azotaemia with intermittent use of SKF 8542 suggests there is some reversible effect on renal blood-flow.

The diuretic response to the combination of SKF 8542 and chlorothiazide is excellent and all patients lost their ascites. The drug was active within a few hours of administration, and, unlike spironolactone, need not be given on consecutive days to obtain a diuretic response. In no patient could the administration of SKF 8542 be related directly to the production of hepatic precoma or coma. The maximal effective dose was between 150 and 200 mg. daily, given in two doses daily. Long-term follow-up of four patients showed only one patient who reaccumulated ascites while on combined SKF 8542 and chlorothiazide therapy. There have been no toxic effects with 14 months' continuous use of the drug.

SKF 8542 is an effective diuretic in patients with cirrhosis and intractable ascites, particularly when given in combination with a proximal tubular diuretic of the thiazide series. The similarity to spironolactone suggests a distal tubular site of action through a mechanism not dependent upon the blockade of aldosterone.

Summary

The effect of triamterene (SKF 8542), a new pteridine diuretic, alone and in combination with chlorothiazide has been assessed in 10 patients with ascites due to cirrhosis of the liver. When given alone SKF 8542 produced only a small sodium diuresis without clinical alteration of the ascites. However, when combined with chlorothiazide the previous diuretic resistance to both diuretics individually was abolished and a satisfactory control of ascites was achieved in all cases.

The similarity of action to spironolactone suggests it acts on the distal renal tube, although potassium depletion did occur and supplements were necessary when the drug was combined with chlorothiazide. SKF 8542 significantly increased the sodium diuresis in four patients already receiving spironolactone and chlorothiazide. This observation confirmed previous suggestions that SKF 8542 produces a sodium diuresis independently of an antagonism of aldosterone.

Glomerular filtration rates were reduced by an average of 30% during continuous combined diuretic therapy with SKF 8542 and chlorothiazide, but reverted to control levels when intermittent therapy was given. No direct evidence of nephrotoxicity was found. Two patients have been maintained for 14 months on intermittent SKF 8542 and chlorothiazide without adverse side-effects.

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RHEUMATIC HEART DISEASE COMPLICATING PREGNANCY

THE REMOTE PROSPECTS

BY

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The purpose of this communication is to consider the remote effects of child-bearing on women afflicted by rheumatic heart disease.

A prospective study of rheumatic heart disease complicating pregnancy was begun in the National Maternity Hospital on January 1, 1948. During the following eight years 539 pregnancies were observed in 385 women. Distinctive features of the series were the high parity of the mothers and the fact that therapeutic abortion was never performed. This combination of circumstances provided an unusual opportunity to observe the effects of child-bearing on the course of the disease and at the same time to assess, albeit in a negative sense, the value of therapeutic abortion.

Immediate Results

The immediate results have been published (Drury *et al.*, 1954; O'Driscoll *et al.*, 1957). Some points relevant to the present context are worthy of reiteration. Deaths that occurred during pregnancy or within an arbitrary period of one year of confinement were regarded as having been related to pregnancy. There was no such death in 475 booked cases and 7 deaths in 64 unbooked cases. Not one of the 7 women who died had been seen at the hospital previous to admission in heart failure. At that time the period of gestation was 16 weeks or more in every case (Table 1). The mothers were notable for their comparative youth and low parity. The woman with 10 children died from rupture of a classical caesarean section scar several weeks before term.

TABLE 1.—Details of Seven Fatal Cases

	23	24	25	27	28	37	39
Age	1	1	1	2	1	3	10
Gravida	1	1	1	2	1	3	10
Gestation in weeks on admission	30	16	31	32	30	20	30

The conclusions were that adequate care can virtually eliminate maternal deaths from this disease, and that therapeutic abortion is a dangerous substitute for adequate care.

Remote Results

Whether repeated child-bearing and the consequent stress of caring for a young family would materially affect the remote prospects of these mothers remained in doubt. In order to answer this question a follow-up of the 378 women who survived delivery by more than a year was undertaken in January, 1961. All had then been delivered between 5 and 13 years previously. Of the 378 women, 356 (94.2%) were traced, 16 (4.2%) had emigrated, and 6 (1.6%) were untraced. The emigrants went to Britain (12), U.S.A. (3), and Canada (1). On

hearsay evidence all are alive but we have been unable to contact them. No recent information could be elicited in respect of the six untraced women, nor could they be identified among the registered deaths in Ireland.

