and systemic lupus erythematosus, would have to be considered. Recurrence of myocardial infarction and the onset of pulmonary infarction are other possible causes of confusion, but in our patients there was no difficulty in excluding these conditions. Congestive cardiac failure may reproduce two radiological features of the syndrome—namely, enlargement of the cardiac shadow and pleural effusion—but the syndrome should be suspected and diagnosed on the other more specific manifestations. The electrocardiogram is often unhelpful, since features of pericarditis may be overshadowed by those of extensive myocardial infarction; delay in disappearance of ST shifts was noted in three of our cases.

Aetiology.—The cause of the syndrome is unknown. Dressler (1959) argues that anticoagulant therapy, by causing leakage of blood into the serous cavities, might produce irritant pericarditis and pleuritis; but he notes that 11 patients in his series of 44 did not receive anticoagulants prior to the onset of the complication. Gery, Davies, and Ehrenfeld (1960) have found anti-heart antibodies in the serum of one patient suffering from the syndrome, thus supporting the suggestion of Dressler (1956) that it may be the result of an autoimmune reaction. Probably it should be regarded as a pericardial and pleural reaction to non-specific myocardial damage, and, as such, has the same aetiology as the post-commisurotomy syndrome.

Treatment.—In these days it is probable that most patients developing the syndrome will be receiving anticoagulant therapy. Even if it is agreed that anticoagulants do not cause the syndrome, the question of stopping them still arises because of the risk of precipitating haemorrhagic cardiac tamponade in the presence of pericarditis; Dressler (1959) reports a death from this cause, although it might be noted that the patient also had haemothorax, haemoperitoneum, and red blood cells in the urine, suggesting that there was an excessive bleeding tendency. The risk of precipitating haemorrhagic cardiac tamponade with anticoagulants must be weighed against the risk of recurrent infarction and thrombo-embolic complications without anticoagulants. If the autoimmune hypothesis of aetiology is correct it would clearly be desirable to give steroids. Three of our five patients received prednisolone; two showed a satisfactory response, but in the third prednisolone had to be stopped after seven days because of the onset of congestive cardiac failure. Dressler (1959) reported some success with prednisolone, although relapse was common when the drug was stopped; such a relapse occurred in one of our patients; this suggests suppression rather than elimination of the pathological process. Dressler (1959) also mentions that relief of pain with prednisolone is an important form of symptomatic treatment. As with anticoagulants, the benefit of steroid therapy is uncertain in the post-myocardial-infarction syndrome.

Prognosis.—All five patients eventually made a satisfactory recovery. Dressler (1959) also comments on the good prognosis. If the increased risk of cardiac tamponade is excluded the prognosis becomes that of the original myocardial infarction. The syndrome, however, prolongs the stay of the patient in hospital and increases discomfort during that time.

Summary

The clinical features are described of five patients who developed the post-myocardial-infarction syndrome. It

closely resembles the post-commisurotomy syndrome, and is characterized by continued pericardial friction, prolonged pyrexia, persistently raised E.S.R., and chest pain of pleuro-pericardial type. Less constant features are pericardial effusion and pleurisy with or without effusion.

The post-myocardial-infarction syndrome probably complicates less than 1% of all cases of acute myocardial infarction. Although the prognosis is good, the patient's recovery is delayed for months.

Aetiology and the problems of treatment with anticoagulants and steroids are discussed.

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SEQUELAE OF URINARY INFECTION IN PREGNANCY

A FIVE-YEAR FOLLOW-UP

BY

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Infection of the urinary tract is relatively common during pregnancy and might be expected to lead, in some cases at least, to recurrent urinary infection or chronic pyelonephritis; it thus seemed worth while to review a number of patients five years after an attack of urinary infection during pregnancy to determine how many showed evidence of recurrent infection or chronic pyelonephritis at this time.

Material and Methods

Of 80 consecutive patients with definite evidence of urinary infection in pregnancy, diagnosed and treated in Queen Charlotte's Maternity Hospital at least five years previously, 50 were available for study. The other 30 either could not be traced (19) or were unwilling to come back to hospital for reassessment (11); no details of their present health or the number of deaths, if any, in the group are known. The investigations included: (1) full clinical examination, including blood-pressure readings, protein estimation, microscopy, and culture of the urine; (2) intravenous pyelography; and (3) a modification of the "pyrexal" test described by Pears and Houghton (1959). This was performed in 22 of the patients who had recurrent urinary infection or

showed radiological abnormalities at the follow-up examination. Blood-urea estimations were normal in all cases.

