Where the prognosis is poor, the opportunity for observation of various characteristics is correspondingly limited. Furthermore, the node-free groups are small (Table XIII). It suffices to say, therefore, that the respective rates of 22% for males and 16% for females in nasopharynx and oropharynx cases, and 24% for males and 13% for females in hypopharynx and post-cricoid cases, follow the same trend as was observed for cervical invasion before treatment. The fact that these rates are so much lower than the comparable ones shown for the tongue and mouth cases is attributable to the shorter average duration of life. In the event of any future development of more effective methods of controlling the primary lesion they could not be regarded as an authentic estimate of potential lymph node involvement.

Discussion

Summarizing the findings, then, it would seem that in the treatment of cancer of the tongue, mouth, and pharynx female patients may be expected to respond much better than males and to resist lymphatic spread more successfully. In none of the aspects investigated—namely, long-term survival, incidence of post-operative mortality, primary recurrence, secondary lymph nodes before and after treatment of the primary lesion—has any evidence against this thesis emerged.

The fact that such sex differences in prognosis are demonstrable makes it obvious that, in the presentation of the results of treatment, omission of the sex and age distribution may well affect the deductions to be made from survival rates. Failure to keep this in mind may conceivably be the cause of some misinterpretation, since, in making comparisons, a higher survival rate attributed to improved technique may be due merely to differences in the sex ratio in the sample.

Furthermore, the need for the incorporation of an age-factor correction cannot be too strongly emphasized, particularly in countries where there is a rapidly increasing proportion of old people in the population. The consequent rising proportion of deaths from intercurrent diseases invalidates the crude mortality rate for purposes of treatment evaluation.

Revelation of differences in behaviour inevitably arouses speculation regarding the causes. Three obvious lines of inquiry seemed to be: (a) the possible effect of oestrogen changes; (b) the comparative incidence of syphilis; and (c) the respective standards of oral hygiene. Analysis of the results on a pre- and post-menopausal basis failed to reveal any real difference. The cases in which a Wassermann test had been made were invalidated for statistical purposes by the policy of clinical selection. Investigation of dental sepsis could not be undertaken in a survey of retrospective character, but there is a strong suggestion from various sources that the standard of oral hygiene is appreciably higher in women than in men.

It may be that investigation of possible local influences would yield only a partial solution, and that the differences now demonstrated are merely a cogent example of the fact that the female, although lacking equal physical strength, is nevertheless fundamentally possessed of greater stamina than the male. In a comparison of male and female mortality trends, Martin (1951) showed that the disadvantage experienced by males has been increasingly enhanced during the past few decades. An analogy is to be found in various other species in which there is an excess mortality of males over females.

Despite the fascination of speculation, the initial function of the statistician is to indicate where such sex differences in prognosis exist, in the hope that medical research workers from other fields may be induced to explore some of the by-ways.

Summary

Three groups of cancer cases—673 in the tongue, 916 in the buccal cavity, and 550 in the pharynx—treated by radium or deep x rays at the Christie Hospital and

Holt Radium Institute, Manchester, during the years 1932 to 1942 inclusive are analysed separately by sex ten years after treatment, for the purpose of demonstrating a marked difference in prognosis.

Survival rates are given in terms of the whole group irrespective of the degree of clinical involvement at the time of treatment, and also in relation to the presence or absence of extension of the disease to cervical lymph nodes. Relevant factors, including post-operative mortality, incidence of recurrence, and incidence of cervical lymph nodes before and after treatment of the primary lesions are investigated.

In all the directions explored the same trend emerges in support of the thesis that a much better response to treatment is manifest in women than in men. Women are also less prone to develop metastases. Some possible influences are considered.

The opinion is expressed, that, in the presentation of the results of treatment of malignant disease, failure to state the sex and age distribution may result in fallacious deductions when comparisons are being made between different series of cases. Attention is also directed to the inadequacy of the crude survival rate for purposes of long-term evaluation, and the necessity for incorporating an age-factor correction is emphasized.

I am indebted to Dr. Ralston Paterson, from whose criticism of my original draft I derived much benefit; to Dr. Edith Paterson for helpful suggestions; to Professor Victor Lambert for useful advice; and to my assistants in the medical statistics department for their aid with the analyses, graphs, and typing of the paper. I wish to record, too, my appreciation of the encouragement and courageous interest of the late Dr. Margaret C. Tod during her terminal illness.

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CANCER OF UTERUS: RELATIVE INCIDENCE OF TYPES

BY

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Carcinomas of the uterus are commonly divided into three groups: (1) epidermoid carcinoma of the cervix; (2) adenocarcinoma of the cervix; and (3) endometrial carcinoma of the "body." The first and third groups together account for over 90% of uterine carcinomas.

Cases under Review

During the past four years 1,612 uterine specimens have been examined in this hospital. These were composed of endometrial curettings, 1,135; uteri, 286; and cervical biopsies, 191. During this period carcinoma of the body has been diagnosed in 34 cases, epidermoid carcinoma of the cervix in five cases, and adenocarcinoma of the cervix in one case.