Of the 356 women traced, 308 (86.5%) were living. Their average age was 40.7 years, and their average parity, viable infants only, was 4.7. The other 48 (13.5%) women had died. Their average age at death was 38.3 years (Table II), their average parity was 5, and the average period by which they survived the last reported pregnancy was 5.3 years.

TABLE II.—Age at Death

Age in years	25-29	30-34	35-39	40-44	45-49	55
No. of deaths	5	11	11	10	10	1

In four cases death was due to coincident disease—namely, cancer of parotid gland, rupture of pulmonary angioma, pulmonary tuberculosis, and hypertension with cerebral haemorrhage. Forty women died from causes related to heart disease—namely, heart failure (25), embolism (12), post-operative valvotomy (2), and sub-acute bacterial endocarditis (1). The cause of death was not clearly recorded in four cases.

During the last reported pregnancy the effort intolerance in 245 women was classified as grades I and II, and in 111 as grades III and IV. In the first group there were 15 (6%) deaths, three from coincident disease. In the second group there were 33 (30%) deaths, one from coincident disease, and in four the cause was not clearly recorded.

Discussion

The seven women who died during pregnancy or within a year of delivery were comparatively young and of low parity. Since all were emergency admissions in heart failure after the sixteenth week of gestation, none was suitable for therapeutic abortion. If this procedure had been employed in the series it would inevitably have been on the mothers who in the event survived. Its use might have resulted in additional fatalities. One of us has elsewhere seen three deaths caused by this operation. Fitzgerald *et al.* (1951) in a series of 460 cases at Cook County Hospital lost only three mothers, each after therapeutic abortion. Morgan Jones (1951) in a series of 352, recorded eight deaths due to heart disease and two following termination of pregnancy. C. Bramwell, in his foreword to Morgan Jones's book, referring to the improved results in Manchester, stated: "This is probably partly attributable to the fact that, as our knowledge of the subject increased, we became more and more reluctant to interfere with the normal course of pregnancy." Yet rheumatic heart disease continues to figure as a main indication for therapeutic abortion.

After an interval of between 5 and 13 years 308 women were still living at an average age of over 40 years in spite of the fact that they had borne an average of almost five children. The average age of the women who had died was a little less and their families were of similar size. These figures show that women with rheumatic heart disease can have several children without reducing their life-span. Jensen in 1938 (quoted by Gorenberg and Chesley, 1953) stated that it could not be shown that pregnancy alters the course of rheumatic heart disease. Boyer and Nadas (1944) were unable to demonstrate any effect of parity upon the age at death

in this disease. Bunim and Appel (1950) concluded that there was no difference in the age at death between parous and nulliparous women observed at the clinics of the New York Heart Association. Morgan Jones (1951) wrote: "There is still no evidence that, in the majority of cases, pregnancy leads to more than a temporary deterioration in the cardiac condition or that repeated pregnancies appreciably shorten life. In the present state of our knowledge, there is, therefore, no justification for discouraging pregnancy in these cases on the ground that, if the patient survived, life may be shortened." Gorenberg and Chesley (1958) decided that there is nothing to suggest that the heart is damaged by child-bearing or that the course of rheumatic heart disease is accelerated. Yet women often receive dire warning against bearing more than an arbitrary number of children and are sometimes sterilized to ensure this.

Rheumatic heart disease is one of the major causes of maternal mortality in the British Isles. This situation will continue until it is realized that the correct approach to the problem lies in adequate medical care and not in interruption of pregnancy. In this regard we agree with Gorenberg and Chesley, writing of America, that "there is a dichotomy between what can be done and what often happens."

Summary and Conclusions

During a period of eight years (1948-56) 385 mothers with rheumatic heart disease were observed in the course of 539 pregnancies. Seven died during pregnancy or within one year of delivery. Their average age was 29 years and four were primigravidae. A follow-up of the 378 survivors was undertaken five years later (1961). During the interval 48 had died. The average age at death was 38.3 years and the average parity was 5. The average age of the 308 who were still living was 40.7 years and the average parity 4.7. Of the 22 who were untraced, 16 are known to have emigrated.

It is concluded (1) that early diagnosis and adequate supervision can virtually eliminate the immediate hazards of pregnancy in cases of rheumatic heart disease; (2) that if a mother survives the immediate hazards her expectancy of life is not materially altered; and (3) that therapeutic abortion contributes to neither the immediate nor the remote welfare of mothers suffering from this disease.

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