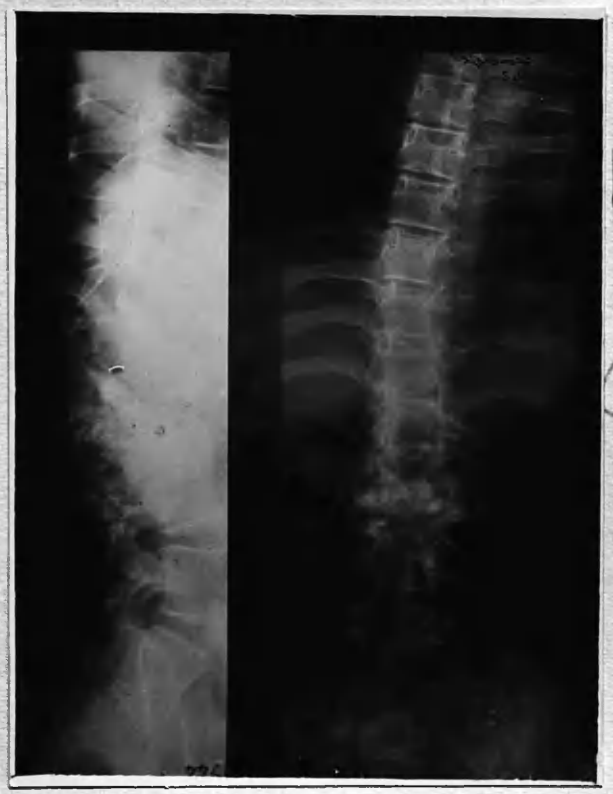
CASE NO. 73. A.H. Age 3 years.

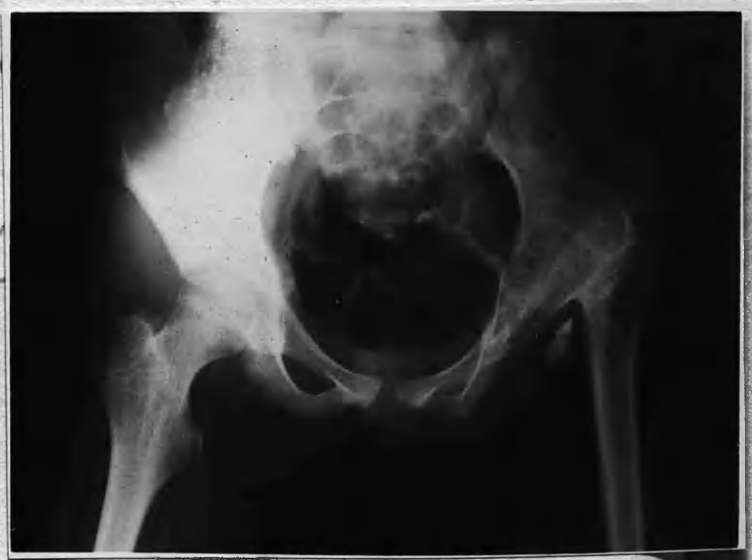
Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Dorsal vertebrae.	1½ years.	Immobilisation on spinal frame.	Disease of 9th to 12th vertebrae. 11th and 12th vertebral bodies absorbed. Commencing recalcification.	(a) Nil. (b) Nil. (c) Limitation of all spinal movements. Kyphosis. (d) Nil.	A lesion in which activity is rapidly diminishing. Note: Plastic operation on cranial vault, at ½ year. Spastic paraplegia of right hand and arm.

CASE NO. 74. R.B. Age 3 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Dorso-lumbar vertebrae.	2 years.	Immobilisation on spinal frame till recently. Now immobilised in plaster jacket.	Very complete absorption of 12th dorsal and 1st lumbar vertebral bodies. Collapse with some recalcification. Diminishing abscess showing some calcification.	(a) Nil. (b) Nil. (c) Small kyphosis. Very limited spinal movements. No spasm. (d) No clinical evidence of abscess.	Sub-active lesion. General condition very poor and development much below normal.





