the summated Hodgkin's and lymphosarcoma and reticulosarcoma results previously shown separately. This is done in Table VII. The differences between the survival rates for the equivocal and unequivocal groups are not significant at the fifth, tenth, or fifteenth years.

TABLE VII.—Comparison of Unequivocal and Equivocal Groups

Clinical Stage	Group	Age-corrected Survival Rate (%)		
		5 Years	10 Years	15 Years
Localized	Unequivocal	53.6	44.0	41.0
	Equivocal	49.3	38.1	36.7
Generalized	Unequivocal	16.8	11.0	10.5
	Equivocal	15.1	8.2	8.2

Conclusions

According to the criteria of cure defined above there is evidence from the series of cases here reported that the two major groups of lympho-reticular disease—Hodgkin's disease and lymphosarcoma and reticulosarcoma—are equally curable. Nearly 40% of patients who present with clinically localized disease are curable, while the outlook is certainly not hopeless even for those who have generalized disease at the time of treatment. In both of these categories the prognosis is more favourable for women than for men.

It is interesting to note that, whether the clinical diagnosis or the histological report be equivocal or not, the prognosis is remarkably consistent both for localized and for generalized lymphadenopathies. It would seem, therefore, that whatever the type of lympho-reticular disease, and despite clinical and histological disputation, the urgent need is for radical x-ray therapy with curative intent, especially in those cases with localized disease.

What is needed is the opportunity to give radical treatment to the majority rather than the minority of patients suffering from these diseases. Early recognition

of this complex group of diseases, coupled with appropriate action, would improve still further the overall cure rates already achieved.

Summary

The customary caution inherent in published survival rates for malignant disease obscures the very possibility of permanent cure. When the expectation of life of a group of patients free of disease becomes similar to that of the general population of the same sex and age constitution we are entitled to speak then of cure.

Survival studies of substantial numbers of patients 5, 10, and 15 years after treatment indicate that nearly 40% of those suffering from localized Hodgkin's disease are indeed cured. Since almost identical cure rates are obtained for patients with lymphosarcoma and reticulosarcoma, it is urged that, whatever the histological disputation, all these lympho-reticular lymphadenopathies require immediate radical x-ray therapy while they are still localized if the opportunity for cure is not to be lost.

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LONG-TERM TREATMENT OF CHRONIC PYELONEPHRITIS IN CHILDREN

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In the past the majority of patients with chronic pyelonephritis were treated by means of short-term administration of antibiotics and sulphonamides whenever there was an acute flare-up of infection. No treatment was given between acute attacks. In this way permanent sterilization of urine was achieved in only approximately 10% of all patients (Orsten, 1960). Helmholtz (1941) was the first to recommend the protracted administration of small doses of sulphathiazole for chronic urinary infection. Addis (1948) used this method for the treatment of chronic pyelonephritis with remarkable success. Stansfield and Webb (1954) were among the first paediatricians to report on the advantages of long-term therapy. They used sulphadimidine for the treatment of chronic pyelonephritis in children, and recommended that it should be administered for at least two months; when the disease had been present longer than two months they recommended that treatment should be for at least six months. Marshall and Johnson (1946) discussed the effect of nitrofurantoin on chronic infections of the urinary tract in children. Good results were claimed after several months of treatment.

In spite of these promising results, long-term treatment did not at first become generally accepted. This was probably due to a justified apprehension of secondary reactions if full doses were given over a long period, or of bacterial resistance if only small maintenance doses were used. These problems have been the subject of several papers, especially those by Haschek (1959) and Dumittan (1960), who agree that long-term administration of small amounts of antibacterial agents is only rarely associated with the appearance of resistance in urinary bacteria.

Present Series.—The series comprised 20 children, of whom 11 were girls. They were under observation from 1954 to 1959. At the time of their first admission to hospital they were aged 3 to 14 years. Judging from the history, the disease had lasted from three months to 10 years. Seven had had the disease for less than one year, another seven from one to three years, and the remainder from 5 to 11 years. All but three—those with short histories of only three to six months—had first been treated elsewhere, some of them only as outpatients. Eleven had been wrongly diagnosed—four as

chronic glomerular nephritis, two as appendicitis, two as enuresis, two as recurrent cystitis, and one as rheumatic fever.

