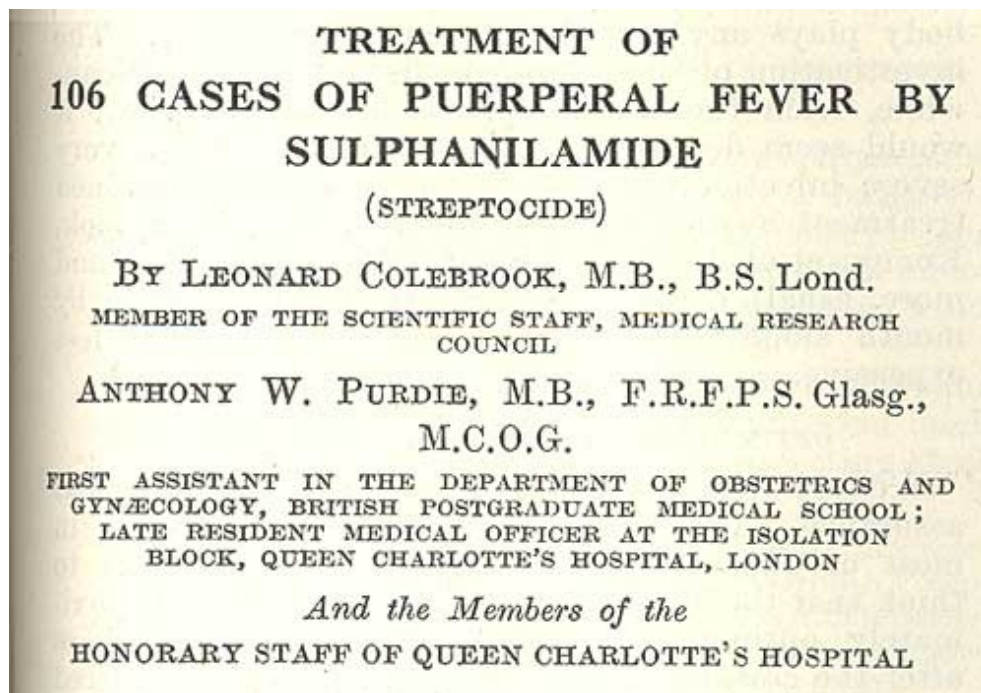


Colebrook L, Purdie AW (1937). Treatment of 106 cases of puerperal fever by sulphanilamide. *Lancet* 2:1237-1242 & 1291-1294.

Key passages

IS THE HIGH RECOVERY-RATE DUE TO CHEMOTHERAPEUSIS ?

How far are we justified in attributing the high recovery-rate in this series of cases (and in the series previously treated by sulphamido-chrysoidine and P.S.) to the chemotherapeutic agents employed ? Although this question was discussed at some length in our report dealing with the red dyes (1936b) its importance justifies some further comment.

Our experience of puerperal infections by the hæmolytic streptococcus at Queen Charlotte's during the past seven years—comprising some 700 cases, investigated more fully, we believe, than any previous series of cases—leaves no room for doubt that the clinical results observed since the beginning of 1936 have been very much better than those obtained before that time. The improvement has shown itself in the greatly diminished death-rate, in the more rapid decline of pyrexia, and in the much lower incidence of parametritis and pelvic cellulitis. The beginning of this period of improved results coincided with the introduction of the new remedies. But there is also some evidence—not conclusive, we think—that the puerperal infections by hæmolytic streptococci have been on the average a little less severe during the same period. As Gibberd (1937) expressed it there has been somewhat less tendency for the infections to assume an "invasive character"—i.e., to extend beyond the genital tract tissues by the blood stream or the general peritoneal cavity. In Gibberd's opinion it was almost impossible, in view of this diminished invasiveness of the streptococcus, to arrive at any decision as to the parts played respectively by that fortuitous change in the disease process and by the new chemotherapeutic remedies. That conclusion seemed to us so important that we re-examined our data from a new angle—determining the mortality-rates among all the cases in which there was unmistakable evidence of "invasiveness." Such evidence was considered to be present in cases having hæmolytic streptococci in the blood stream (positive blood culture)—with or without signs of generalised peritonitis in addition. We do not contend that the segregation of "invasive cases" by this

criterion gives us data entirely satisfactory for statistical analysis, but they seem to us good enough for the detection of big effects—and probably the best that we can obtain from human puerperal fever. The figures and mortality-rates (for which we are indebted to our colleague R. M. Fry) are shown in Table III. It will be seen that among the 22 septicæmic cases treated by the red dyes and sulphamido-

Some cases treated by the red dyes and sulphamamide, although they were "invasive cases," the death-rate has been very much lower than among the cases in the same category observed during the years 1932-35. This suggests, we think, that the reduction in case-mortality (among these cases at any rate) has been effected more by the treatment employed than by lack of invasiveness of the streptococci.