Urinary Infection During Pregnancy.—The infection was most common in the first pregnancy, but the onset of symptoms was more frequently seen in the third trimester than in the second. Most of the patients had clinical evidence of renal infection, more often on the right side than the left; half of them also had symptoms of an infection of the lower urinary tract. Five had no symptoms or signs apart from the urinary findings, but one of these subsequently underwent right nephrectomy for chronic pyelonephritis with hypertension. *Escherichia coli* was the organism found most frequently. Sulphonamides were used more often than any other drug, but eight patients were treated with potassium citrate only. The urine was not always examined after a course of treatment, and patients were sometimes discharged with active urinary infection.

Follow-up

Clinical Findings

The time of occurrence of urinary infections in the 50 patients up to the time of this follow-up examination is shown in Table I. Two had suffered urinary infections in childhood; one of these had undergone removal of an infected hydronephrotic kidney soon after the pregnancy, and the other was still suffering from recurrent attacks of urinary infection; this is in keeping with Woodruff and Everett's (1954) findings that urinary infections in pregnancy followed childhood infections only when these were recurrent or associated with lesions of the urinary tract.

Thirty-nine patients had experienced more than one attack; it would therefore seem that the urinary infection of pregnancy is usually only one episode in a recurrent disease. The first attack occurred before pregnancy in 19 and during pregnancy in 20; this suggests that pregnancy may have initiated the recurrent infection in one-half (20/39) of these cases. Only 11 patients gave a history of a single attack of urinary infection without recurrent or residual symptoms or signs.

While the blood-pressure was higher than would be expected for healthy women of a similar age-group, the significance of this finding is limited because of the small number in the series and of the differences in the method of recording the blood-pressure of the patients and controls.

The findings in catheter specimens of urine at the time of follow-up are shown in Table II. Because the urine was centrifuged before microscopy the presence of scanty leucocytes was ignored. Ten patients had definite urinary infection; only one of these had symptoms at the follow-up examination, but eight gave a history of attacks of recurrent urinary symptoms since

TABLE I.—Time of Occurrence of Urinary Infection in 50 Patients

Single attack during pregnancy	11
Recurrent attacks	39
Attacks began	
{ In childhood	2
{ Before pregnancy	17
{ During	20

TABLE II.—Findings in Catheter Specimens of Urine at Follow-up of 50 Patients

Normal	32
Abnormal	16
Leucocytes + bacteria cultured	10
Leucocytes	4
Bacteria cultured	2
Catheter specimen of urine not obtained	2

the infection in pregnancy five years previously; the final catheter specimen of urine obtained after treatment of the infection at that time had shown leucocytes in three and leucocytes and positive bacterial culture in four of these patients, but no further treatment had been given. In five of the eight the history was suggestive of recurrent renal infection, and these probably have chronic pyelonephritis (Table IV, Cases 2, 3, 4, 6, and 10).

Radiological Investigations

In 43 of the 50 cases "plain film" examination of the whole urinary tract was undertaken, followed by intravenous pyelography, routinely using 20 ml. of 45% sodium diatrizoate ("hypaque"). Seven patients were not examined—two because of a past history of allergy, and five because they failed to attend for the investigation. A careful assessment of the size of the kidneys was made and evidence of parenchymal contracture was especially sought.

Abnormal findings were noted in 19 of the 43 cases (Table III). A radiological diagnosis of chronic pyelonephritis was made in one patient because of overall contracture of the renal parenchyma with persistent irregularities in the margins of the minor calices, which

TABLE III.—Results of Intravenous Pyelography in 19 Abnormal Cases

Chronic pyelonephritis with contracture of parenchyma and slight caliceal dilatation	1
Caliceal, pelvic, and ureteric dilatation	2
dilatation	4
Ureteric	2
Developmental anomaly of ureter	2
Ureterocele (unilateral)	1
Vesical diverticulum	1
Fundal indentation of bladder	9
Total abnormalities	22

Fundal indentation of the bladder and dilatation of the upper renal tract occurred together in three patients.

were slightly dilated, especially in the mid-zone. She gave a history of recurrent infection of the upper urinary tract over the past six years; and urine examination at follow-up showed no bacteria and an increased leucocyte count which the injection of pyrexal did not increase.

When caliceal, pelvic, or ureteric dilatation was reported a persistent dilatation throughout the examination was implied; a transient apparent dilatation was not regarded as pathological.

Of the nine patients with dilatation of some part of the upper urinary tract six had suffered recurrent attacks of urinary infection, including the patient in whom a radiological diagnosis of chronic pyelonephritis was made. A urinary infection at the time of follow-up was found in one of the two patients with caliceal, pelvic, and ureteric dilatation, in both the patients with ureteric dilatation, but in none of the patients with caliceal dilatation alone.

Dilatation of the upper urinary tract in pregnancy is predominantly hormonal in origin, but is also due in part to pressure of the uterus on the ureters; the persistence of this dilatation for long periods after pregnancy cannot be explained by a continuation of either of these factors. It seems probable that infective fibrosis of the walls of the calices, pelvis, or ureter occurs during pregnancy, and this prevents the normal disappearance of the dilatation of these structures. This also would explain the frequency of persistent dilatation of the upper urinary tract (9/43) in patients who had suffered a urinary infection in pregnancy. Although infection

is more likely to persist in an abnormal urinary tract, dilatation of the calices, pelvis, or ureter does not necessarily indicate the presence of a chronic pyelonephritis.