Methods

Proteinuria, Urinary Cell-excretion, and Bacteriological Examination of Urine.—Proteinuria was tested for each day: (1) in the first morning sample by the addition of salicylsulphonic acid, (2) in the 24-hour collection with Esbach's technique. Addis counts were performed on 12-hour collections obtained during the nights that the children had slept and had not passed urine. The urine was collected in the morning by spontaneous voiding after careful cleaning of the perineum and vulva in girls or the prepuce and glans penis in boys. The urine for bacteriological cultures was obtained in girls by catheter, in boys by mid-stream specimen.

Renal Function.—Endogenous creatinine clearance was used for estimation of the glomerular filtration rate. The average value from a 24-hour collection was recalculated per 1.73 sq.m. body surface area. An index of the tubular reabsorption of water in each kidney was determined from the value of the ratio of the concentrations of plasma and urine endogenous creatinine according to the formula $R = (1 - \frac{P}{U}) \times 100$, where P and U are the plasma and urine creatinine concentrations respectively. The advantage of this ratio lies in the fact that it does not require the quantitative collection of urine. The urine from each kidney was obtained by ureteral catheters introduced into the pelvis. The lowest normal value of R under the conditions of oliguria at the time that the catheters were inserted is 98%. This method has been described previously (Hradcova and Schück, 1960). The kidneys' maximal ability to concentrate was measured after a 24-hour period of fluid deprivation; with this technique the lower limit of the normal is S.G. 1028. The maximal ability to dilute was measured after an intake of 500 to 1,000 ml. of water, according to the age and weight of the child.

X-ray Examination.—Intravenous and ascending pyelography, micturition urethrocytography, and pneumoretroperitoneum were carried out according to routine techniques.

Findings on Admission

Urine.—When admitted to our clinic all children had positive findings in the urine. Proteinuria was invariably present, though in only two patients was it as high as 2–4 g./24 hr. The white-cell excretion rate was always increased. Most of the patients also had microscopic haematuria, occasionally due to renal stones. Casts were not seen (Fig. 1). In all the children the urine culture was positive; 13 had only one organism, of which seven were *Escherichia coli*, two had *Proteus* and *Ps. pyocyanea*, and one each had *Streptococcus faecalis* and *Staphylococcus pyogenes*. The urines of the remaining seven children were infected with several organisms; these were the same as those mentioned above and in roughly the same proportion.

Renal Function.—The glomerular filtration rate was normal in all but three of the children. These three were among the eight who had bilateral disease; their glomerular filtration rates varied between 42 and 67 ml./min./1.73 sq.m. and the non-protein nitrogen (N.P.N.) between 56 and 98 mg./100 ml. Impairment of the maximal ability to concentrate was striking

(Fig. 2); it was reduced in 75% of cases. It was normal in some of the patients with unilateral disease. The maximal ability to dilute was impaired in three cases, the specific gravity of urine dropping, at the most, to S.G. 1004, 1005, and 1006.

Radiological Findings

All the children had abnormal intravenous pyelograms (I.V.P.). On the basis of the I.V.P. findings, cystograms, ascending pyelography, and occasionally pneumoretroperitoneum, the patients were divided into two groups. In the first group (eight children) there was no evidence of obstruction of the urinary tract. The changes were unilateral or bilateral, with delayed or poor excretion of the dye, pelvic and ureteric dilatation, kinking hydro-ureter with hydronephrosis, vesico-renal reflux, and congenital dysplastic kidneys.

In the second group (12 children) there was evidence of urinary-tract obstruction. In one patient the kidney did not excrete and there was a staghorn calculus in the pelvis. The other 11 suffered from hydronephrosis with hydroureter—four of them bilaterally and seven unilaterally. The causes of obstruction were: ureteric valves, stones in the ureter or in the urinary bladder,

FIG. 1.—Addis count in children with chronic pyelonephritis before long-term therapy: number of white and red cells in a 12-hour collection of urine. The normal count is 1,000,000 white cells and 500,000 red cells. In all patients the number of leucocytes was greater than 11,000,000. Haematuria was found in 75% of cases; in some this was partly due to the presence of stones.

FIG. 2.—Maximal ability to concentrate the urine. Fifteen of the 20 cases had some impairment.

stenosis of the ureteropelvic junction, and sclerosis of the neck of the urinary bladder.

Treatment

All eight children in the first group and 2 of the 12 in the second group were treated medically; the remaining 10 in the second group were treated both medically and surgically.