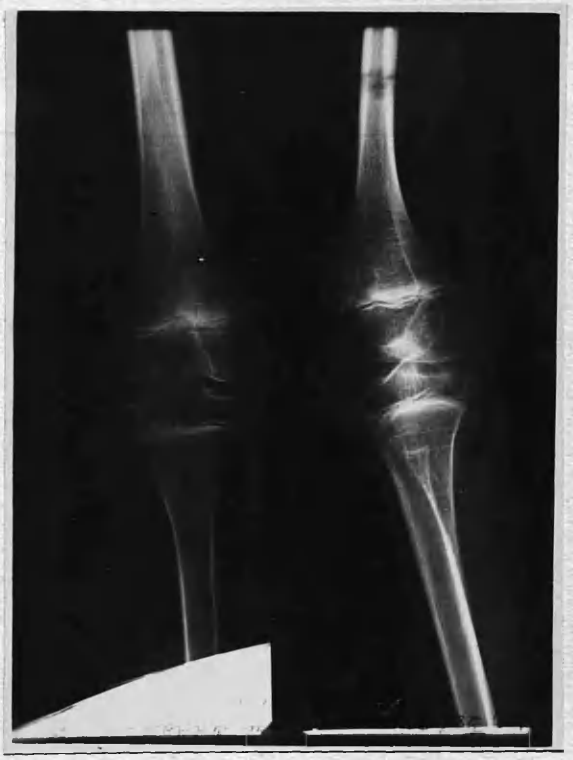


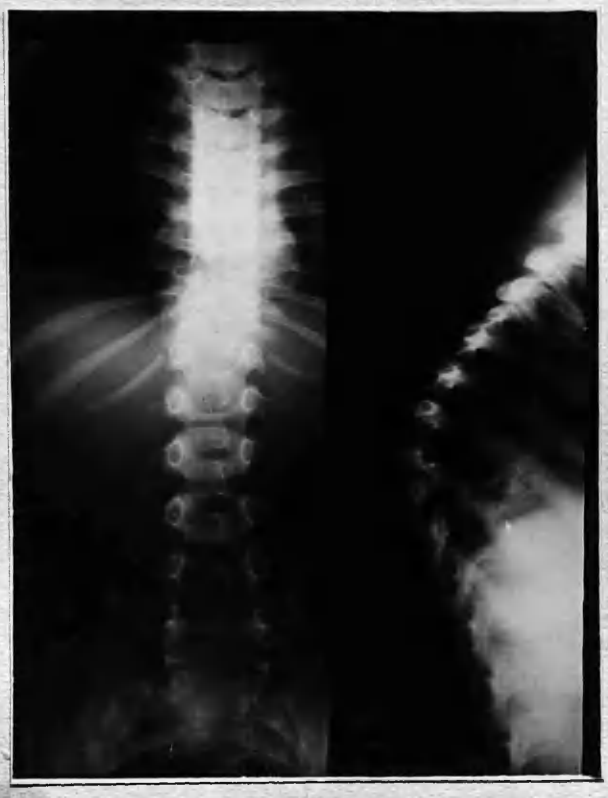
CASE NO. 75. M.D. Age 6 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Right Knee Joint.	3 years.	No reliable history of early treatment. History of "aspiration" and scar on outer aspect of knee. Recent immobilisation in plaster splints.	Marked erosion of inner epiphyseal condyle extending into inner and posterior aspect of diaphysis. Bone detail generally masked.	(a) Nil. (b) Spasm round knee joint with pulpiness and pain on movement. (c) Movement very slight. (d) Nil.	Lesion remains active. General condition good.

CASE NO. 76. E.S. Age 12 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Right Hip Joint and Lumbar Vertebrae.	Hip—9 years. Spine—7 years.	No history available of treatment of hip joint disease. Immobilisation and hyperextension on various spinal frames. Recent fixation in plaster spinal jacket.	Hip: Loss of head and neck of femur with acetabular erosion and dislocation. Small calcified abscess. Ankylosed—good bone detail. Spine: Complete destruction of three lumbar bodies. Good collapse. Butterfly psoas abscess, well calcified.	(a) Nil. (b) Nil. (c) Spinal movements good above lesion. (d) Palpable psoas abscess.	Healed and healing lesions. General condition fairly good but much muscular atrophy.



