Considering the group of 41 men as a whole, only 18 (44%) had no objective evidence of any organic disease. In the remainder there was evidence of abnormal pulmonary function and/or the presence of established lung disease or heart disease. The implications of the finding of a high rate of organic disease in men in this income group between the ages of 50 and 60 are discussed.

We wish to acknowledge the assistance of Dr J. B. L. Gee and Dr. L. G. Bentivoglio in the exercise pulmonary diffusing capacity measurement. Dr. R. G. Fraser kindly reported on the radiographs, and we are indebted to our technical staff for many of the measurements and determinations made.

We are particularly grateful to Brig. Murray of the Salvation Army, Montreal, and his chaplain, without whose help and co-operation this study could not have been undertaken.

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Rheumatoid Disease in Children

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ABSTRACT

Data relative to 102 patients seen between 1940 and 1960 with infantile rheumatoid arthritis were analyzed. The systemic nature of the disease and variable early clinical picture make early diagnosis very difficult. Only 20% had articular symptoms at the onset. The youngest was aged 6 months and there was a greater incidence of onset in the first two years of life. Particular attention was paid to the site of original joint involvement as compared with the subsequent final joint pathology. Spindle fingers or swollen proximal interphalangeal joints appear late in the disease but are usually diagnostic of infantile rheumatoid arthritis. Diagnosis is essentially a clinical one; laboratory tests are of little diagnostic value. Prognosis is related to the age of onset, on institution of therapy, and systemic manifestations. Of these patients 50% were functionally normal at the time of follow-up, 25% had mild residual disability and 25% were severely crippled.

THE term "Still's disease", as an eponym for infantile rheumatoid arthritis, is inaccurate and misleading. It is inaccurate, because it ignores the contribution of Cornil,[20] who described the condition 10 years previously, in 1864. The name is also misleading since it implies that rheumatoid arthritis in children is usually associated with extensive visceral lesions and a bad prognosis. In this respect, it would be more precise to compare Still's disease with Felty's disease,[31] since the two eponyms describe, respectively, unusually severe varieties of infantile and adult rheumatoid arthritis. However, such severe varieties are the exception and not the rule. It is now well accepted that infantile rheumatoid arthritis frequently has a favourable prognosis and that, indeed, it is only rarely associated with such widespread lesions as pericarditis, splenomegaly and hepatomegaly.[50]

TABLE I.—COMPARISON OF ADULT AND JUVENILE RHEUMATOID ARTHRITIS

More common in children	*More common in adults*
Acute onset	Morning stiffness
Systemic manifestations	Joint pain
Rash	Subcutaneous nodules
Large joint involvement	Centripedal joint involvement
Intermittent course	Long periods of activity

Although there are noteworthy points of distinction between infantile and adult rheumatoid arthritis (Table I), the differences are minor, and are due to the differences in the hosts rather than in the disease;[45] indeed, the pathological process and the sex incidence of rheumatoid arthritis are essentially unchanged from infancy to senility. The immediate purpose of the clinical investigation described in this report was to clarify the natural history of rheumatoid arthritis in children. The analysis of the infantile form of the disease and the observation of the development of joint deformities in early life would automatically improve our

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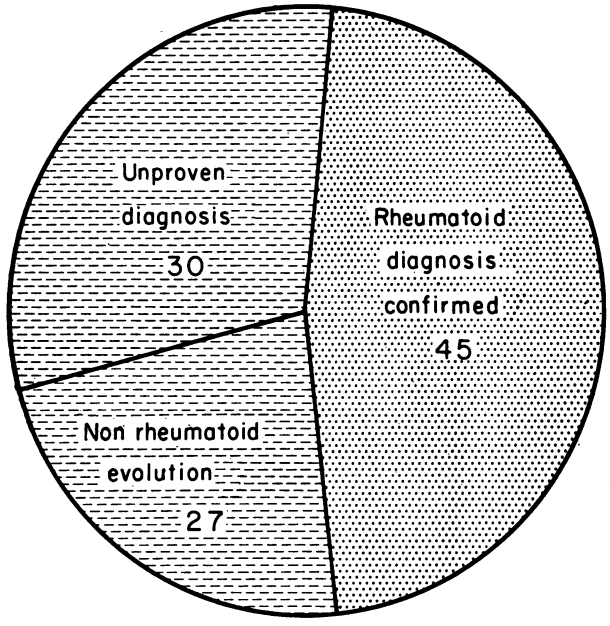


Fig. 1.—Distribution of patients at the St. Justine Hospital from 1940 to 1960. One hundred and two patients were discharged with the diagnosis of juvenile rheumatoid arthritis.

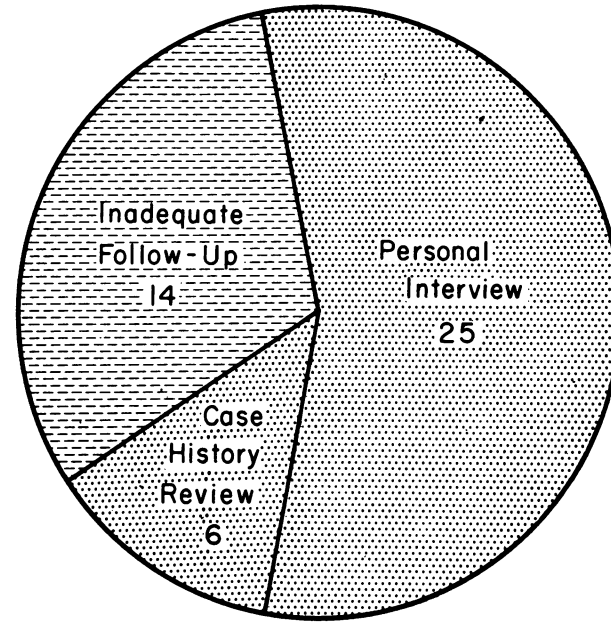


Fig. 2.—Distribution of patients: 45 cases of juvenile rheumatoid arthritis.

understanding of the more common, adult form of rheumatoid arthritis.

This review is based on an analysis of 102 patients seen at the St. Justine Hospital, Montreal, over the past 20 years with a discharge diagnosis of infantile or juvenile rheumatoid arthritis (Fig. 1). Thirty charts were immediately discarded, since they were inadequately documented to justify the diagnosis. Another 27 patients were excluded at the time of follow-up, when the subsequent evolution of their illness clearly indicated a different diagnosis. The remaining proved cases of juvenile rheumatoid arthritis total 45, and represent 44.1% of those originally so diagnosed. Such a percentage of error compares favourably with that noted in other reported series and illustrates rather eloquently the protean early clinical picture of juvenile rheumatoid arthritis and the considerable difficulties in establishing an accurate early diagnosis.[8] Among these 45 confirmed cases of juvenile rheumatoid arthritis (Fig. 2), 31 had a well-documented follow-up of one year or more; the analysis of these patients forms the basis of this report.

Juvenile rheumatoid arthritis is a relatively rare disease, and no reported series can be expected to be large enough to permit a statistically valid analysis. Indeed, according to Ogilvie,[53] statistics are either too good to be true, or too true to be good. None the less, a collection of data is not an end in itself: the information contained in these 45 case records must be organized and interpreted; otherwise it merely represents scattered information.[47] In spite of their limited number, the observations made on these patients were summarized in percentages, whenever possible.

AGE OF ONSET

Larger series[41] usually reveal an equal incidence of onset before and after seven years of age.[25] Our series (Fig. 3) illustrates the constant higher incidence of onset in the first two years of life;[33] the youngest patient was two months of age. The age distribution demonstrates, once more, that rheumatoid arthritis belongs to no specific age groups;[7, 39, 48, 52] indeed, the proportion of new cases is almost the same throughout life, with a slightly higher incidence in women between the ages of 50 and 55, and a slightly lower incidence in children.

PRECIPITATING FACTORS

Precipitating factors were sedulously sought and were recorded only when parents were very definite concerning their occurrence (Table II). It is our

TABLE II.—PRECIPITATING FACTORS IN 45 CHILDREN WITH RHEUMATOID ARTHRITIS

Recent infection		4%
Trauma		2%
Definitely no precipitating factor		65%
Positive family history		58%
Arthritis	33%	
Related disease	25%	

opinion that many previously described associated factors[68] were likely coincidental, or were part of the prodromal clinical picture. There was, however, a strong suggestion of a hereditary factor,[4] with a definite family history of arthritis and related diseases.