The patient with a vesical diverticulum experienced recurrent attacks of cystitis during and after pregnancy. A small ureterocele was found in one patient who had cystitis before and during pregnancy. It is of interest to note that in another patient investigated after this series had been completed a large unilateral ureterocele was found which contained two calculi.

The fundus of the bladder normally presents a smooth and rounded outline in the intravenous pyelogram of the normal pregnant woman. The degree of convexity of this margin depends on the degree of bladder-filling.

Intravenous pyelogram of a patient delivered five years previously. No lesion is noted in either kidney or ureter, but the bladder shows a deep fundal impress.

Occasionally the uterus makes a shallow impress on the vesical fundus which may be more pronounced when the uterus is anteverted and anteflexed. In nine patients in the present series there was a wide and deep impression of apparently extrinsic origin on the fundus of the bladder (see Fig.) which was much larger than the impress made by a normal non-pregnant uterus. Examination of these patients revealed no pelvic tumour. It was thought that an enlarged uterus must be pressing on the bladder, but bimanual palpation and the passage of a uterine sound showed the uterus to be within normal limits of size or in one case slightly enlarged. The cause of the vesical impress has not been determined. The appearances strongly favour a slight increase in the bulk of the uterus without its cavitory length being increased. At the follow-up, urinary abnormalities were present in six of the nine patients showing this bladder impress, and three of these also had dilatation of the upper urinary tract.

Pyrexal Test

Pears and Houghton (1959) found that the intravenous injection of a bacterial pyrogen, pyrexal, into patients with chronic pyelonephritis increased the urinary cell count; this response may occur in patients with acute pyelonephritis but not in normal patients or in those with non-infective renal disease. The value of this test lies mainly in the detection of chronic renal infection when urine examination is otherwise normal; it was performed on 22 patients with either a history of recurrent urinary infection or of abnormal urinary or radiological findings at the time of follow-up. The method used for this investigation was similar to that described by Pears and Houghton.

The cell counts reported by Pears and Houghton did not differentiate between renal epithelial cells and leucocytes, and did not include squamous epithelial cells or red cells. We have counted all these types of cells separately, and it is apparent that different patients react to pyrexal with different cellular responses.

An increased urinary cellular excretion was found in 12 patients (Table IV), and five of these had a history suggesting recurrent renal infection. Nine had a urinary infection at the time of follow-up, but after treatment only four were still apparently infected when the pyrexal test was performed; this confirms that the urinary cellular response to the injected pyrogen may occur in the absence of obvious urinary infection.

TABLE IV.—Patients With Increased Urinary Cellular Excretion After Injection of Pyrexal

Case No.	History	Catheter Specimen of Urine at 5-Year Follow-up	History of Recurrent Renal Infection	Treatment with Antibiotic (Before Pyrexal Test)	Increase in Urinary Cellular Excretion After Pyrexal	Intravenous Pyelogram
1	Pyelonephritis in 2 pregnancies	Infection	—	+	Leucocytes, epithelial and red blood cells	Bladder dent
2	" during and after 2 pregnancies	"	+	+	" " "	Systolic contraction of normal pelvis
3	" " " " 3rd pregnancy	"	+	+	" " "	Bladder dent
4	" " " " pregnancy	"	+	—	Leucocytes and epithelial cells	No appreciable disease
5	" in 1st pregnancy	"	—	+	" " "	Dilatation right ureter and bladder dent
6	Urinary infection in 1st pregnancy. Symptoms in upper and lower urinary tract since	"	+	+	" " "	Relative stasis in right renal pelvis
7	Urinary infection in 4th pregnancy	"	—	—	" " "	No appreciable disease
8	" " " " 3rd pregnancy Symptoms in lower urinary tract since	Normal	—	—	" " "	Not done. Allergy
9	Pyelonephritis in 1st pregnancy. Recurrent symptoms in lower urinary tract since	Infection	—	+	Leucocytes	No appreciable disease
10	Urinary infection in 3rd pregnancy. Symptoms in upper and lower urinary tract since	"	+	+	"	Bladder dent (Fig. 1)
11	Pyelonephritis in 1st pregnancy	Leucocytes and red blood cells	—	—	"	No appreciable disease
12	Symptoms in in lower urinary tract since	Normal	—	—	"	Bifid type left pelvis and calices

Although Pears and Houghton found an increased urinary cellular excretion after the injection of pyrexal in patients with chronic pyelonephritis, it is possible that a patient with any type of chronic urinary infection—for example, urethritis or cystitis—may respond in this manner. In this series the numbers of renal epithelial cells and leucocytes have been counted separately, for it was thought that if there was an increase in both the renal epithelial cells and the leucocytes after pyrexal the chronic urinary infection would probably be situated in the kidney substance. There was an increase of both these types of cell in eight patients and of leucocytes alone in four; the significance of this is not clear, but in four out of the five patients with chronic pyelonephritis an increase in epithelial cells was found. Ten patients had no significant change in the urinary cellular excretion rate after the injection of pyrexal, and none of these showed any clinical evidence of chronic urinary infection.