We would submit, further, that if it cannot be stated *with certainty* at present that the drugs in question have played an important part in the control of the infection in our puerperal cases, we are nevertheless justified in regarding that conclusion as *highly probable* if we take into account not only the clinical data here presented but also certain collateral evidence. The collateral evidence we have in mind is of three kinds:—

(1) The fact—now demonstrated in many laboratories all over the world—that these drugs, sulphamido-chrysoidine, P.S., and sulphamamide, are certainly able to control experimental infections by hæmolytic streptococci in laboratory animals—viz., mice, rats, and rabbits—not only when given at the same time and by the same route as the infecting streptococci but when given by a

TABLE III

DEATH-RATE FOR ALL BLOOD-POSITIVE CASES (HÆMOLYTIC STREPTOCOCCI) WITH OR WITHOUT GENERALISED PERITONITIS

Year.	Cases.	Deaths.	Death-rate (per cent.).
1932	14	13	93
1933	24	18	75
1934	26	15	58
1935	18	12	67
Totals	82	58	Aver. 71
1936 and first* quarter of 1937 (Prontosil and sulphamamide treatment) ..	22	6	27.3

* The cases for 1936 and first quarter of 1937 only were chosen because Gibberd's analysis (1937) had dealt with that period.

different route (including the oral) and after an interval of some hours.

(2) The fact that a curative effect in human beings has been demonstrated beyond all reasonable doubt in two distinct classes of infection by hæmolytic streptococci: (a) in acute meningitis (proven by culture from the cerebrospinal fluid); and (b) in certain extremely chronic infections of subcutaneous tissue and of bone which had previously proved resistant to all therapeutic measures. The evidence with regard to meningitis is that whereas before the introduction of sulphamido-chrysoidine recovery was a rare

event—Gray (1935) has computed it at 3 per cent. ; he was able to find only 66 recoveries in all the literature since 1901—there have been no less than 26 recoveries reported during the past few months. ^{27 30 1 16 21 13 23 7 26 19 20 2 3 24} Another case in the care of L. N. Silverthorne of Toronto was seen by one of us (L. C.) but has not yet been reported. The evidence with regard to chronic infections consists only of a few isolated cases, but in these the immediate response to treatment by sulphanilamide after years of suppuration was so dramatic that it was almost

impossible to resist the conclusion that the drug was directly responsible for their recovery.

These cases comprise the one already reported by us (Purdie and Fry 1937) of chronic infection of the skin and subcutaneous tissues which had refused to heal for three years following puerperal sepsis but healed completely within six weeks under treatment by sulphanilamide; and another case of very extensive suppuration (not puerperal in origin) involving cellular and bony tissues of the pelvis, with many sinuses which had persisted for several years. One of us (L. C.) was privileged to see this case in New York by the courtesy of Dr. Hugh Auchinloss, but it has not yet been reported. The patient's rapid recovery under treatment by sulphanilamide was very remarkable; and it is perhaps worthy of note that the chronicity of the lesions did not interfere with the curative influence of the drug.

(3) The fact that the blood of patients under treatment by sulphanilamide (and to a smaller extent by the red dyes) acquires a very greatly enhanced power of killing hæmolytic streptococci, even when these are of high mouse virulence. This observation, first reported by one of us (L. C.) with Buttle and O'Meara (1936), has since been confirmed many times by our colleague E. D. Hoare. Although we do not know that this greatly increased capacity to kill the streptococci is a sine qua non for the checking of the infective process there can be little doubt that, when present, it must assist the checking.

To sum up, while we admit that a diminished severity of the infective process may have been in part responsible for the satisfactory results observed in these 100 cases, there seems to us very little doubt that the treatment by sulphanilamide has also played an important part. To make an even approximate estimate of the proportionate influence of these two factors would be worthless. There is, in our view, abundant support for the continued use of sulphanilamide or sulphamido-chrysoidine and P.S. in puerperal infections by hæmolytic streptococci, but not for their use in similar infections due to other organisms (apart from the *B. coli* infections of the urinary tract). In order to avoid the prolonged administration of these drugs to unsuitable cases, with risk of toxic effects, we would again urge the importance of a bacteriological examination of a vaginal swab taken as early as possible from every case of puerperal pyrexia.