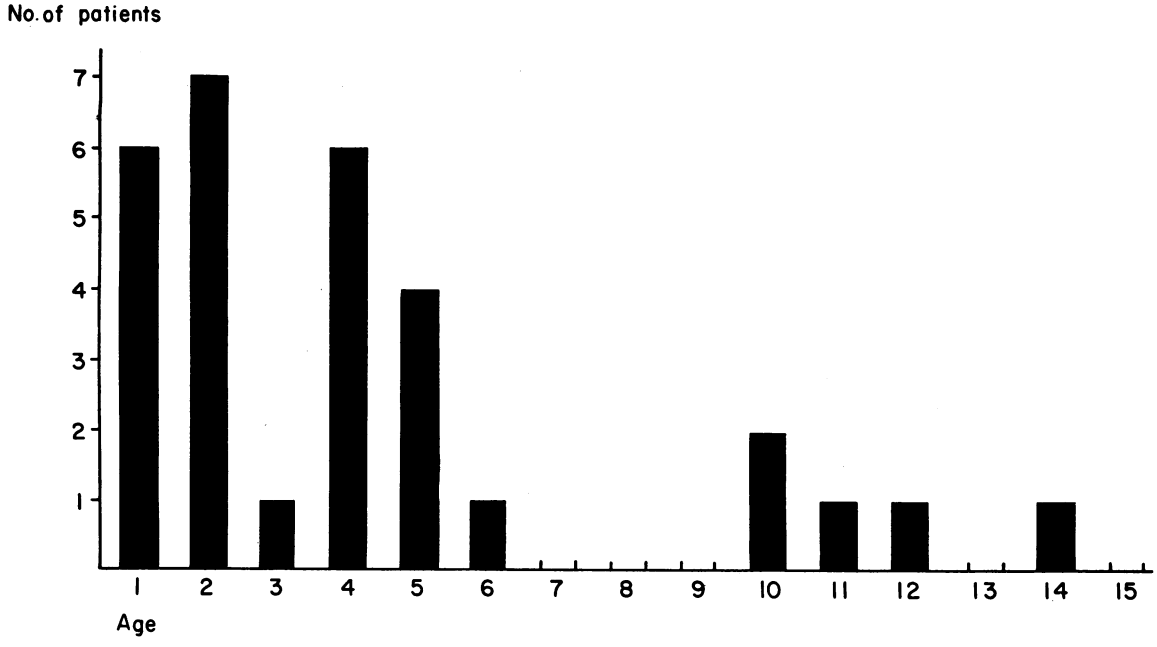


Fig. 3.—Age of onset.

CLINICAL PICTURE

No clinical picture is totally characteristic of rheumatoid arthritis in children;[21, 27] an almost endless variety of clinical manifestations is possible.[34] In some instances the early clinical manifestations are exclusively systemic, with a particularly abrupt onset and a complete absence of joint signs for many months. The latter type of clinical picture has been labelled the infantile type of juvenile rheumatoid arthritis (Table III). There is also an adult type with a more insidious onset and obvious joint signs; and a third, or mixed type. Generally speaking, the infantile form is more common in the early years of life, while the adult and mixed forms have a better prognosis and are more frequent in the pre-school child.

TABLE III.—TYPES OF JUVENILE RHEUMATOID DISEASE

	Average age at onset
Infantile	
(Acute onset, systemic signs)	20%—1½ years
Adult	
(Insidious onset, local joint signs)	40%—3½ years
Mixed	
(Articular signs, mild systemic signs)	40%—4½ years

SYSTEMIC MANIFESTATIONS

The basic lesion of rheumatoid arthritis is in the collagen of the connective tissue; subsequently, almost every system may become involved. The distribution and the severity of non-articular signs and symptoms attest most eloquently to the systemic nature of rheumatoid arthritis (Table IV). In this respect it would be more precise to speak of rheumatoid disease rather than rheumatoid arthritis.

The diagnosis "fever of unknown etiology" is a relatively common first diagnosis. An elevated temperature is often the most dominant early clinical feature of infantile rheumatoid arthritis; the fever may be constant and very high, or it may be intermittent. The more common diagnoses then encountered are the collagen diseases, infectious diseases, Hodgkin's disease, septicemia and encephalitis.

A rash is not uncommon in juvenile rheumatoid arthritis. The rash is highly variable and may even be urticarial; more commonly, however, it is evanescent, and it characteristically fluctuates with the temperature.

TABLE IV.—SYSTEMIC MANIFESTATIONS

Fever		55%
Rash		35%
"Still's disease"		0%
Miscellaneous:		
Eye lesion	15%	
Lymphadenopathy	10%	
Splenomegaly	3%	
Hepatomegaly (jaundice)	10%	
Obvious heart pathology	10%	
Lung infection	10%	

The complete clinical picture of Still's disease,[46, 64] with hepatomegaly, splenomegaly, pericarditis and arthritis, was never observed in this group of patients. This low incidence of this variant of the disease warrants an explanation and requires emphasis. Most published reports on juvenile arthritis[12] have originated from hospitals for chronically ill children, with a 5% to 10% incidence of so-called Still's disease and a mortality rate of 5%.[3] The patients in this report were seen in a hospital for acute treatment; they represent by far the most common variety of infantile rheumatoid arthritis—the clinical picture that is usually encountered in actual practice. If one awaits the complete clinical picture described by Still, the diagnosis of juvenile rheumatoid arthritis will not only be delayed, it will frequently be missed altogether.

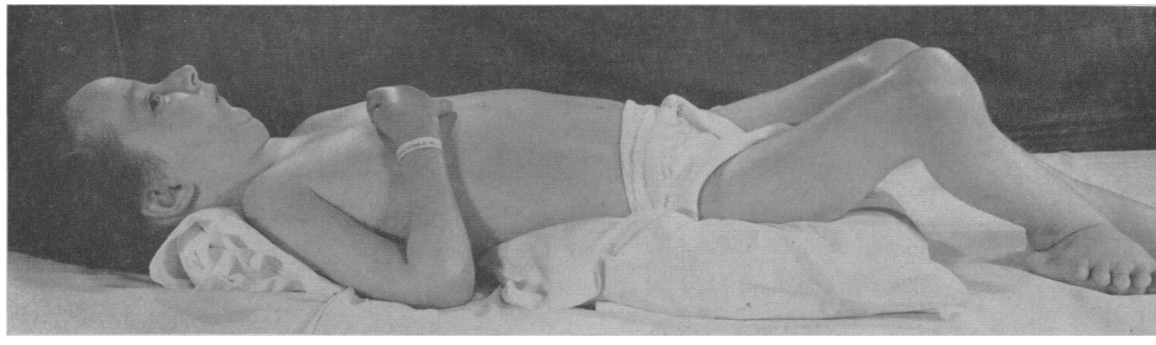


Fig. 4.—Crippling variety of infantile rheumatoid disease; complete invalidism with fixed deformities, a "bird jaw" and gross muscle atrophy. An early age of onset and systemic involvement had indicated a bad prognosis.

Three patients had eye lesions; one of these had a unilateral lesion that progressed to complete blindness. Their joint deformities were most disabling, illustrating once more the association between systemic manifestations and a poor prognosis (Fig. 4; Table X, column 2).

It is important to appreciate that the gross muscle atrophy commonly observed in some patients (Fig. 4) is not the atrophy of disuse. The pathological process extends far beyond the articulations and the connective tissue of muscles and peripheral nerves; it also affects the central nervous system directly, as suggested by cerebrospinal fluid changes.[74] It is interesting to note that the aberrations in cerebrospinal fluid cell count and cerebrospinal protein do not parallel serological alterations, nor are they closely related to the duration or the severity of the arthritis.

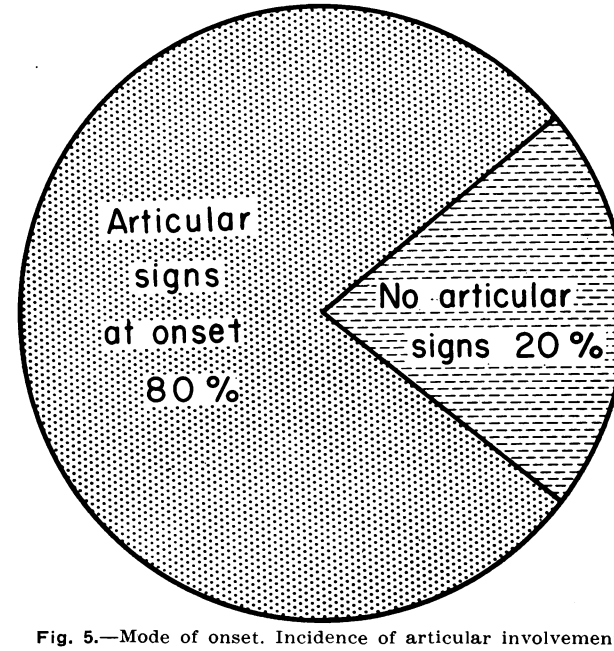


Fig. 5.—Mode of onset. Incidence of articular involvement.

JOINT MANIFESTATIONS

Joint involvement is most variable.[76] At the time of onset, 20% of our patients had no articular signs whatsoever (Fig. 5); the first clinical sign of the disease were articular in only 80% of patients.

