SEX AS A FACTOR IN THE PROGNOSIS OF HODGKIN'S DISEASE

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Physicians have long recognized that malignant lymphogranulomatosis, or Hodgkin's disease, occurs but one-third as frequently in women as it does in men. In the course of a previous study (1) it was noted that not only was this condition less common but that it also appeared to be less malignant in the female sex. As this was merely an impression, however, the literature was reviewed for statistical evidence bearing on this point.

Gemmell (2) in 1923 was impressed by the fact that Hodgkin's disease occurs less frequently in women but did not realize that its severity is also lessened. He studied 57 cases in females, gathered from the literature and from his own experience, and pointed out that the patients usually showed varying degrees of oligomenorrhea up to complete amenorrhea. Of 10 parous patients, 6 dated the onset of their disease from a pregnancy. In approximately half of the series the disease was first observed during a period of physiological amenorrhea—in 10 cases before puberty, in 8 after the menopause, in 5 during pregnancy, and in 2 during lactation. Gemmell recorded post-mortem studies on four patients, one of whom showed marked atrophy of the genital organs despite the fact that she was but thirty-one years of age. Others have reported similar cases, as exemplified by the twenty-two-year-old patient described by McAlpin and Von Glahn (3). As a result of his studies, Gemmell postulated that ovarian function furnishes a relative protection against the inroads of Hodgkin's disease.

STATISTICAL INVESTIGATION

For the present study, 204 cases of Hodgkin's disease occurring in women were collected from the abundant literature on this subject. To secure a comparable series in men, 180 cases were tabulated from the same sources. In this way it was possible to rule out the effect of variations in therapy on the prognosis and course of the disease, as the patients in each series received approximately the same treatment. Five hundred recorded cases were briefly reviewed for sex incidence and it was found that Hodgkin's disease occurs three times as often in men as in women, which confirms other published statistics.

The average survival period in 63 fatal cases in women was found to be 3.4 years, reckoning from the onset of the disease to the death of the patient. This figure was reached despite the inclusion of 6 cases in children less than ten years old, an age at which the patients were physically but not physiologically females. Four (66.6 per cent) of these young patients died in less than nine months, which obviously lowered the survival period for the entire group. In comparison, the average duration of the disease in 104 males dying of lymphogranulomatosis was 2.3 years, indicating that the woman with Hodg-
Hodgkin's disease survives, on the average, one and one-half times as long as the man with the same disease.

Most authors have recognized the fact that persons with Hodgkin's disease may live from ten to twenty-five years even without therapy. It was deemed of interest, therefore, to investigate so-called "longevity" in this condition. Fig. 1 graphically portrays the findings for this phase of the study.

More than three-quarters of the women live more than three years after the appearance of the disease; over one-half survive more than five years and nearly one-fifth are still living after ten years. The figures for men are very much lower for each group. In fact, the proportion of women living more than five years is greater than of men living three years, and the number of women surviving over ten years is nearly twice that of men surviving over five years.

Figs. 2 and 3 are closely related and may be discussed together. Fig. 3 shows the age of onset of Hodgkin's disease in males and females. The significant finding here is the absence of any appreciable difference between the two sexes. Most of the cases appear between the second and fourth decades of life. Fig. 2 shows the number of patients of each sex in each age group dying in less than three years. In men the figure is approximately 25 per cent for the first three decades of life; it rises abruptly to twice this during the next twenty years, and is erratic from then on. In women quite a different situation exists. During the first ten years of life, when the female physiology
most closely resembles that of the male, 37.5 per cent of the patients die in less than three years. The mortality then slowly decreases to about 8 per cent between thirty and fifty years and again ascends as sexual activity decreases. The fact that 92 per cent of the women developing Hodgkin's disease between the ages of thirty and fifty years will live for more than three years is seldom recognized.

![Graph showing percentages of patients of each sex in each age group dying of Hodgkin's disease in less than three years after onset.]

**FIG. 2. PERCENTAGE OF PATIENTS OF EACH SEX IN EACH AGE GROUP DYING OF HODGKIN'S DISEASE IN LESS THAN THREE YEARS AFTER ONSET**

![Graph showing age of onset of Hodgkin's disease in males and females.]

**FIG. 3. AGE OF ONSET OF HODGKIN'S DISEASE IN MALES AND FEMALES**

**COMMENT**

These findings suggest that women have some protection against Hodgkin's disease and that this is in some way associated with adult female physiological activity. The marked difference in the average survival period between the two sexes, the greater “longevity” in women, and the low three-year mortality during the period of greatest physiological activity all offer support to this assumption.
Women differ from men in two major functions—menstruation and gestation. It is tempting to theorize that these activities have an important bearing on the more favorable prognosis in the female sex, though no substantial proof can be offered at this time that these are the only factors involved.

Gemmell, as stated previously, felt that the ovary played an essential rôle, but this would hardly explain the long survival periods enjoyed by some men, as, for example, the patient of Wile and Stiles (4), who lived eighteen years. Desjardins (5) treated one patient, who developed lymphogranulomatosis after the menopause, with ovarian extract but failed to arrest the process. Gemmell's finding of oligomenorrhea and amenorrhea in women with Hodgkin's disease is of little importance, as many chronic wasting diseases are accompanied by such symptoms.

During both menstruation and pregnancy the other endocrine glands are also in a state of hyperactivity and this may have some bearing on the problem. Furthermore, the human economy is very complex and even functional differences that are in no way related to the endocrine system may afford a protective factor in women.

The fact that these findings do not apply to lymphosarcoma is another link in the chain of evidence that these two conditions are separate entities.

CONCLUSION

Hodgkin's disease is not only less frequent but also less malignant in women than in men. That glandular activity exerts a restraining influence on the condition in women can only be suggested.

BIBLIOGRAPHY