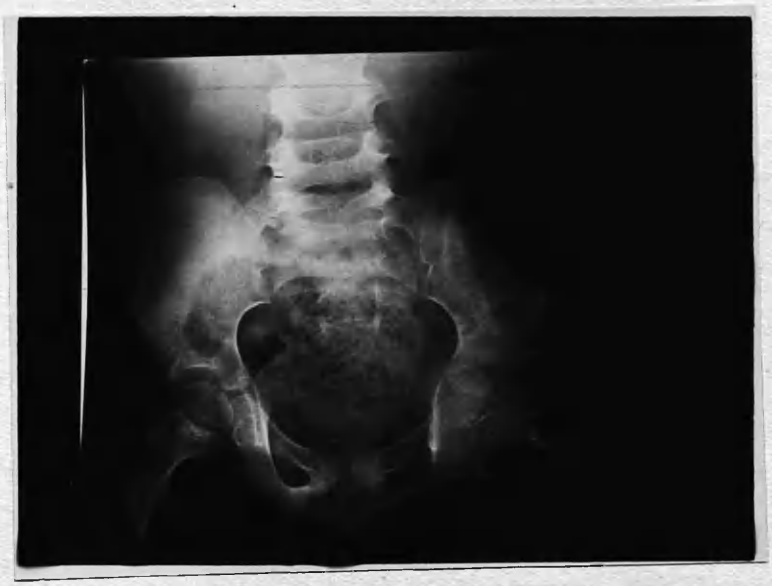


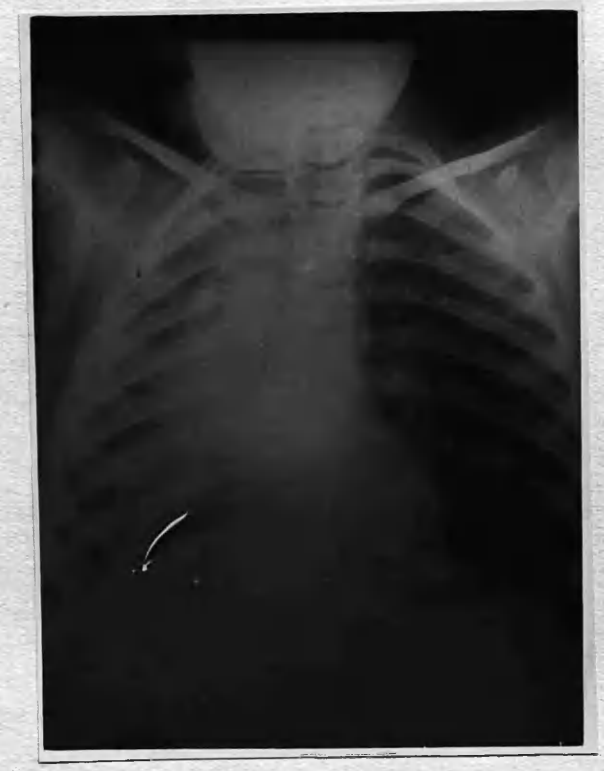
CASE NO. 77. J.S. Age 9 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Right Knee Joint.	6 years.	Immobilisation from 1926 till 1928 with apparent good recovery. Some fleeting symptoms in 1928—observed for a time—apparent subsidence. Pain and swelling returned in 1930. Immobilised since then.	No bony abnormality. Presumably purely synovial.	(a) Temperature irregular to 99·4°F. Pulse 80—100. (b) Nil. (c) Flexion extremely limited. No spasm behind knee. (d) Nil.	No evidence of present activity of disease but repeated relapses make an assessment of final quiescence very difficult.

CASE NO. 78. C.H. Age 5 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Dorsal Vertebrae.	3½ years.	Long-continued immobilisation on spinal frames and plaster bed. Lately—fixation in plaster spinal jacket.	Destructive disease of 8th to 12th dorsal vertebral bodies. Two bodies almost entirely absorbed. Destructive process apparently not extending but no evidence of recalcification or efficient approximation of fragments. Spinal abscess—? increasing.	(a) Some irregularity of temperature to 99·8°F. Pulse 80—100. (b) Nil. (c) Spinal movements in abeyance. No spasm. (d) No clinical evidence of abscess but note radiological report.	Lesion remaining apparently active. Little or no evidence of a healing process.



