DEEP X-RAY THERAPY IN **SPONDYLITIS**

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Since late 1947 a joint clinic has been conducted at the Rheumatism Centre and at the Christie Hospital and Holt Radium Institute for the investigation of cases of ankylosing spondylitis and their treatment by x rays. This paper concerns 332 cases seen under this joint arrangement and the changes observed in 275 of these following x-ray therapy.

The clinical picture of ankylosing spondylitis has been fully described in several recent publications (Polley and Slocumb, 1947; Mowbray et al., 1949; Parr et al., 1951), and notably in those of Hart et al. (1949, 1950). During the course of the present study patients whose disease conformed to the classical picture were labelled "typical" spondylitics, but there were some patients whose illness differed in various ways from this and who were classed as "atypical" spondylitics in the absence of a satisfactory alternative diagnosis. Some of the patients seen in the spondylitis clinic were found on further investigation to be suffering from conditions unrelated to spondylitis, such as bone disease, disk prolapse, and spinal cord lesions, but these have been excluded from this study. During the analysis of the spondylitic cases a "borderline" group was also introduced between the "typical" and 'atypical" groups. X-ray therapy was not advised in a number of the atypical cases although many had been referred for this, and one of our purposes was to find out if that policy was in fact justified. X-ray treatment was also not given to typical cases in which the spondylitis appeared to be inactive.

Of the 332 cases, 242 were considered to be typical, 59 atypical, and 31 borderline. Some of the features of these cases are set out in Table I.

About one-quarter of the patients in each group gave histories of rheumatic complaints among relatives; in the typical group 35% of these were of fairly definite or probable ankylosing spondylitis, compared with 19% in the atypical group, but the difference is not significant (P>0.16). The incidence of iritis in the three groups did not differ significantly. true incidence of involvement of the hands and feet in ankylosing spondylitis may be somewhat higher than is indicated owing to the inclusion of some typical cases in the borderline group, but if these groups are combined the incidence of 34 in 273 cases (12.5%) contrasts with the incidence of 52.5% in the atypical group. Tendinitis and tendon nodules were noted very rarely in typical spondylitics but were found in 12% of the atypical patients. Ball's modification of Rose's serum differential agglutination test (Ball, 1950) gave strongly positive results in 12% of the 50 atypical patients tested. Ball (1952) reported positive results with this test in 44.2% of 642 unselected cases

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	Typical	Borderline	Atypical
Total No. of Cases	242	31	59
Males	197	28	45
Females	45	3	
Family history:	43	3	14
Definite animitating and delicit			١ .
Definite ankylosing spondylitis Probable	13	0	3
Miscellaneous rheumatic complaints	10	0 8 3	.0
Miscellaneous rneumatic complaints	43	8	13 3 0 31
Definite history of iritis	19	3	3
Probable ,, ,, ,.	4		0
Hands or feet involved	12 2	22	31
Tendon lesions	2	1	7
Differential agglutination tests	125	22	50
Strongly positive	3	0	6
Weakly or doubtfully positive	4	Ŏ	Ĭ
Negative	118	22	43
Clinical status: Mean disability score* before treatment after Duration of symptoms when treated:	6.04 ±2.24 3.84 ±2.16	7·91 ± 1·81 5·31 ± 2·70	6·4±2·36 4·92±2·75
5 years or less	62	8	14
More than 5 years	150	20	21
X-ray grade:†			
<u>I</u>	43	3	6
II	167	25 0 3	41
ш	31	0	1
Not known	i	3	2
Sacro-iliac joints normal but change	_	_	_
elsewhere	0	0	6
X-ray films normal	ŏ	ŏ	š
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of rheumatoid arthritis attending hospital. This suggests that the atypical group is not largely composed of patients with rheumatoid arthritis affecting the spine in spite of the high incidence among them of involvement of the hands and feet.