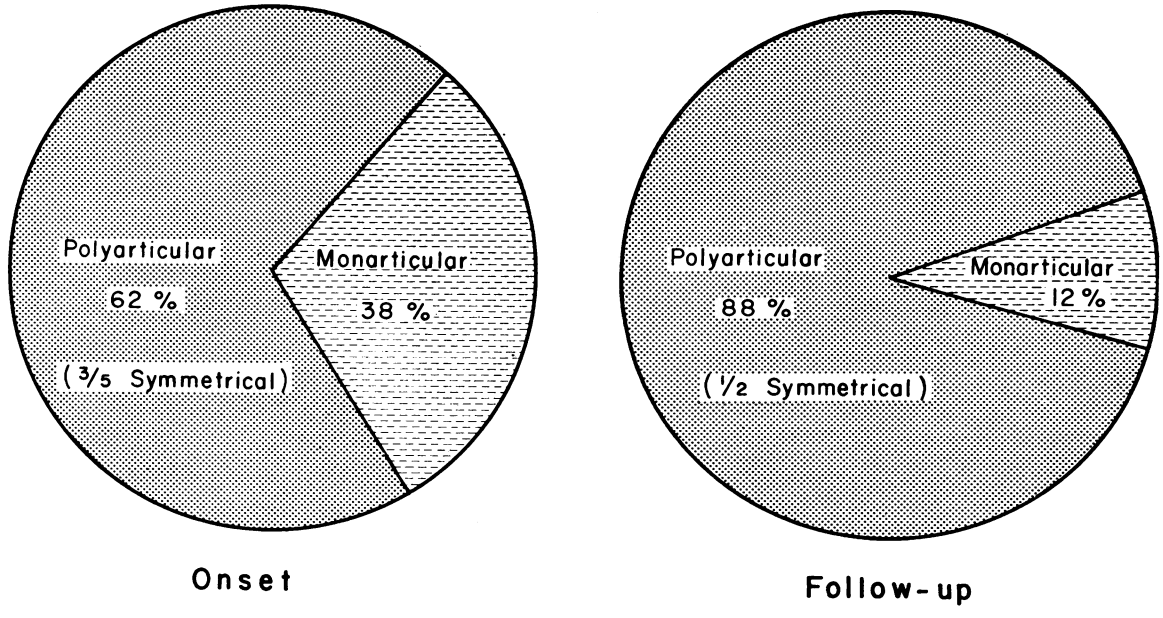
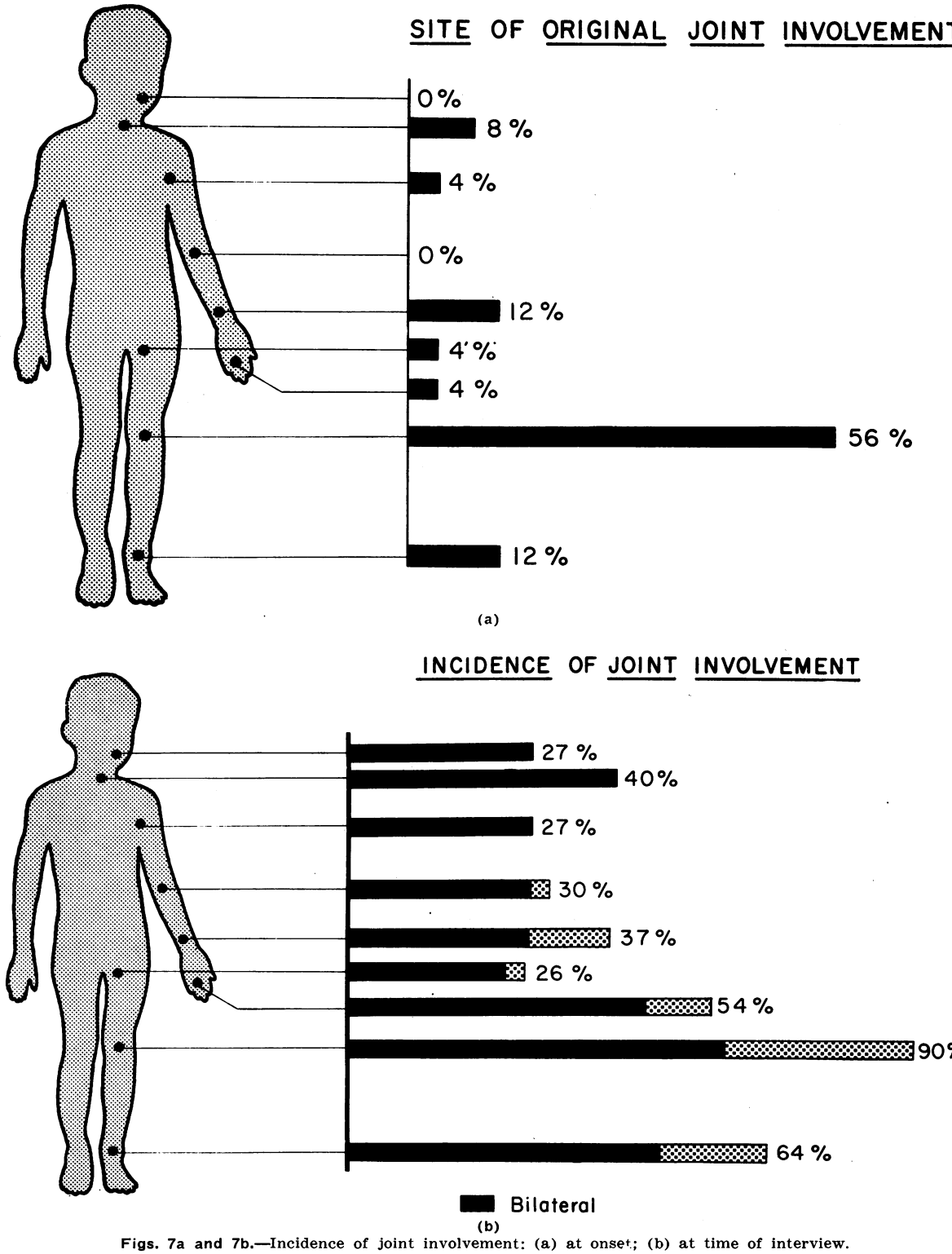


Fig. 6.—Incidence of monarticular involvement. At onset. At interview.



Figs. 7a and 7b.—Incidence of joint involvement: (a) at onset; (b) at time of interview.

Among this latter group, joint involvement was monarticular in 38% of patients at the time of onset (Fig. 6); at the time of interview, however, monarticular signs were noted in only 12%. Such a monarticular distribution had persisted in the latter cases for an average of 3½ years. In the majority of cases, however, polyarticular signs develop within a few months. Similarly, the incidence of symmetrical joint involvement[71] decreases with time, being noted in only 50% of patients at the time of examination (Fig. 6). Characteristically, the centripedal migration of joint involvement commonly observed in adults was not noted in these children.

Order of Joint Involvement

The sequence or order of joint involvement was carefully noted (Fig. 7a). The commonest site of

original joint involvement was the knee, followed by the wrist and ankle.[65] Occasionally the original articular symptoms were cervical and a painful torticollis was the first clinical manifestation of rheumatoid arthritis.[49]

TOTAL JOINT INVOLVEMENT

Joint involvement in general showed a predilection for the knee and the weight-bearing joints

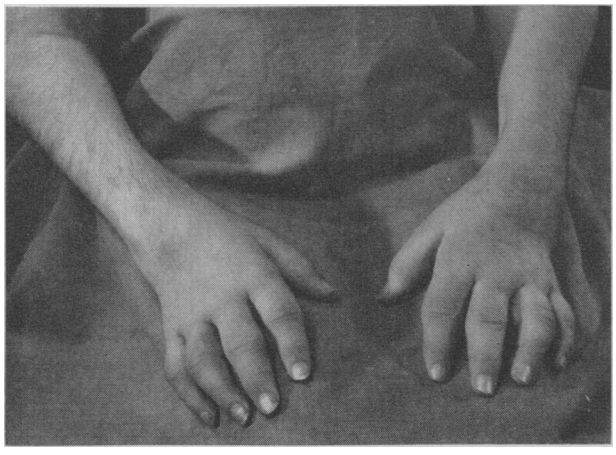


Fig. 8.—Spindle fingers in infantile rheumatoid arthritis are often late to appear, but they are found in no other collagen diseases of children; note forearm hirsutism due to cortisone medication.