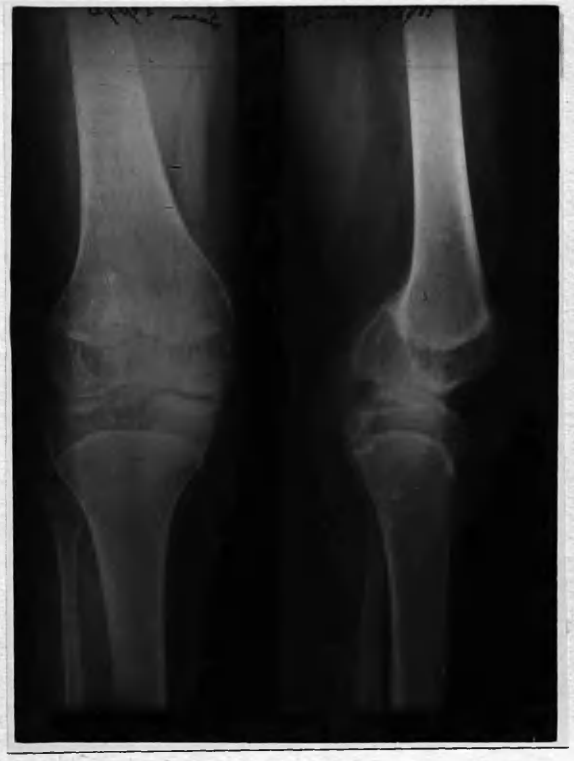


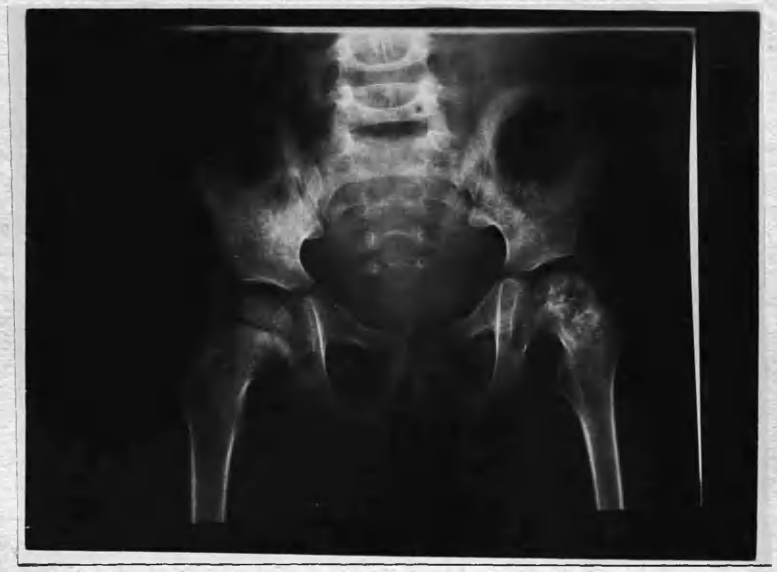
CASE NO. 79. W.L. Age 4 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Right Hip Joint.	1½ years.	Immobilisation in plaster splint after onset. Extension on Pyrford frame.	Progressive absorption of head of femur with erosion of acetabulum. Disease active. Widespread osteoporosis.	(a) Temperature swinging to 99·8°F. Pulse 86 to 108. (b) Pain on attempted movement. (c) Movements very limited. Spasm. (d) Nil.	Definitely active and progressive lesion.

CASE NO. 80. E.C. Age 12 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Ribs and costal cartilage. (? periosteal).	1 year.	Abscesses which formed over various ribs and costal cartilage have been aspirated or incised with good healing.	No radiographic evidence of bone lesion.	(a) Nil. (b) Nil. (c) Nil. (d) Small fluctuant swelling over 10th right rib posteriorly—receding.	Disease possibly sub-active in one area but generally quiescent. Child ambulant and in excellent general condition.