Discussion

Clinical examination of the patient is quite unreliable both for diagnosis and for estimating the results of treatment of urinary infection. Of the 10 patients in this series who at follow-up examination had undoubted urinary infection, only one had symptoms or signs attributable to it. A history of recurring episodes of urinary infection was more significant, being obtained on direct questioning in 8 out of the 10 patients.

Repeated examination of the urine for leucocytes and bacteria over a period of time is essential; the risk of causing infection by repeated catheterization can be avoided by using mid-stream instead of catheter specimens of urine. Stansfeld (1954) showed that the average number of leucocytes in the urine of 115 patients with chronic pyelonephritis was only 2–3 per high-power field, and that leucocyte counts of over 50/c.mm.—equivalent to about one in every 5–10 high-power fields—are rarely, if ever, encountered in normal urine. It is probable that only very small numbers of leucocytes in the urine should be regarded as normal; the presence of larger numbers must always be looked upon with suspicion and an attempt made to confirm their presence and determine their origin. Infection of the renal tract is usually associated with large numbers of bacteria in the urine; and although contamination also causes the presence of bacteria in the urine, infection can be distinguished from contamination by estimating the numbers of organisms in fresh specimens of urine, either by direct bacterial counts (Kass, 1957) or by counting the numbers of colonies that grow in culture (Wood *et al.*, 1960). True bacilluria, such as Kass showed to accompany acute pyelonephritis, always gives a very high bacterial count, while accidental contamination is associated with low counts only.

The pyrexal test was positive in 9 out of the 10 cases in which urinary infection was found at follow-up examination, whether or not subsequent treatment had rendered the urine sterile. It would seem that this test is a worth-while aid in the search for latent infections of the urinary tract. It is possible that differential counts of renal epithelial cells and leucocytes may help to locate the infection, high counts of renal epithelial cells suggesting that the kidney is involved.

Radiological studies are of value in revealing the presence of congenital and acquired abnormalities of the urinary tract, some of which are amenable to

surgical treatment. The significance of the deep fundal indentation of the bladder found in nine of our cases is not yet clear.

It is difficult to obtain proof that the treatment of long-standing chronic pyelonephritis alters the course of the disease. Infection often recurs after treatment, and in these patients intrarenal changes and bacterial resistance of antibiotics may limit the effectiveness of treatment. As chronic pyelonephritis may begin in pregnancy, adequate care and follow-up of all pregnant patients with urinary infection may help to diminish the incidence of this disease.

Summary and Conclusions

A study has been made of 50 patients five years after a urinary infection in pregnancy.

Thirty-nine suffered from recurrent urinary infections. In 20 of these pregnancy had apparently initiated the infection.

There were abnormal radiological findings in 19 patients, and their significance is discussed.

Urinary infection was found in 10 of the 50 patients at the time of follow-up. Clinical evidence suggested that five of these were suffering from early chronic pyelonephritis; two others had undergone nephrectomy for unilateral chronic pyelonephritis, making a total of 14% of patients with chronic pyelonephritis in the series.

The pyrexal test was performed in 9 out of the 10 cases with active urinary infection at the follow-up examination, and was positive in them all.

The clinical state of the patient is unreliable in estimating the cure of a urinary infection, which is best determined by the persistent absence of leucocytes and organisms in the urine. The risk of causing infection by repeated catheterization can be avoided by the use of mid-stream urine. Chronic pyelonephritis may begin in pregnancy, and adequate treatment and follow-up of all pregnant patients with urinary infection may help to diminish the incidence of this disease.

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“Rather interesting stories lie behind the selection of some trivial names, as in the case of barbituric acid. This was the discovery of the chemist, Baeyer, who came upon the new compound as a combination of maleic acid with a breakdown product of uric acid. He wrote later that he was enamoured at the moment of a charming lady named Barbara, and so he decided to call the new compound “barbituric acid” in her honour. The story does not end there, for later the physician von Mehring took a trip to Italy shortly after discovering the hypnotic properties of diethylbarbituric acid, and, as he approached the city of Verona, he was struck with the idea of naming this compound Veronal.” (Dr. LLOYD C. MILLER, Ph.D. (director of revision, *U.S. Pharmacopeia*), “Doctors, Drugs, and Names.” *J.A.M.A.*, July 8, 1961.)