(Fig. 7b). There was a characteristically high incidence of cervical lesions[38] while shoulder and wrist lesions were almost always bilateral. The hands were rarely the site of original joint involvement, but they were commonly affected in well-established cases.[11] The first joints involved were usually the metacarpophalangeal joints, more frequently in the index finger. Although swollen proximal interphalangeal joints or spindle fingers (Fig. 8) appear after metacarpophalangeal involvement, they are none the less a most useful diagnostic sign, since they are found in no other collagen diseases of children; thus spindle fingers, if present, should confirm the diagnosis of infantile rheumatoid arthritis. One should not expect to observe spindle fingers too frequently, however, since they are less common in children than in adults who have had their disease for an equal period of time. There were no examples of "mains en lorgnette" or "opera-glass hands", sometimes seen in comparably severe cases of adult rheumatoid arthritis.[70]

TABLE V.—GROWTH DISTURBANCES

1. Generalized:	
Height	13%
Weight	23%
2. Local:	
Premature ossification of epiphyseal centres	30%
Local shortening:	
Bradydactylia	10%
"Bird-jaw"	10%
Local lengthening	3%

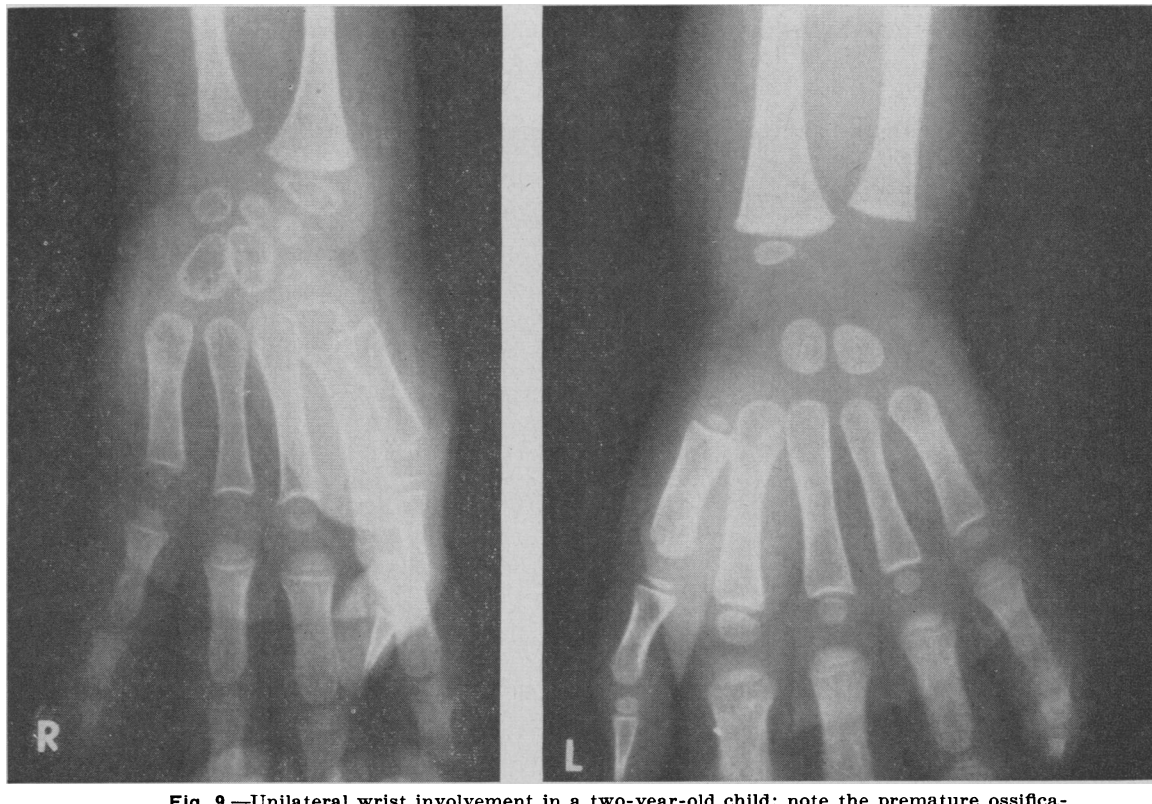


Fig. 9.—Unilateral wrist involvement in a two-year-old child; note the premature ossification of epiphyseal centres on the involved side (R).

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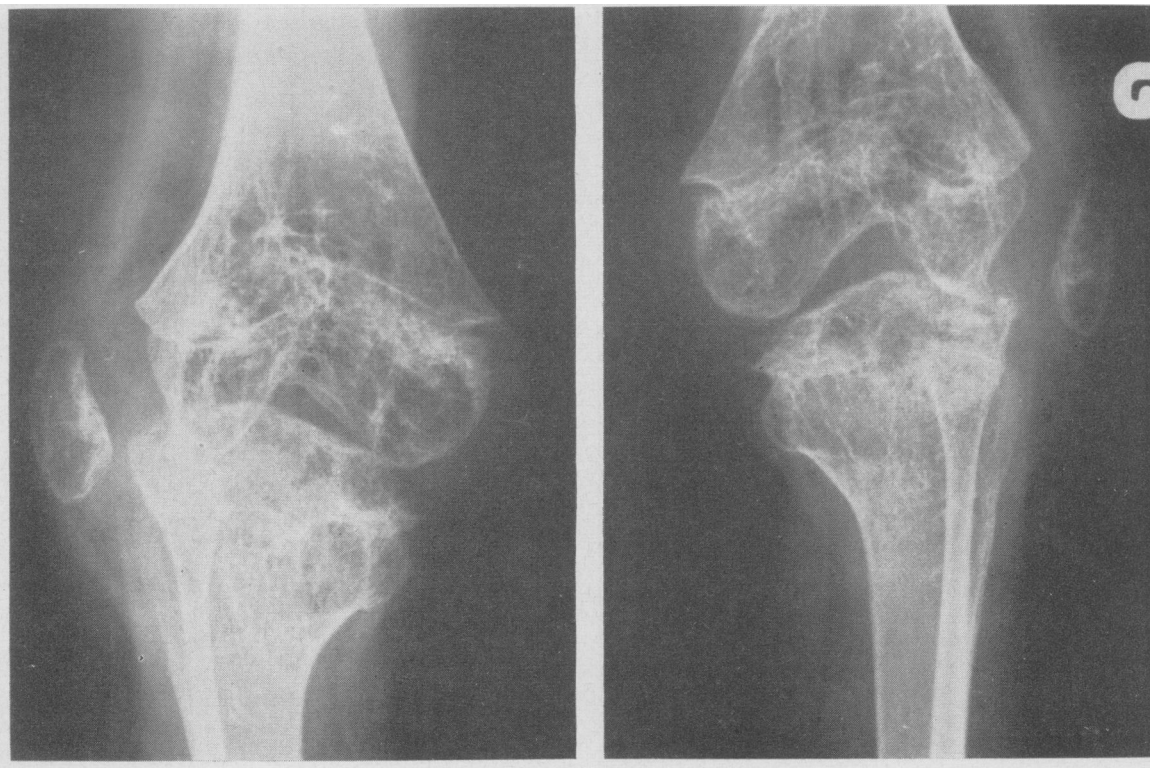


Fig. 10a

GROWTH DISTURBANCES

Growth disturbances were not uncommon (Table V).[2, 44] Dwarfism is usually most marked in the extremities and is usually associated with a severe form of arthritis and obvious systemic involvement. The decrease in height is frequently accentuated by hip and knee flexion deformities.

Local growth disturbances are more common than generalized ones, although they are sometimes less obvious. Local hyperemia and hypervascularity can, on rare occasions, stimulate an epiphyseal plate, or hasten the ossification of epiphyseal centres; this is particularly well seen (Fig. 9) in unilateral wrist lesions.