Technique of X-ray Treatment

The x rays were generated at 250 kV with a half-value layer of 1.63 mm. of copper, the focus-skin distance being 50 cm. It has been our practice, even when symptoms were confined to one level of the back, to treat the whole spine and the sacro-iliac joints through rectangular applicators 7.5 cm. in width, the length being adjusted so as to ensure close apposition of these to the skin.

Previously, smaller fields were used to treat local painful regions of the spine, but this method was abandoned because, although the treated area might be painless after treatment, further lesions in the vicinity often developed or were disclosed during treatment. The sacro-iliac joints were treated through a single applicator, 15 by 12 cm., contiguous with the lowermost spinal field.

Almost all these patients were treated as out-patients, a dose of 150 r (measured with back-scatter) being given to the skin surface of each field at each weekly visit for ten weeks. Serious radiation sickness occurs infrequently with this low dosage, having caused curtailment of treatment in only four of these patients. It was also hoped that this dosage would decrease the likelihood of haematological complications, particularly in patients requiring retreatment at a later date.

Peripheral joints were treated through parallel opposing fields, a maximum skin dosage of 150 r being delivered to each field weekly for ten weeks. In treatment of the carpus and tarsus, as in the spine, large fields covering the whole of these groups of small joints proved most successful. For the tarsus, fields approximately 25 by 12.5 cm., to include the whole foot and ankle-joint, were used.

Localized painful lesions over bony prominences such as ischial tuberosities, adductor tubercles, and iliac crests, and painful costochondral junctions, were given single exposures through small fields to a dose of 500 or 600 r.

Method of Assessment

For analysis, the patient's status was assessed in terms of constitutional disturbance, pain, range of movement, and general functional capacity. In order to obtain some quan-

Treated patients only (see text).
 Grade II=Sacro-iliac joints only involved. Grade II=Sacro-iliac joints nvolved + slight or moderate change in spine or elsewhere. Grade III=Sacro-iliac joints involved + severe and extensive change in spine or elsewhere.

titative expression of disability before and after treatment for statistical analysis as a check on the general clinical assessment of the case, the patient was given a numerical score for each of these features, scores of from 0 to 2 being awarded for increasing degrees of constitutional disturbance, of from 0 to 3 for pain of increasing severity, and of from 0 to 3 for increasing impairment of spinal movement. Functional capacity was scored in five grades—from grade 1, in which the patient was fully employed or employable in normal work and able to undertake normal physical recreations for his or her type, to grade 5, in which he was confined to bed unable to look after himself. The total or "disability score" was taken to represent a measure of the patient's disability.

Patients considered to be "much improved" had complete or almost complete freedom from pain after treatment, the associated constitutional disturbance was abolished or significantly decreased, and they usually gained weight. The general functional capacity of the patient was increased, and in cases without extensive radiological changes the range of movement often, but not invariably, improved. Photographic records of the range of back movement done in some cases gave valuable objective evidence of this (Figs. 1 and 2).

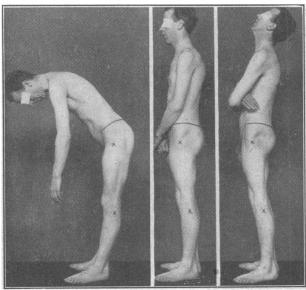


Fig. 1.—Before x-ray treatment.

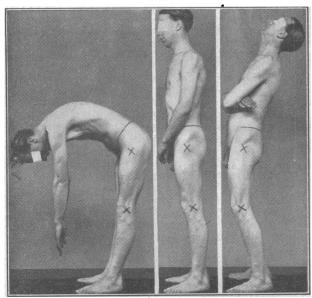


Fig. 2.—Two months after x-ray treatment

"Slightly improved" signified less improvement in these respects, usually implying persistence of pain of significant degree in the treated area. A smaller number of cases were included in this category, since, although the treated areas were much improved, the beneficial effect was overshadowed by the development of new lesions elsewhere. Improvement was usually first noted about the middle of the course, and maximum improvement within the first two months or so after treatment, though a few cases continued to improve for about six months.