Medical treatment was begun with full doses of antibiotics to which the bacteria were most sensitive. After being discharged, the children remained under our control as out-patients and were given 0.5 g. of sulphaurea five times a day during the first week of each month for 6 to 24 months, with the exception of two children whose treatment was terminated after three months. During the last year sulphaurea was in some cases replaced by sulphamethoxypyridazine, 0.25 to 0.5 g./day.

Effect of Treatment.—A successful cure was considered to have been achieved when after the completion of treatment there were no complaints, the complete urine analysis and bacteriological findings were persistently negative, and renal-function tests as well as an I.V.P. were normal.

Patients without Obstruction

In this group with no anatomical obstruction to the urinary tract long-term administration of antibiotics and sulphonamides was completely successful in six of the eight children. In one child treatment was successful except for recurrent isolated bacteriuria.

In the remaining patient treatment was unsuccessful. She was a 13-year-old girl with congenital dysplastic kidneys and chronic pyelonephritis, with retarded development, weight 29 kg. and height 140 cm.; the disease remained active, with erythrocyte sedimentation rates (Westergren) ranging between 50 and 80 mm./hr. and 70 and 105 mm./2 hr. Renal function gradually deteriorated, the glomerular filtration rate fell to 17 ml./min./1.73 sq.m. of body surface area, tubular reabsorption of water dropped to 93.6%, she was unable to dilute below S.G. 1005 or concentrate above S.G. 1009. The failure of all therapeutic efforts in this case was probably due to congenitally abnormal kidneys with a superimposed pyelonephritis of eight years' duration. Her treatment has so far lasted two years.

Patients with Obstruction

In the second group, in which there was evidence of obstruction of the urinary tract, two children were treated with long-term administration of antibiotics and sulphonamides only; the other 10 were all treated both with surgery and with long-term antibiotics and sulphonamides.

Children Treated with Long-term Antibiotics and Sulphonamides Only.—Both children were cured. One was a 7-year-old girl with a history of dysuria and recurrent fever for 11 months due to recurrent urinary infection. She had bilateral hydronephrosis and hydroureter. The obstruction was caused by bilateral congenital ureteric valves. After one year's treatment there were no residual functional, bacteriological, or radiological abnormalities except for the continued presence of the ureteric valves. The second patient was an 8-year-old boy with a three-months' urinary infection associated with a small stone in the left renal pelvis. Later it descended to the lower end of the ureter and

caused acute hydroureter. Eventually the stone was excreted. Treatment was continued for six months.

Children Treated by Surgery and Long-term Antibiotics and Sulphonamides.—Obstruction of the urinary tract was relieved by surgery in all 10 patients. After operation all were given antibiotics and sulphonamides for several months. Three were cured. Fig. 3 shows the change in the ability to concentrate the urine which occurred in an 8-year-old boy with recurrent renal stones, hydronephrosis, narrowing of the uretero-pelvic junction, and chronic pyelonephritis on the right side. He was treated for a year and watched for another year.

Fig. 3.—Values of maximal ability to concentrate during 24-hour period of fluid deprivation in an 8-year-old boy with recurrent renal stones, hydronephrosis, stenosis of uretero-pelvic junction, and chronic pyelonephritis on the right side. Before operation the maximal ability to concentrate was normal because little urine was being formed on the right side. After the first nephrolithotomy and the removal of the sclerotic tissue from the renal hilus, followed by three short courses of antibiotics throughout the next year, the ability to concentrate remained reduced. After the second nephrolithotomy long-term therapy was commenced. The maximal ability to concentrate returned to normal. The Addis count and I.V.P. findings also returned to normal.

In three children renal function and the x-ray findings returned to normal, the urine was microscopically negative, but organisms continued to be found on culture. In another three children with advanced bilateral hydronephrosis some improvement was obtained. In these children renal function and x-ray findings improved but pyuria remained, or, conversely, the content of white cells and urine culture were nearly normal but the functional capacity was still moderately reduced. These six patients have been treated for 6 to 18 months; their treatment continues. The treatment failed in one patient (a girl aged 10); after a plastic operation on an enormous hydronephrosis on the right side and subsequent medical treatment for 18 months the urinary results were normal and overall renal function was within normal limits. The separate tubular reabsorption of water in the hydronephrotic kidney, however, dropped in the second year after operation from 98.1% to 96.9%, which pointed to severe damage of the kidney, and at the same time the blood-pressure rose from 120/70 to 150/100 mm. Hg. Because of this a nephrectomy was performed, after which the blood-pressure immediately fell, and it remained normal (100/60) throughout the next two years.