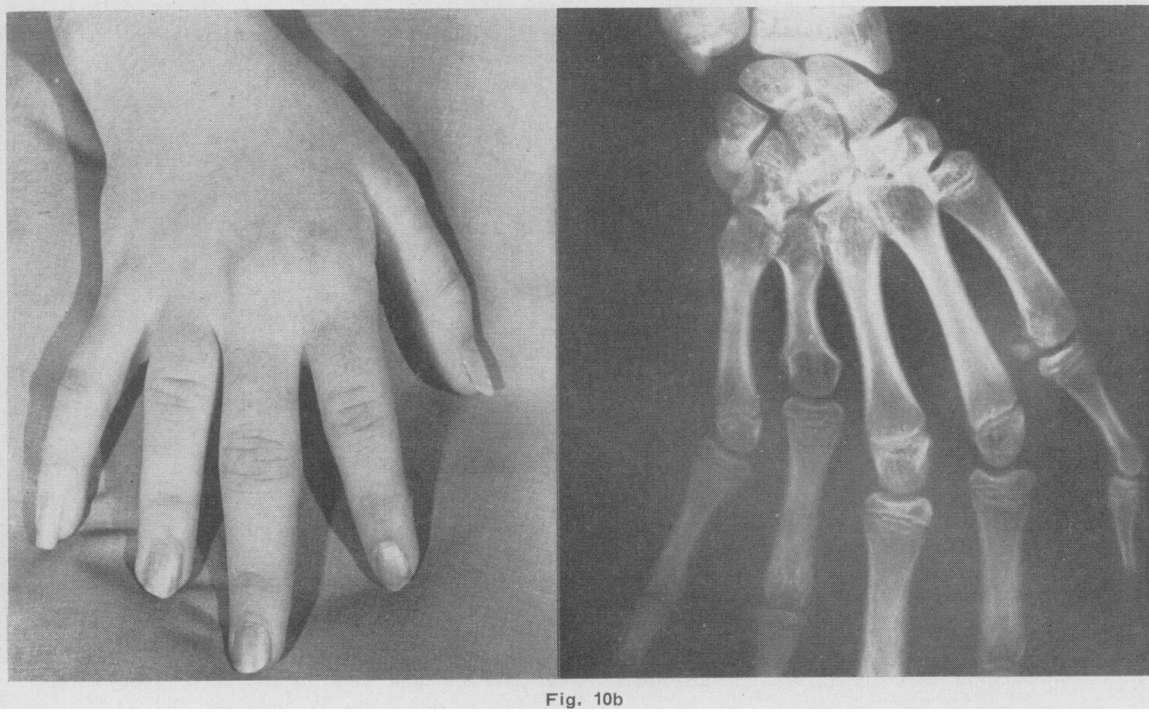


Fig. 10b

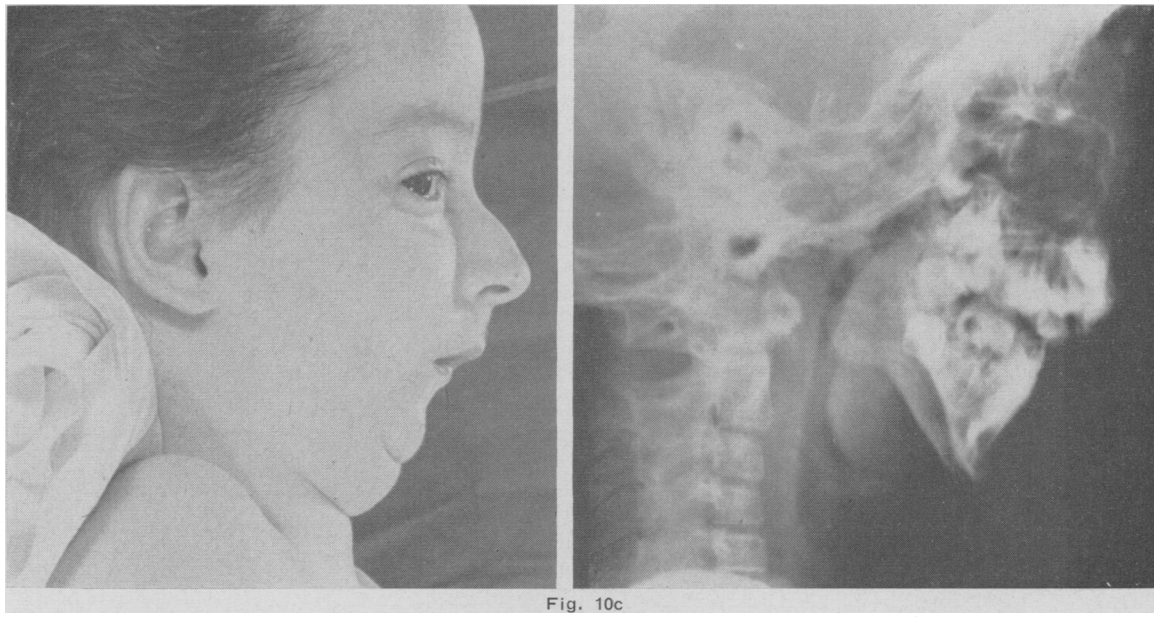


Fig. 10c

Figs. 10a, 10b and 10c.—Local growth disturbances secondary to invasion of epiphyseal plates: (a) Distorted articular surfaces; (b) local shortening or bradydactylia of ring finger; (c) "bird jaw".

More commonly, however, the rheumatoid process invades the epiphysis and later the epiphyseal plate, destroying it completely or partially. Clinically, this leads to distorted articular surfaces (Fig. 10a) or local shortening. The two common sites of local shortening are the fingers and jaw. Bradydactylia (Fig. 10b) is the most common type of local growth disturbance and is usually noted in the ring and little fingers. A "bird jaw" (Vogelgesicht) is not uncommon in severe forms of juvenile arthritis (Fig. 10c). This deformity is progressive; it is secondary to temporomandibular joint involvement and invasion of the condyles which normally provide the forward and down-