The patients were assessed before and one month after completion of treatment and at intervals thereafter, in the first instance one year, but before this when necessary. They were in all cases instructed to report to the clinic should relapse occur before their appointments fell due.

Results

The numbers of patients treated in the three groups and their status after treatment are shown in Table II.

TABLE II

	Typical		Borderline		Atypical	
	Male	Female	Male	Female	Male	Female
Total No. of cases No. treated	197 175	45 37	28 26	3 2	45 27	14
Much improved after treatment	124	25	16	2	9	2
Slightly improved after treatment	41	10	6	0	9	2
No change after treatment	3 7	1 1	2 2	0	5 4	3

As the proportions of males and females much improved after treatment do not differ significantly in either the typical or the atypical groups (P=0.69 and =0.64 respectively) the figures for males and females have been grouped together in the subsequent analysis.

The proportion of patients much improved after treatment is very significantly higher in the typical than in the atypical group (P<0.00001). The distributions of the disability scores in the two groups before treatment tested by the χ^2 method do not differ significantly (P<0.96), but a highly significant difference in these is apparent after treatment (P<0.0008). This difference is due to a significant increase in the proportions of patients in the typical group in the lower disability classes after treatment, whereas in the atypical group the proportions are not significantly altered.

In Table III a further analysis is made of patients in the typical group much improved after treatment.

Elevation of the blood sedimentation rate above 20/200 mm. Westergren is no guide to whether a patient will be improved after x-ray therapy. Hart et al. (1949) came to a similar conclusion. We recommend x-ray treatment only in cases in which the ankylosing spondylitis

TABLE III.—Analysis of Typical Cases

	No.	Treated	Much Im- proved	P
B.S.R. >20/200 mm	162 68 12*	141 60	98 }	>0.7
Peripheral joints: Treated concurrently with spine Treated separately		32 30	17 14 }	>0.6
Age < 45 years when treated: Duration 5 years or less > 5 years Age 45 years or more when treated: Duration 5 years or less > 5 years		57 109 5 41	47 71 }	< ∙01
Radiological Grade I " " II " " not known	43 167 31 1	38 149 24	33 101: 14 }	<0.01 0.38 <0.0

^{*}Fleven of these patients were treated, and eight were considered to be much improved after treatment.

appears "active," as we have been unimpressed by the results of treatment of patients with little pain, either spontaneous or on movement, or constitutional disturbance, though they may have severe limitation of movement and extensive radiological changes typical of the disease. This means that judgment of the "activity" of the disease must be largely based on clinical criteria.

As might be expected, the probability of improvement after treatment is higher in patients whose symptoms are of short duration. That the duration of symptoms rather than the age at which treatment is given is the factor concerned is suggested by the observation that among patients with symptoms of more than five years' duration the proportions much improved after treatment in the age groups above and below 45 years are almost identical. In keeping with this is the finding that significantly fewer patients were much improved after treatment when radiological changes were also present in the spine or elsewhere than when changes were confined to the sacro-iliac joints—a finding similar to that of Smyth et al. (1941a). It should be added that no such relationship between duration of symptoms and improvement after treatment can be shown in the atypical group, in which improvement appeared to be related to the age of the patient and unconnected with duration of symptoms, but this impression was not confirmed statistically.

Seventeen patients in the typical group have been given second courses of treatment to previously treated areas, 15 of these to the spine and sacro-iliac joints. Seven of these 17 patients were much improved after treatment, a significantly smaller proportion than after the first course (P<0.02).

We do not yet know how long the improvement after treatment will be maintained in most of these patients, but up to February, 1953, 56 of the typical cases had relapsed, and in 44 of these relapses areas treated in the first course were involved.