In those patients from both groups in whom treatment was successful pyelonephritis had been present for three months to nine years; they were treated from 3 to 18 months and were observed subsequently for up to three years (Fig. 4).

Discussion

The administration of long-term antibiotics produced a complete cure in 11 children; initially all had had abnormal intravenous pyelograms. In six the radiological changes were particularly severe, and included

the ureters and pelves, is associated with infection without obstruction, long-term administration of antibiotics or sulphonamides may cause the reflux and dilatation to disappear. It appears, therefore, that in such circumstances the radiological abnormalities are the result of the infection and not its cause (see Table).

It is of interest that the effect of treatment in the first group, where there was no evidence of obstruction of the urinary tract, was so much better than in the second, in which there was obstruction, even though this had been relieved surgically. It is probable that in the second group the obstruction had caused more irreversible damage to the kidney because of the increased pressure and stasis of urine proximal to the obstruction. Kidneys can be destroyed by obstruction in the absence of infection. It is clear that when there is unequivocal evidence of obstruction of the urinary tract it should be removed. If there is uncertainty about the presence of obstruction, conservative treatment may demonstrate that the radiological abnormalities are reversible.

Summary

Twenty children with chronic pyelonephritis were first treated with full doses of the antibiotics to which the bacteria were most sensitive, and then by long-term administration of sulphonamides. This therapy was always supplemented

in cases of proved obstruction of the urinary tract by surgical relief of the obstruction. The duration of the disease ranged from 3 months to 10 years, the duration of the treatment from 3 to 18 months. Six months to three years have elapsed since the termination of therapy in the successful cases. Eleven children were cured and seven were substantially improved; in two cases the treatment had no effect.

In six children with dilated ureters and pelves, or vesico-renal reflux, but no evidence of obstruction, the abnormal radiological appearances disappeared after prolonged treatment with sulphonamides.

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FIG. 4.—Eleven children with chronic pyelonephritis who were cured by treatment. The disease lasted three months to nine years; treatment lasted 3 to 18 months. Cases 4, 6, and 7 were also treated surgically. Medical observation after treatment lasted six months to three years.

vesico-renal reflux and dilatation of the ureters and pelves, though there was no evidence of obstruction. Nevertheless, treatment with long-term antibiotics and sulphonamides cured not only the infection but also the abnormal radiological appearances (see Table). It follows that when vesico-ureteric reflux, or dilatation of

Cured Children with Marked Radiological Changes Associated with Chronic Infection in the Urinary Tract

Case	Sex	Age (Years)	X-Ray Findings		Long-term Treatment (Months)
			Before Treatment	After Treatment	
1	F	8	Micturition urethrocytography Left vesico-renal reflux and dilata- tion of left ureter*	No reflux. I.V.P. normal	12
2	F	8	I.V.P. Dilatation of both pelves and ureters	Normal	18
3	M	3	I.V.P. On left side poor excretion of dye and dilatation of pelvis; dilatation and kinking of ureter	"	3
4	M	8	I.V.P. Dilated left ureter and pelvis; ure- terolithiasis	"	3†
5	M	8	I.V.P. Dilated left ureter	"	9
6	F	7	I.V.P. Delayed excretion of dye and dilatation of right pelvis and ureter. Left side: no excretion. Mic- turition cysto- gram normal	Normal except for indentations of both ureteric walls suggestive of valves in both ureters. Micturi- tion cystogram normal	12

* Cystoscopy on admission showed chronic cystitis with trabeculated bladder without residual urine, left ureteric orifice incompetent. After treatment cystoscopy showed a normal bladder.
† Spontaneous elimination of the stone.

Physiotherapy and remedial gymnastics have become organized professions in Great Britain only within the last 60 years. Details of careers in the professions are given in *The Physiotherapist and the Remedial Gymnast*, a revised illustrated booklet in the "Choice of Careers" series recently issued by the Central Youth Employment Executive. (Prepared by the Ministry of Labour and the Central Office of Information, No. 52, obtainable from H.M.S.O. or book-sellers, price 1s. 3d. net.)