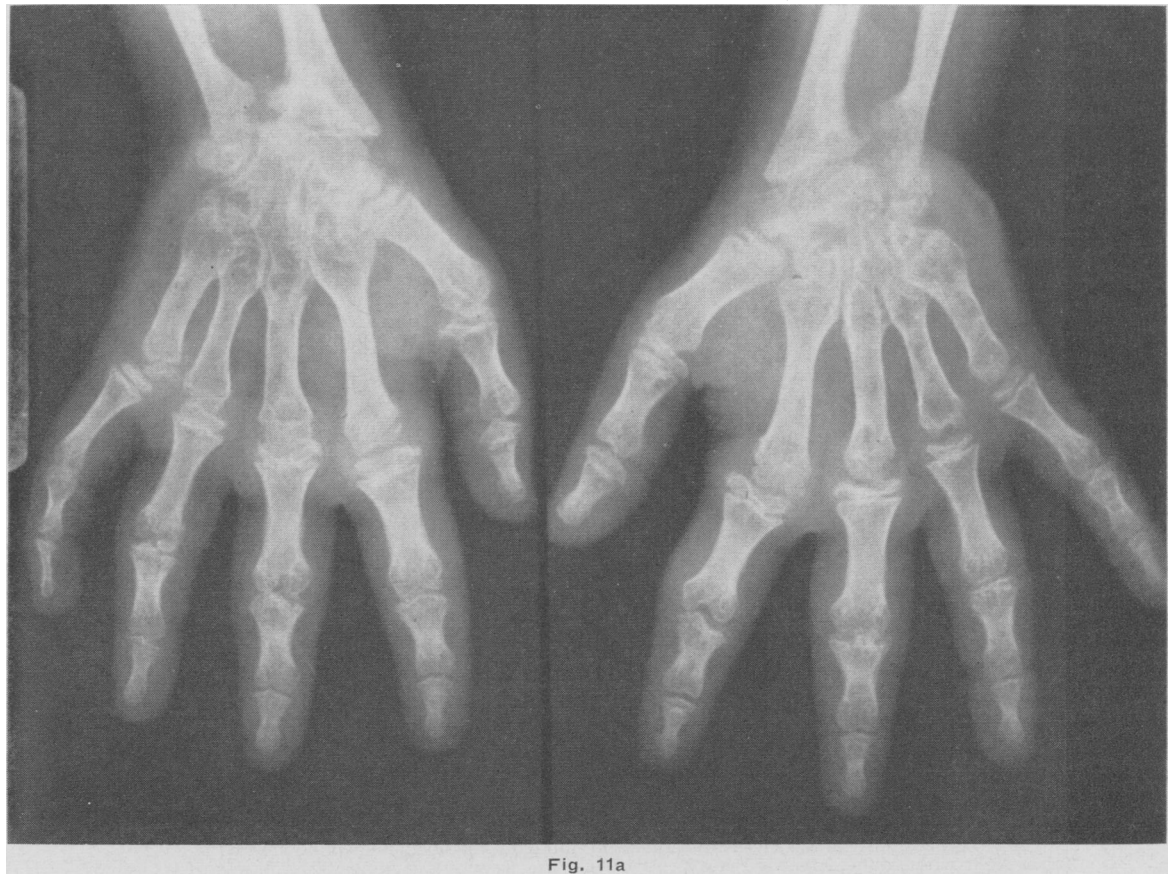


Fig. 11a

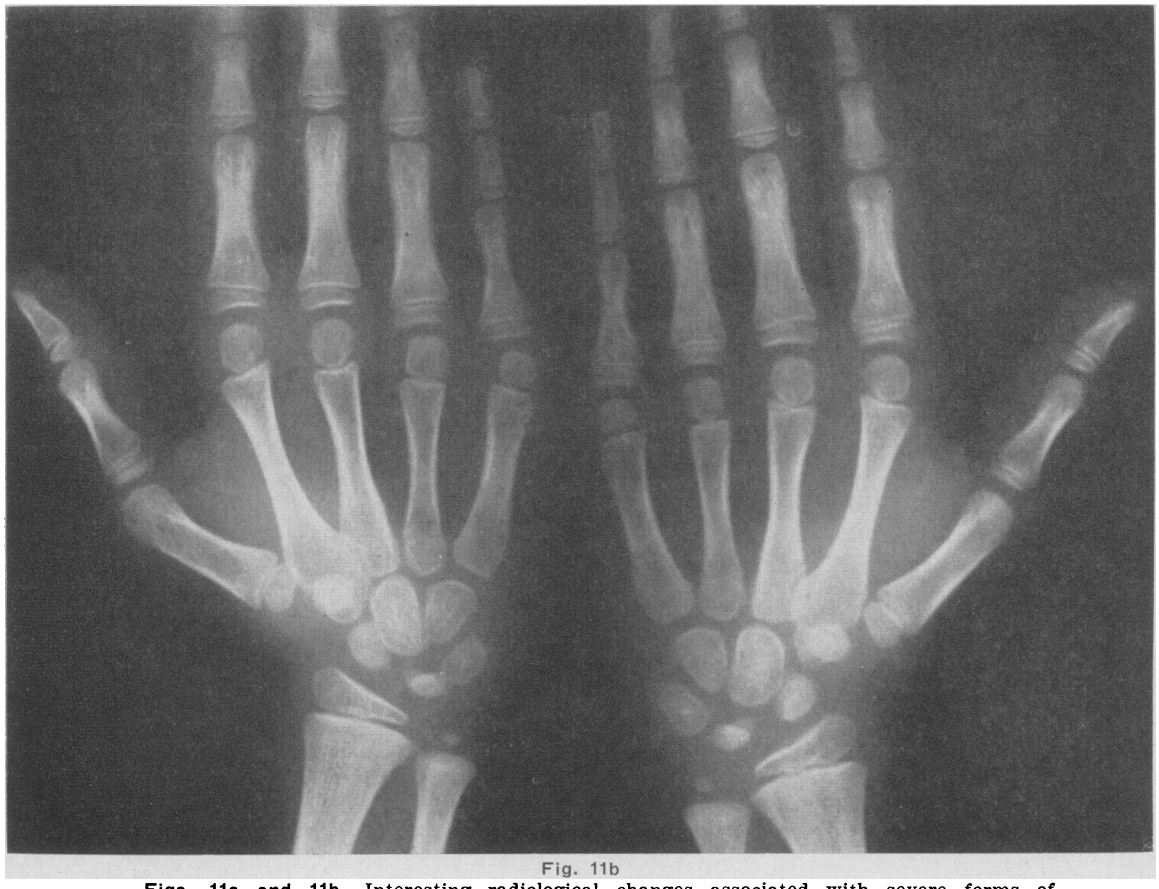


Fig. 11b

Figs. 11a and 11b.—Interesting radiological changes associated with severe forms of infantile rheumatoid arthritis: (a) cystic type of osteoporosis; (b) subperiosteal new bone—note phalanges.

ward vector of growth in the jaw.[28] There is usually an overbite (a Class II type of malocclusion) with protruding upper teeth and crowding of the lower teeth; there may even be encroachement of the pharyngeal space in more severe cases.

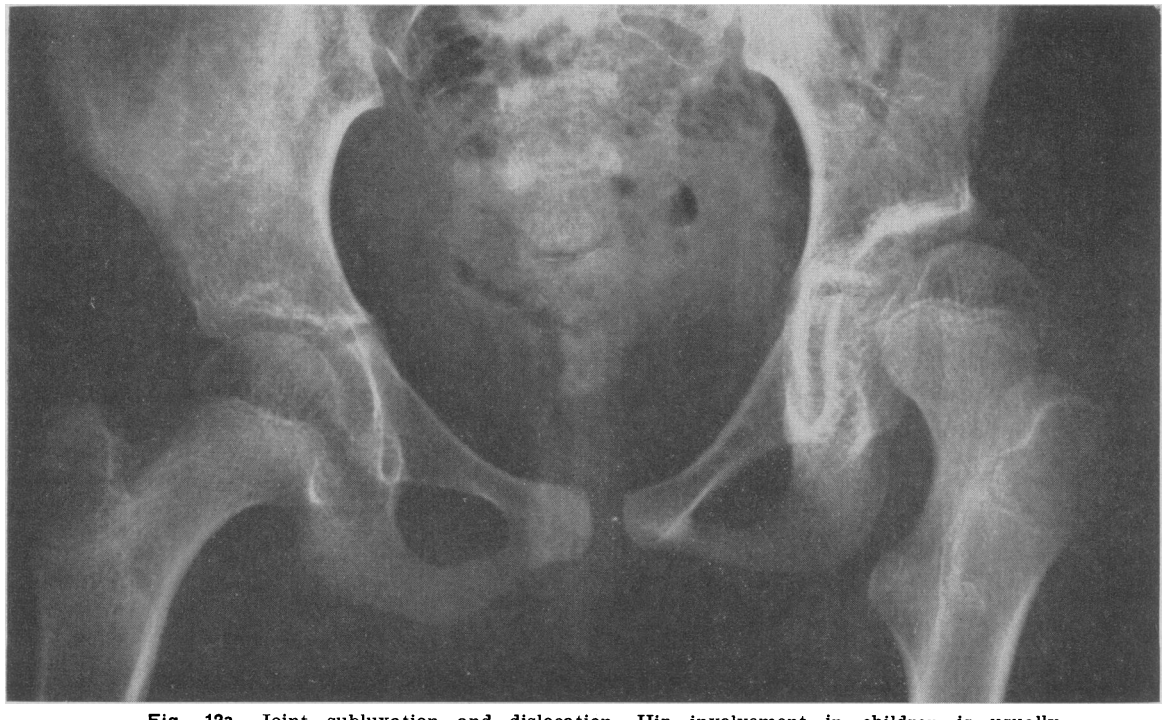


Fig. 12a.—Joint subluxation and dislocation. Hip involvement in children is usually associated with subluxation and not protrusion.

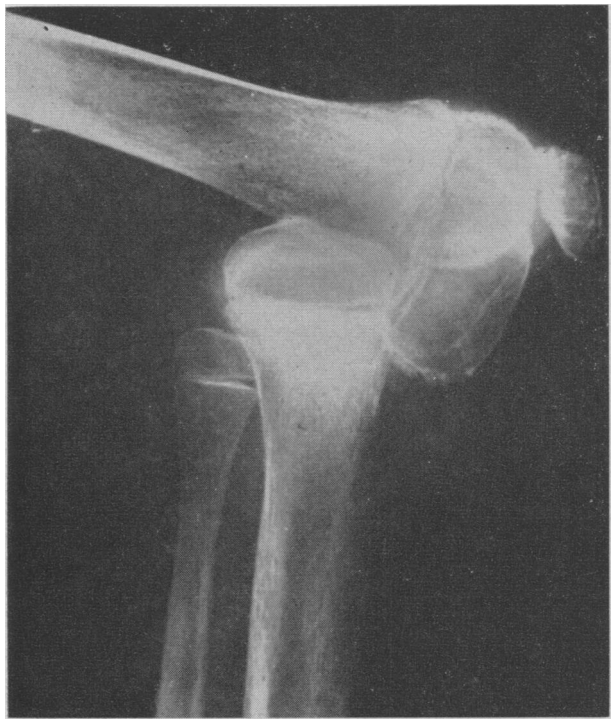
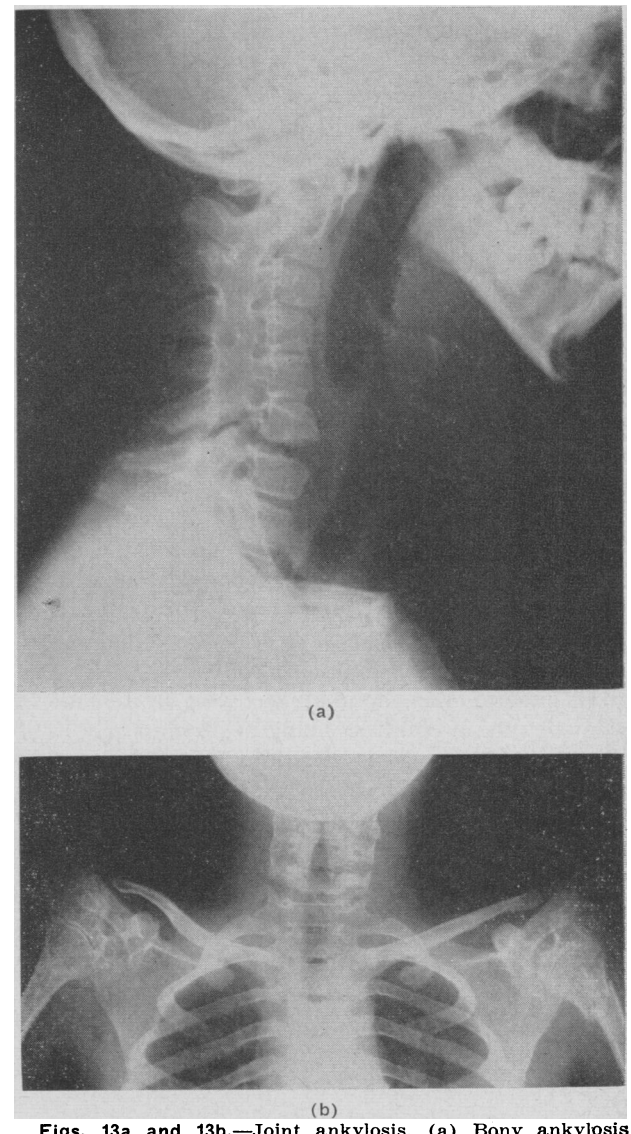


Fig. 12b.—Joint subluxation and dislocation. Complete dislocation is exceptionally rare and was only encountered in the knee.