Thirty-two of the relapsed patients had been regarded as much improved after treatment, and of these none relapsed in the first six months after treatment, whereas five of the slightly improved patients relapsed during this period. Of the seven patients much improved after a second course of treatment, one has so far relapsed in the second six months after its completion; four of these patients have not yet been seen six months after treatment. It is unlikely that many more patients have had major relapses without our learning of these, as relapsed patients have usually been anxious to have further x-ray treatment, which in this region is entirely controlled from the Christie Hospital and the Holt Radium Institute.

Complications of X-ray Treatment

These relate to 301 courses of treatment given to 275 individuals. Twenty-five patients received two courses, 21 of these to the spine, and one patient has had three courses to the spine.

The only serious haematological complication encountered was in a man aged 44 whose haemoglobin prior to x-ray treatment was 64% (9.5 g. per 100 ml). After seven weekly treatments to the spine and sacro-iliac joints profuse bleeding occurred from a rectal polyp and he rapidly became severely anaemic, requiring repeated transfusion. Sternal marrow examination revealed an aplastic picture, and no improvement in either the blood count or marrow appearances occurred with A.C.T.H. treatment. His spondylitis was little if any improved after treatment, and he was maintained in indifferent health by regular blood transfusions, to which he showed gradually diminishing response, dying with extensive haemochromatosis two and a half years after treatment.

In one patient inactive pulmonary tuberculosis seemed to be reactivated by treatment to the spine, and on being informed of his extensive pulmonary disease he committed suicide in a fit of depression. Since this occurrence routine radiographs of the chest have been taken before x-ray

therapy to the spine, and seven other known cases of inactive pulmonary tuberculosis have been treated without complication.

Two other patients have died. One was a woman aged 57 with atypical spondylitis and features of Cushing's syndrome. Hypertension was present before treatment, and after nine weekly treatments to the spine and a single exposure of 600 r to the sternum and sterno-clavicular joints she complained of increasing weakness, tiredness, anorexia, and loss of weight. Albuminuria, azotaemia, and greatly reduced renal function were detected. She died at home in heart failure two months after treatment.

The other was a man aged 39 whose arthritis appeared typical of spondylitis. He had an associated inactive chronic pyelonephritis with hypertension and azotaemia, and, though much improved in respect of his spondylitis after treatment, he died in uraemia eight months later.

It is possible that in both these patients x-ray therapy may have accelerated the renal failure, although the radiation dosage to the kidneys in these cases was considerably less than that found to produce permanent renal drainage in man by Kunkler et al. (1952).

Permanent amenorrhoea after treatment occurred in 13 of the 47 females treated, and probably also in three further cases; 13 of these were below the age of 45. Temporary amenorrhoea lasting up to one year occurred in three other cases, all below 35. Since this high incidence of post-treatment amenorrhoea was disclosed by analysis of these cases, a tangential field method of treatment of the sacro-iliac joints in females has been adopted. Radiation to the ovaries should be less by this technique, but too few cases have so far been treated to assess how often it results in amenorrhoea.

No other serious complications were noted.

Other Treatment

The patients were encouraged to lead as normal lives as possible within the limits of their disabilities. They were instructed in the performance of breathing exercises and simple measures aimed at correction of deformity, such as sleeping supine on a firm bed and gradually decreasing the number of pillows, and were advised to avoid prolonged stooping and heavy lifting in a flexed position. Some of the more severely disabled patients with potentially correctable deformities were also given a more intensive course of reablement as in-patients of the Devonshire Royal Hospital in Buxton. Eight patients, all with severe bilateral involvement of the hips, were referred for hip surgery, and one was referred for spinal osteotomy.