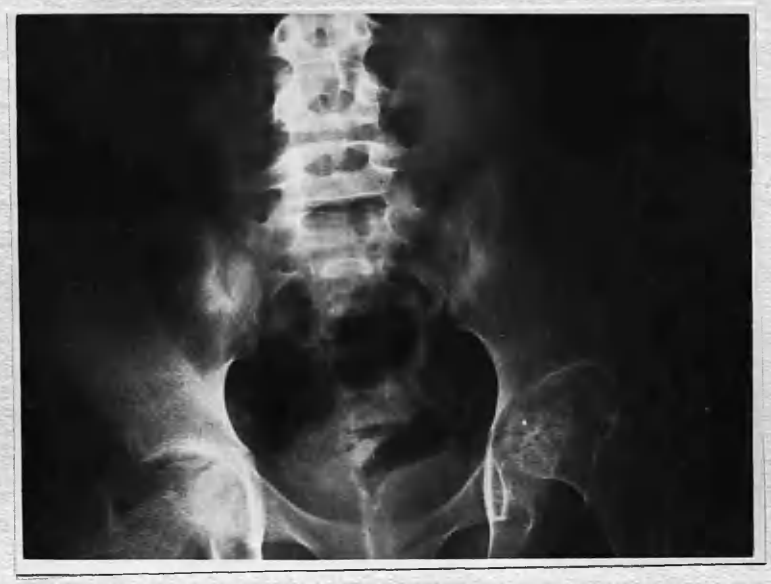


CASE NO. 81. E.G. Age 13 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Right knee joint.	12 Years.	No reliable history of early treatment. Ambulant and considered "quiescent" in 1929. Acute relapse in March, 1932.	Loss of joint space. Some irregularity of medial articular surfaces of femur and tibia. General haziness and poor bone detail.	(a) Nil. (b) Nil. (c) Joint fixed. No flexion possible. (d) Nil.	A moderately active lesion. General condition good.

CASE NO. 82. G.L. Age 2 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Left hip joint.	1½ years.	Plaster splint fixation followed by extension on Pyrford frame.	Epiphyseal head and neck of femur eroded and excavated. No acetabular erosion. No abscess.	(a) Temperature irregular to 99·4°F. Pulse 90 to 120. (b) Some pain on rotation of femur. (c) Rotatory movements limited. (d) Nil.	A localised active lesion.

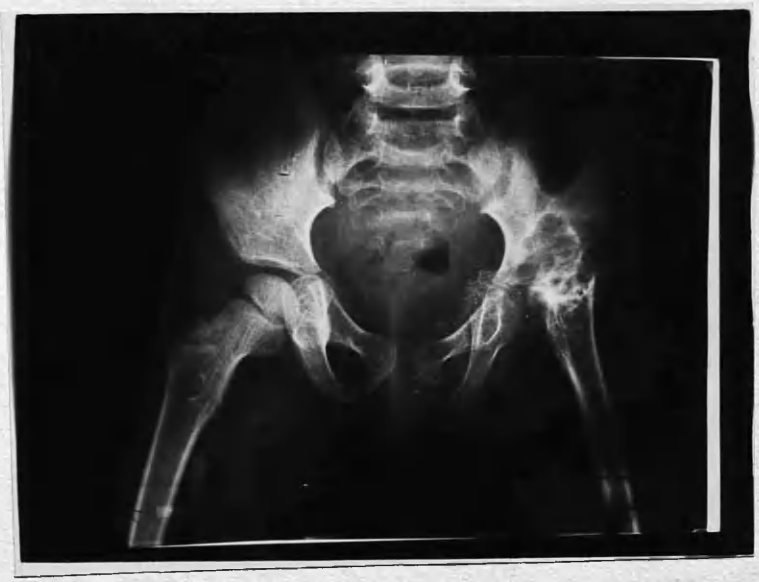


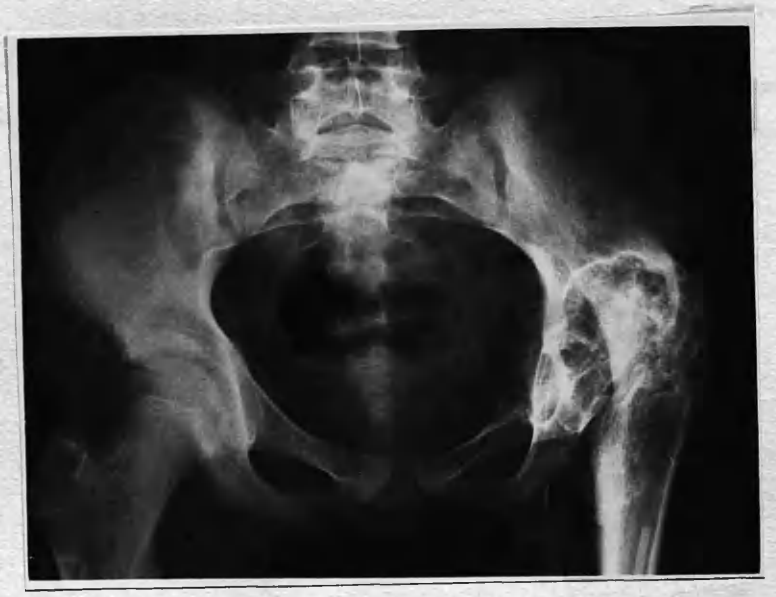
CASE NO. 83. C.W. Age 13 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Left hip joint.	8 years.	Immobilisation in various splints. Abscess of thigh present and aspirated since 1930.	Loss of head and part of neck of femur. Little acetabular erosion. Banana - shaped abscess in thigh—partly calcified.	(a) Nil. (b) Nil. (c) Hip ankylosed. (d) Abscess too thick to aspirate.	Lesion not definitely quiescent—note abscess history.