Figs. 13a and 13b.—Joint ankylosis. (a) Bony ankylosis is rare; the commonest site is the cervical spine; it is occasionally observed in the knee. (b) Fibrous ankylosis is more frequent, particularly in the hips and upper extremities. Note the spontaneous fracture of the humerus.

RADIOLOGICAL PICTURE

Radiographic signs are late to appear.[73a and b] The first alteration is an osteoporosis which is sometimes quite extensive, even in the absence of radiological evidence of articular involvement.[51] The next stage is one of resorption of the subarticular cortex. Later, small periarticular bone cysts develop; as already noted, these changes are frequently first seen in the metacarpal head of the index finger.[30] In advanced cases one may note articular disorganization and a cystic type of osteoporosis (Fig. 11a).

Another interesting radiologic sign which is late to appear, and which is more common in the hand, is the formation of subperiosteal new bone (Fig. 11b). On occasion, there is considerable remoulding and widening of the bones so affected.

Complete destruction of larger joints is usually preceded by subluxation. In the knee, for example, the subluxation is associated with a flexion deformity; in the hip, there is frequently widening of the joint line and there appears to be an exuberant synovial pannus which seems to push the femoral head out of the acetabulum (Fig. 12a). It is interesting that rheumatoid arthritis of the hip frequently results in subluxation of the femoral head in the child, while it commonly causes protrusion in the adult. Complete joint dislocation (Fig. 12b) was seen in only one patient, in whom it was noted in both knees.

Certain joints, such as the cervical spine (Fig. 13a), and sometimes the knees, will proceed to complete bony ankylosis; on the other hand, fibrous ankylosis is the usual type of ankylosis in the hips and upper extremities (Fig. 13b). The association of such ankyloses and osteoporotic bones predispose these patients to pathological fractures (Fig. 13b). Such spontaneous fractures may occur in bed, above a long leg-cast, or they may occur as a complication of forceful joint manipulation.

LABORATORY INVESTIGATION

The laboratory investigation of rheumatoid patients has been disappointing (Fig. 14). There is no diagnostic laboratory test for juvenile rheumatoid arthritis. The alterations of serum proteins are characteristic but non-specific.[63] The rheumatoid factor test has yielded false positives and false negatives. The same is true for the antistreptolysin titre, which is even less specific. The sedimentation rate is merely a gross index of disease activity. The anemia frequently encountered in rheumatoid arthritis is also non-specific; it is hypochromic but responds poorly to iron.[24] However, it frequently

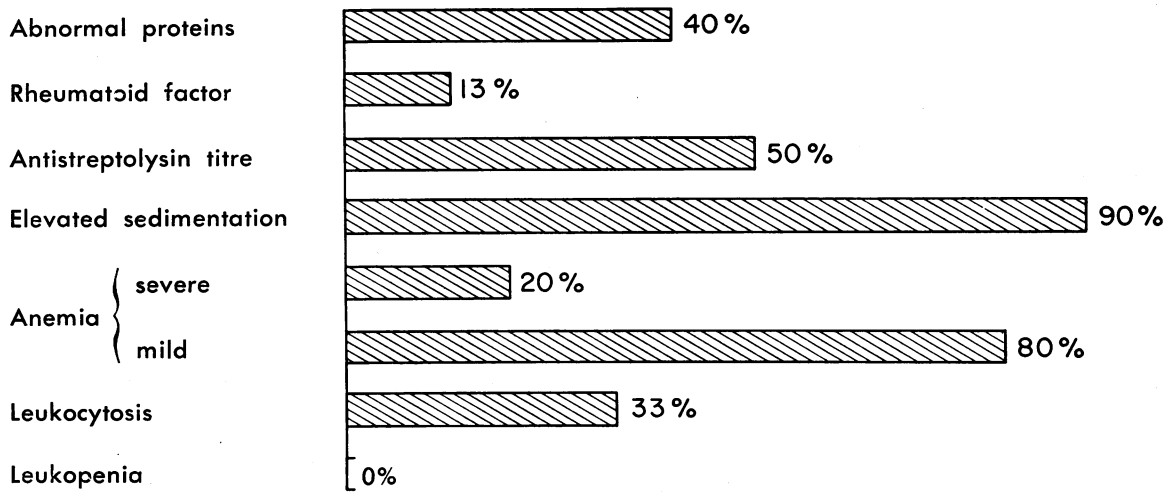


Fig. 14.—Laboratory investigation.

responds to cortisone and is commonly associated with a decreased red blood cell survival time.[24] A very high leukocytosis, or a leukopenia, is usually suggestive of a poor prognosis.

In general, the rheumatoid factor is difficult to demonstrate in children, being positive in only 13%, as compared to 50% of adults with rheumatoid arthritis. This incidence is slightly higher (19%) in the presence of severe or long-lasting disease.[13] More sensitive tests are available[50] but they are too elaborate for current usage. On occasion the rheumatoid factor can even be demonstrated in the joint fluid. There is an obvious need for a practical and sensitive diagnostic test, and the biochemistry department of this hospital has undertaken such an investigation on all patients.

Differential Diagnosis

Since there are no diagnostic laboratory tests, the problem of differential diagnosis is difficult and is essentially based on clinical considerations. The rigid diagnostic criteria[61] suggested for adults by the American Rheumatism Association[18] are, unfortunately, not applicable to children.

The differential diagnosis (Table VI) first rests on the particular type of juvenile rheumatoid arthritis. The systemic or infantile type, with an acute onset and high fever, must be distinguished from acute infections, viral or otherwise. It is important to recall that in these instances joint signs may be mild or late to appear; indeed they rarely dominate the early clinical picture. Three of our patients with this type of the disease had an original diagnosis of encephalitis, while another patient presented a clinical picture indistinguishable from poliomyelitis for three years.

Among the patients who present joint signs predominantly, the obvious distinction is between monarticular and polyarticular involvement. Those with monarticular distribution must be distinguished from cases of post-traumatic synovitis and tuberculosis; the former diagnosis was entertained for a year and a half in one instance; on another occasion, the erroneous diagnosis of tuberculosis of the ankle was corrected two years after an inconclusive synovial biopsy. Indeed the inflammatory, granulomatous character of both disorders can be most confusing. The distinction can only be made by indirect means and after the passage of time, unless a positive culture is obtained from the joint fluid.

Analysis of the joint fluid[59, 60] will facilitate the distinction between rheumatoid arthritis and post-traumatic arthritis, since the cell count and the reaction to glacial acetic acid are quite different in these two conditions.[62]

In those with polyarticular involvement the most difficult distinction is between rheumatoid arthritis and rheumatic fever[29] (Table VII). Although this diagnostic difficulty also exists in adults,[10] it is far more commonly encountered and more pronounced in children. The incidence of heart and joint signs in both of these conditions may impede the distinction for a long time.[55] The essential points of differential diagnosis are well known[69] (Table VII), but in practice it is often true that only the subsequent evolution of the disease unveils the true

TABLE VI.—DIFFERENTIAL DIAGNOSIS

I. Acute onset, systemic manifestations:
   a. Acute infections { Poliomyelitis / Encephalitis / Septicemia
   b. Collagen diseases
II. Obvious articular involvement
   a. Monarticular distribution { Tuberculosis / Post-traumatic arthritis
   b. Polyarticular distribution: rheumatic fever

TABLE VII.—DIFFERENCE BETWEEN RHEUMATOID ARTHRITIS AND RHEUMATIC FEVER

	R.A.	*R.F.*
Flitting arthritis	0	++++
Redness in involved joint	+	++++
Cardiac manifestations	++	++++
Response to salicylates	++	++++
Severe systemic manifestations	+++	+
Gradual joint destruction	+++	0

diagnosis. Francis Bacon could well have been referring to this diagnostic dilemma when he wrote that "time is the mother of truth".

TREATMENT

Most authorities now agree that the clinical end-stage of rheumatoid arthritis is more closely related to the severity of the pathological involvement than to the treatment. None the less it is undeniable that treatment is indicated and may be decidedly beneficial. If the treatment is delayed, the chances of complete recovery decrease considerably.

TABLE VIII.—TREATMENT

Medical

1. *Rest*
   - a. General { Physical / Mental
   - b. Local { Splints / Traction
2. *Improvement of general condition:*
   - a. Eradication of infection foci
   - b. Correction of anemia
3. *Drug therapy:*
   - a. Salicylates
   - b. Butazolidin
   - c. Antimalarial drugs
   - d. Cortisone
4. *Physiotherapy*

Although an absolute cure is rare, remission is possible and may be quite gratifying. For a child, the postponement of a deformity can be invaluable.