Immobilization

Spinal supports were rarely advised, as we have not been impressed by their value in preventing spinal deformity or relieving pain due to established deformity, although a number of patients had been provided with such supports before coming to the clinic. Patients were confined to bed only in exceptional circumstances. The few patients who had been immobilized, particularly those in whom the lower limbs and spine had been immobilized in plaster sometimes because of a mistaken diagnosis of tuberculosis, were as a group strikingly more disabled than the rest of the patients. A similar experience was reported by Swaim (1939). Nineteen patients in our typical group had at some stage been immobilized in bed, in plaster, or on frames for periods of months to years; of these, five were virtual statues with rigid dorsal and lumbar spines and fixed or grossly limited hips, and two of them had practically fixed knees. Only six similar cases were encountered among the remaining 223 patients in the group, and there was no indication from the histories of the immobilized patients that as a group they were examples of more severe disease than the rest of the cases. On the contrary, whereas all six of the patients who had not been immobilized had completely fixed cervical spines, in those cases in which only the lower limbs and lower spine had been immobilized neck

movement was full or only slightly impaired, the gross loss of movement being confined to the parts immobilized.

The case histories of the five patients mentioned illustrate this point.

Case Reports

Case 1.—Man aged 24. In January, 1944, at the age of 18 he developed pain in the right buttock and milder pains in the left shortly afterwards. In October, 1945, tubercle bacilli were found in his sputum, and in January, 1947, lobectomy was performed. In 1949 he began to lose ground, pain in the right buttock increased, and the sputum was again found to be positive. In September, 1949, tuberculosis of the right hip was diagnosed and he was immobilized from the upper dorsal region downwards in an abduction frame. On removal from this after one year, the dorsal and lumbar spines were fixed, the hips ankylosed, and the knees and ankles very limited in movement. Neck movement was full apart from slight restriction laterally, and there was a normal range of movement in the upper limbs. The patient subsequently underwent Girdlestone's operation on the right hip with good results.

Case 2.—Man aged 20. In 1943, when 15 years old, he developed fleeting pains in the low back, knees, and left heel, and left-sided sciatica. After unsuccessful treatment with salicylates and physiotherapy, ankylosing spondylitis was diagnosed in December, 1945. At this time the lumbar spine was straightened, dorso-lumbar extension was absent, and other movements were about three-quarters of normal range. Neck movements were full. There was minimal painful limitation of hip movement, all other limb joints being normal. He was immobilized in plaster beds from the upper dorsal region downwards from January to August, 1946, and again from January to November, 1947. At the end of this period the lower dorsal and lumbar spines, both hips, and both knees were fixed. Neck movement was full, and, apart from some limitation of external rotation of the right shoulder and slight fusiform swelling of fingerjoints, the upper limbs were normal.

Case 3.—Man aged 42. In 1934, at the age of 27, he developed pain in the buttocks, which persisted in spite of physiotherapy and spread to the low back. In 1943 a plaster spica was applied to the right hip for two to three months, and reapplied for a further six months in 1944. On removal of this, the left-sided pain increased, and in January, 1945, he was immobilized in a Pearson bed and later in an abduction frame, and then for nine months from the head downwards on a plaster bed. Contrary to instructions, he continued to move his neck, though the plaster prevented extension. On removal from the plaster bed his lumbar and dorsal spines were stiff; extension of the neck was absent, but he had a useful range of other neck movements. Both hips were fixed, the knees had a full range, and the upper limbs were normal apart from minimal limitation of the shoulders. He still suffered pain of moderate severity, but by perseverance he regained a little movement in the spine and left hip. Deep x-ray therapy to the spine, sacro-iliac joints, and left hip early in 1950 resulted in complete relief of pain, which has been maintained.

Case 4.—Man aged 28. In 1938 at the age of 16 he noted pains in the feet followed shortly by pains in the interscapular region and neck, which spread during the following three years to all levels of the spine and to the hips. He was told nothing could be done, and took to bed for three years. At the end of this time his spine was completely fixed, apart from a trace of cervical movement, and his hips were ankylosed in flexion with severe total flexion deformity. Both shoulders had about half the normal range; the remaining joints appeared unaffected.