CASE NO. 84. M.K. Age 9 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Left hip joint.	4 years.	Immobilised from 1928 till 1931 with apparent healing. Acute recrudescence after a fall in September, 1931.	Partial destruction of head of femur. Upward erosion of acetabulum. Bone detail poor—active disease.	(a) Temperature irregular to 99·8°F. Pulse 90 to 104. (b) Pain still present on movement, (c) Movements not possible. Painful spasm. (d) Nil.	Acute lesion. General condition fairly good but rather flabby. (Jewess).



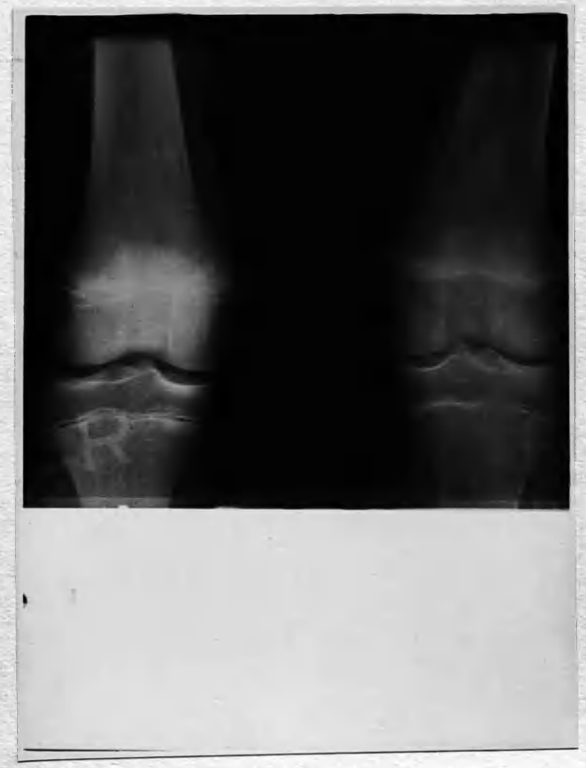


CASE NO. 85. M.H. Age 3 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Right hip joint.	3 years.	Immobilisation and extension on abduction and Pyrford frames. Abscess in thigh aspirated once in December, 1931—thereafter absorbed rapidly.	Almost complete destruction of head of femur. Rarefaction of neck of femur and trochanteric area.	(a) Temperature swinging to 100°F. Pulse 90 to 100. (b) Slight pain and spasm — becoming less. (c) Movements very limited. (d) No evidence of recurrence of abscess.	A lesion of low activity.

CASE NO. 86. E.H. Age 13 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Right hip joint. Pulmonary (tuberculosis of hilar glands).	10 years.	Extra-articular graft to hip joint in 1926. Rested for a time in 1930 on account of occasional pain in joint. No symptoms ~~then~~ since then.	Ankylosis firm with destruction of head and part of neck and erosion of acetabulum. Much calcified abscess shadowing.	(a) Nil. (b) Nil. (c) Joint ankylosed. (d) No clinical evidence of abscess.	Hip lesion apparently inactive. General condition poor. Cough and loss of weight. Calcified hilar glands in each lung.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CASE NO. 87. E.H. Age 12 years.

Site of Lesion.	*Duration of Lesion.*	*Available history of Treatment.*	*Extent and character of Lesion as described in radiographic reports.*	*Evidence of activity* *a Temperature and pulse rate.* *b Pain.* *c Limitation of movement.* *d Abscess formation.*	*Remarks.*
Left knee joint.	1⅓ years.	Immobilisation in plaster splints.	No bony abnormality. Some loss of joint space.	(a) Temperature at night 99·4°F. Pulse 80 to 100. (b) Nil. (c) Flexion movement increasing slowly. (d) Nil.	Some pulpiness and general evidence of incomplete arrest of disease. Note: This joint was excised in September, 1933, on account of pain and swelling. Active erosion of cartilage found at operation.

Leigh and Williams, Ltd.
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