It is important to treat the whole patient and not merely a collection of joints[23, 32] (Table VIII). Rest is probably the most important part of the treatment; bed rest and hospital rest are essential in the more severe forms of juvenile rheumatoid arthritis.[15] Bed rest, however, does not imply mummification,[66] or the enforced, uninterrupted rest advocated by Hugh Owen Thomas. Rather, John Hilton's[37] and Robert Jones' interpretation of rest, a physiological rest, should prevail.[14] The restrained use of physiotherapy can prevent the development of deformities and keep muscle atrophy at a minimum. There is no need for forceful passive manipulations; children will move their own joints much more effectively as soon as they are painless. The intelligent use of splints and appliances will assist in maintaining inflamed joints at rest with a minimal risk of ankylosis in children. Rest and movements are the keynotes of therapy, with emphasis on the former.[67]

Drug therapy is a matter of controversy at the present time.[9] Salicylates are obviously the first line of defence, but the role of more powerful drugs, such as phenylbutazone, antimalarial medication and, particularly, cortisone, remains to be established.[36, 77] In general phenylbutazone and the antimalarial drugs have been used with encouraging results, particularly in children; they should be used whenever salicylates are inadequate, or in the presence of salicylism. The indications for systemic cortisone[43] are rather precise (Table IX), but the advantages of the drug must be carefully weighed against its potential undesirable effects.[26] Severe osteoporosis and other features of Cushing's syndrome are not rare, although they are, fortunately, reversible. Cortisone treatment undoubtedly yields better short-term results, but most authors now believe that the long-term results[72] are not improved by systemic cortisone.[19, 78]

TABLE IX.—SYSTEMIC CORTISONE MEDICATION

I. *Indications:*
   - a. Resistance to salicylates, etc.
   - b. Severe systemic involvement, e.g.
     - Still's syndrome
     - Severe anemia
   - c. Fulminating disease

II. *Complications:*
   - More common and more severe in children

The intra-articular use of cortisone, on the other hand, is enthusiastically recommended. Indeed, salicylates and early intra-articular cortisone medication have controlled most of these patients; such injections may be performed under anesthesia and may be associated with gentle manipulations, followed by splinting.

Forceful mobilizations and fractures of osteoporotic bones should be a thing of the past. Such manipulations are dangerous and almost never provide any permanent gain. If flexion deformities are rigid, osteotomies are to be preferred. On the other hand, there is no need of osteotomy in the case of every flexion deformity; a certain degree of fixed knee-flexion is compatible with good function. In our opinion, there is no indication for surgery before a knee-flexion deformity exceeds the 155° position. If surgery is performed on every knee which cannot extend to 180°, a considerable number of useless osteotomies will be performed, and an even greater number of deformities will recur. This was particularly well illustrated by one patient who had eight technically successful femoral osteotomies. This patient's knee flexion deformity (160°) has once again recurred, but his function is adequate; another osteotomy will be considered only if and when the flexion deformity progresses beyond 155°. It is worth noting that the deformity in this case has not progressed in the past two years in spite of continuing rheumatoid activity.

It is obviously better to prevent[40] such flexion deformities,[5] either medically or by a well-timed synovectomy.[42] The indications for synovectomy are essentially the same for patients with juvenile and adult rheumatoid arthritis.[54] This operation should be performed in the face of resistant symptoms, before the advent of fixed deformities.

PROGNOSIS

There are no absolute prognostic criteria;[1] none the less, certain factors are more commonly associated with a particular type of outcome (Table X, column 1). Although it is true that "once an

TABLE X.

1. *Favourable prognostic criteria*
   - Prolonged remission
   - Absence of systemic manifestations
   - Onset after age of 3 years
   - Monarticular involvement
   - Early treatment

2. *Systemic manifestations and prognosis*

	Incidence of systemic involvement
Crippling disability	90%
Moderate disability	32%
Complete recovery	7%

3. *Age of onset and residual disability*

Crippling disability	2.0 years
Moderate disability	3.5 "
Complete functional recovery	4.7 "

arthritic, always an arthritic", and that certain patients have had exacerbations after 20 years of inactivity, a prolonged remission is always encouraging. The absence of systemic involvement is another favourable prognostic sign (Table X, column 2). An early age of onset, on the other hand, is always unfavourable[76] (Table X, column 3) (see Fig. 4).

END RESULT

The average follow-up period in this study was five and a half years, with a range of one to 15 years. The status of these patients at the time of interview (Fig. 15) suggests that the prognosis of juvenile arthritis is not as gloomy as once was thought. Indeed, the prognosis for life is good, while the prognosis for joint deformity is not bad.

The end result for individual patients, however, is difficult to forecast. Colver's conception[17] that the disease is self-limiting and eventually burns itself out is no longer tenable; one of our patients was in a period of continuous activity for eight years, and instances of 10 and 15 years of unremitting disease activity have been reported.[25]

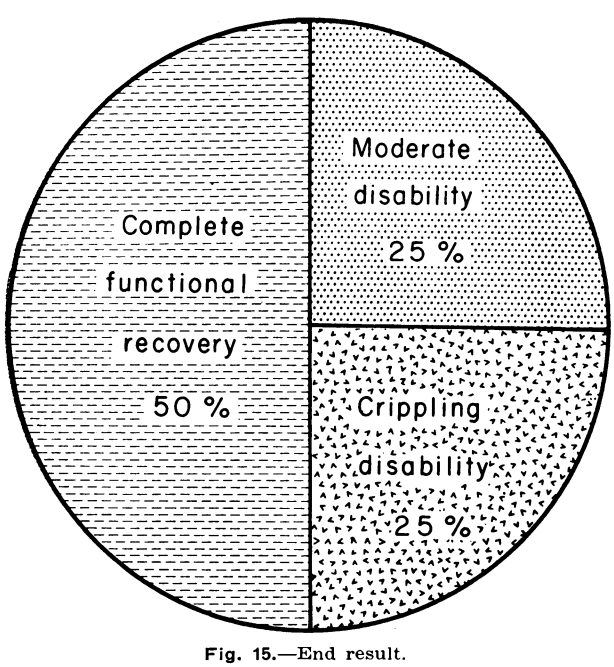


Fig. 15.—End result.

Indeed, although half of our patients were functionally normal on examination, many of them had mild residual deformities (52%) or some suggestion of persistent activity (48%). These patients demonstrate the fluidity[57] and the reversibility[35] of the disease; even in the absence of joint signs, the rheumatoid state clearly persists.

SUMMARY

The clinical picture of juvenile rheumatoid arthritis has been reviewed with particular emphasis on the difficulties of an early diagnosis, the sequence and types of joint involvement, the prognostic criteria, and the end result. Certains suggestions have been made concerning treatment, and the need for a more sensitive, practical diagnostic test has been emphasized.

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Prediabetes and Pregnancy

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ABSTRACT

In a prospective study of perinatal losses associated with prediabetes, 105 pregnancies were followed in women showing mild abnormalities of glucose tolerance. Hypoglycemic agents were not administered in the absence of frank diabetes. All patients were attended at delivery by interns or residents. Only two perinatal losses (1.5%) occurred in complicated cases, one of which might have been avoided. Perinatal losses in unrecognized prediabetics are largely due to associated obstetric factors, and in uncomplicated prediabetes should not differ from nondiabetic pregnancies. Recognition of the prediabetic state allows subsequent complications to be anticipated and treated early. In the absence of frank diabetes, hypoglycemic agents would not improve the immediate fetal salvage. Their value for reducing the incidence of recognized complications or in promoting the remote welfare of the fetus (preventing the ultimate development of diabetes) has not been established. The administration of hypoglycemic agents to the pregnant prediabetic is not recommended in view of the possible teratogenic effect.

THE perinatal mortality for all pregnancies is approximately 2% to 3% in many centres. As recently as 1957 perinatal mortalities exceeding 30% were reported in unrecognized prediabetics.[1-3] Such statistics are difficult to accept when it is considered that the usual figure for perinatal loss in frank diabetics in many centres does not exceed 15%. It was felt that the high losses reported were based on retrospective studies. For this reason a prospective study was undertaken at the Women's Pavilion of the Winnipeg General Hospital.[4]

From July 1, 1958, to June 30, 1959, every staff patient was studied. Glucose tolerance curves were not performed on every patient, but on two-thirds of the patients showing any sugar in their urine and on others with a background suggestive of the prediabetic state; e.g., large babies, poor obstetric histories, or a family history of diabetes.

Six hundred and seventy pregnancies were followed in 642 patients. Three previously known diabetics and 32 patients who were confined elsewhere were excluded. Four hundrd and seventy-six patients who never at any time showed sugar in their urine or an abnormal glucose tolerance curve served as controls. Patients with renal glycosuria and with glycosuria of unknown etiology (no blood sugars performed) were not included in the control group, but were studied as separate groups. Carbohydrate tolerance in pregnancy has been discussed in a previous publication.[4]

Because normal values for blood glucose levels in pregnancy have not been generally accepted, an arbitrary definition of an abnormal glucose tolerance curve was made for the purpose of this study. In terms of true blood glucose, the upper limits of normal for the fasting, peak and two-hour levels were taken as 100 mg. %, 160 mg. %, and 100 mg. %, respectively. The glucose tolerance curves that were considered abnormal were further subdivided into four groups based mainly on the two-hour value. Values of 140 mg. % or more were

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