Case 5.—Man aged 41. In 1940 at the age of 26 he developed persistent low back pain and his back began to stiffen. After some months he was admitted to hospital and kept in bed for six months. Subsequently he wore a spinal brace for one year; his pain eased during this period. In 1943 the left knee became painful, and after some weeks in bed both legs stiffened, although previously the right

knee had been normal. For the next 18 months he remained on traction without any exercises, and at the end of this time the dorsal and lumbar spines were rigid and he had about half the normal range of neck movement. Both hips were ankylosed and the knees severely limited; movement of the upper limbs was normal. Later he was transferred for cup arthroplasty of both hips.

Discussion

Clinicians dealing with large numbers of patients with ankylosing spondylitis are generally agreed that x-ray therapy is of some value in this disease (Kahlmeter, 1930; Hare, 1940; Smyth et al., 1941a; Scott, 1942; Hilton, 1943; McWhirter, 1945; Kuhns and Morrison, 1946; Hart et al., 1949; Parr et al., 1951), and at least two controlled trials have confirmed this clinical impression (Smyth et al., 1941b; Desmarais, 1953), but x-ray therapy does not completely arrest the ankylosing process. The best long-term results are therefore achieved by combining this with systematic exercises, positioning in bed and at work, and other physical measures designed to retain mobility and prevent or correct deformity.

In Desmarais's trial the effects of various doses of x rays and mock therapy were compared in ankylosing spondylitis, rheumatoid arthritis, and osteoarthritis, and it was found that patients with ankylosing spondylitis showed the greatest improvement, those with osteoarthritis derived some benefit, but the course of patients with rheumatoid arthritis was not significantly different from that of untreated controls. The similarity in behaviour after treatment of, peripheral joints treated alone and those treated concurrently with the spine in our typical cases favours the view that the beneficial effect of x rays in ankylosing spondylitis is due to a local action on irradiated tissues and not to an indirect effect mediated through an endocrine or other mechanism, and that the failure of rheumatoid joints to improve is due to a difference in tissue responsiveness to x rays.

The proportion of treated patients with symptoms of over five years' duration is slightly less in the atypical than in the typical group, so that the poor response to treatment in the atypical group cannot be ascribed to longer duration of symptoms, and the similarity of the mean disability scores and the distribution of these scores in the two groups before treatment argue against the results being due to a preponderance of unusually severe cases in the atypical group. The failure of many patients in the atypical group to benefit from x-ray therapy may therefore be due to inclusion in this group of a number of other conditions which resemble ankylosing spondylitis clinically but are unaffected by x-ray therapy.

Conclusion

The results of this study suggest that only patients suffering from typical ankylosing spondylitis benefit from x-ray therapy. It would therefore be desirable to have well-defined clinical and radiological criteria by which typical spondylitis could be distinguished from other conditions which may simulate this disease. Such a differential diagnosis is also desirable, since immobilization usually aggravates typical spondylitis, while it may be helpful in some of the atypical conditions. We are therefore studying the various arthritic conditions which may simulate ankylosing spondylitis with a view to elaborating a satisfactory differential diagnosis.

Summary

On clinical and radiological grounds 332 cases of spondylitis were divided into three groups: 242 "typical" cases conforming to the classical picture of ankylosing spondylitis, 59 cases classed as "atypical" in the absence of a satisfactory alternative diagnosis, and an intermediate group of 31 "borderline" cases. A family history of rheumatic complaints and a history of iritis were found with

equal frequency in the three groups. In spite of a high incidence of involvement of the hands and feet in the atypical group, the comparatively low proportion of patients in this group giving positive results with Ball's modification of Rose's serum differential agglutination test is evidence that the atypical group is not largely composed of patients with rheumatoid arthritis affecting the spine. The adverse effect of prolonged immobilization in typical ankylosing spondylitis is emphasized.

A total of 275 patients received deep x-ray therapy; the proportion much improved after this in the typical group was very significantly higher than in the atypical group. In the typical group, the age or sex of the patient and level of the blood sedimentation rate gave no indication of the probability of improvement after therapy; better results were obtained in patients whose symptoms were of five years' duration or less and in whom radiological changes were confined to the sacroiliac joints. No significant difference was observed in the behaviour of peripheral joints treated alone and those treated concurrently with the spine, suggesting that the effect of deep x-ray therapy in ankylosing spondylitis is a local one on irradiated tissues.

Complications of x-ray therapy included one case of aplastic anaemia, reactivation of pulmonary tuberculosis in one case, permanent amenorrhoea in 13 of the 47 females treated, and possible acceleration of renal failure in two cases.

Reasons are given for ascribing the poor results from x-ray therapy in the atypical group to inclusion of patients with other diseases simulating ankylosing spondylitis.

We are grateful to the many consultants in this region who have allowed us to study their cases during the investigation; to Professor J. H. Kellgren for much advice and helpful criticism; to Dr. Ralston Paterson for provision of facilities for x-ray treatment and follow-up of the patients; to Dr. O. Janus, who saw many of these patients originally in the clinic; and to Miss Marion Russell for help with the statistics.

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Bracken Hill House, The Woods, Northwood, Middlesex, the pioneer hostel of B.R.A. Homes Ltd. (under the aegis of the British Rheumatic Association), is now open. It is designed to meet the needs of industrial workers with early and serious rheumatic conditions for whom bed accommodation at hospitals with rheumatic units is unlikely to be available in the near future. All medical services are provided by Mount Vernon Hospital. Industrial medical officers or the patient's family doctor can apply for accommodation. Cost of beds ranges from £4 15s. to £7 7s. Further details may be obtained from either Bracken Hill House or the British Rheumatic Association, 11, Beaumont Street, London, W.1.

CONGENITAL VALVES IN THE POSTERIOR URETHRA

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A valvular formation of mucosal folds in the posterior urethra is the most often encountered example of the group of congenital anomalies which cause urethral obstruction. A full pathological and clinical description of the condition was given by Young, Frontz, and Baldwin in 1919, yet the lesion has never been widely recognized nor has a satisfactory routine for diagnosis and treatment emerged. I have had the opportunity of operating upon 14 of these valve cases, and the present observations are based upon the study of this series, and of the records of 21 further cases in which the diagnosis has been confirmed by post-mortem examination at the Hospital for Sick Children. All but one of the 14 cases have been treated during the past two years, and it may be of interest to record that during the same period eight cases with other forms of congenital urethral obstructions and four cases of bladder-neck obstruction in young children have come under treatment.

Their Origin

In the characteristic form (Young's type 1) a valve is formed on either side of the urethra by a double fold of mucous membrane, the two meeting in the midline sagittal plane of the urethra, leaving only a small channel anteriorly (Fig. 1). The free edges of the valves are continuous above

posteriorly and ridges conwith nected with the verumontanum: below and anteriorly they fade out on the urethral wall at approximately the level of the external sphincter.

Faint ridges with a similar disposition are evident in the normal male urethra, and have observed that in the embryo they first appear at approximately the 50-mm. stage. The ridges were exceptionally well developed in a 99-mm.

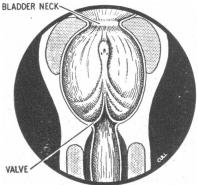


Fig. 1.—Diagram showing the disposition of urethral valves in their most characteristic form. The urethra has been drawn as if it had been opened by a vertical incision of the anterior wall, so that the anterior extremities of the valvular folds are held apart.

embryo which I have examined; they have no discernible function, and after this stage they appear to shrivel spontaneously, but it is clear that it would require only a slight exaggeration of the normal formation with some adhesion of the free edges to bring about the development of an obstructive valve. We are thus dealing with only a minor deviation from the normal, and we should not therefore expect a high instance of multiple congenital anomalies in this disease. In fact, the accompanying abnormalities are chiefly those consequent upon the obstruction.

From this evidence of their origin, it will be manifest that congenital valves will constitute an obstruction to the urinary passages almost from the time that urine is first formed and long before the complete differentiation of the nephrons. A free flow of urine is not, of course, essential