The age distribution of the cases of adenocarcinoma of the endometrium is shown in the Table. The mean age

was 55 years. The marital status was 26 married and 9 single. The age distribution of the cases of epidermoid carcinoma of the cervix is also shown in the Table. The mean age was 45 years. Three were married and two were single.

Age Distribution of 34 Cases of Adenocarcinoma of the Endometrium and Five Cases of Epidermoid Carcinoma of the Cervix

	31-	36-	41-	46-	51-	56-	61-	66-	71-	76-80
Adeno-carcinoma		3	2	3	13	4	3	3	2	1
Epidermoid carcinoma	1		2		1	1				

The relative incidence of cases of carcinoma of the body and the cervix is 7:1. This ratio is so different from the textbook figures that the following points must be noted.

Firstly, the patients are drawn from a selected portion of the community, as this hospital deals almost entirely with the upper- and middle-income groups of Cork City and surrounding country. Secondly, the cases considered to be carcinoma of the endometrium are only those showing frank histological evidence of carcinomatous change; any case showing only atypical hyperplasia was excluded. The fact that the cases were collected over a period of four years would seem to exclude any chance selection in a short period. It would also exclude, to a large extent, the possibility of a number of cases of carcinoma of the cervix having been "missed." To bring the figures to accepted proportions over a hundred cases of cervical carcinoma would have had to escape notice, and, so far as we are aware, no patient in this series who was not diagnosed as carcinoma of the cervix has returned with this condition. Lastly, the age distribution and mean age of both groups are typical. It would thus seem reasonably certain that in this series there is an actual and well-marked reversal of the usually accepted frequency of carcinoma of the body and of the cervix.

To determine whether the atypical distribution was due to an increase in the number of cases of endometrial carcinoma or to a decrease in cases of cervical carcinoma a comparison was made with the figures of the Dublin maternity hospitals (*Irish Journal of Medical Science*, 1949, 1950, 1951). The incidence of endometrial carcinoma occurring per hundred operative gynaecological cases in the Dublin maternity hospitals was compared with that occurring in this hospital, and was found to be very similar. This fact indicates that the variation in our figures is due to an absolute decrease in the number of cases of epidermoid carcinoma of the cervix.

The Dublin reports also show that their relative incidence of the two types of uterine carcinoma is that generally accepted—that is, a preponderance of cervical carcinoma.

Discussion

Figures quoted for the relative incidence of the different types of uterine carcinoma vary, "but broadly it may be said that cervical carcinoma is three or four times as common as endometrial, and that cervical epidermoid carcinoma is at least ten times as common as cervical adenocarcinoma" (Willis, 1948). Novak (1952) gives the proportion as one endometrial carcinoma to eight cervical carcinomas.

It is becoming generally acknowledged that uterine carcinoma has socio-economic and racial distinctions. Stock (1947) has shown uterine carcinoma to be more common among the lower social class in England. He does not, however, distinguish between carcinoma of the endometrium and cervix. Clemmesen and Nielsen (1951) bring evidence to show that cervical carcinoma is more common in the lower socio-economic group, and that its incidence in rural areas approximates to the wealthier areas in the towns. The opinion that cervical carcinoma is more frequent in

the lower-income group is also expressed by Lombard and Potter (1950). They state that "in a sample obtained from a gynaecologist who permitted a study of the records of his wealthy patients . . . the sample was small . . . owing to the fact that only a very small percentage of his private patients had carcinoma of the cervix." Again, Hall *et al.* (1950) found that, while the usual accepted relative incidence of the types of uterine cancer was valid for ward cases, in their private patients endometrial carcinoma was more frequent in the ratio 2:1. Corscaden and Gusberg (1947) also noted that in the private-patient group carcinoma of the endometrium was more common than carcinoma of the cervix.

While showing a much higher proportion than in any of the series quoted, our figures do agree in demonstrating that the usually accepted relative incidence of carcinoma of the endometrium to the cervix does not hold good for all sections of the community. They can also be used to show that in the socio-economic group concerned the disproportion observed is due to an absolute decrease in cases of cervical carcinoma rather than to an increase in endometrial carcinoma.

From the findings of the authors quoted and from our admittedly small group of cases it seems that one definite fact arises—that cancer of the cervix is more common in the lower socio-economic group. Our figures can do little more than suggest that the incidence of endometrial carcinoma may be much the same in all groups.

The reason for this low incidence of cervical carcinoma is obscure. Lombard and Potter (1950) list five factors which they claim have definite significance in the development of cervical carcinoma: marriage before the age of 20 years, unrepaired lacerations, last child born to women before the age of 25 years, syphilis, and individuals divorced or separated at any time. We considered these factors in relation to the class of patient dealt with in this hospital, and it was found, from a sample of married women, that the average age of marriage was 27 years; thus two factors—marriage before the age of 20 years and the last child born before 25 years—do not apply. Divorce and separation are exceptionally rare, as is syphilis. Of all these factors it is only unrepaired laceration of the cervix which might operate.

The relationship of cervical lacerations to cervical carcinoma is still undecided. An interesting contribution in this field is that of Gagnon (1950). This author investigated the medical histories of a large number of nuns, "women whose social state and mode of life protect them from the usual causes of cervicitis or chronic irritative lesions." He found that the ratio of endometrial carcinoma to that of cervical cancer was 6:1, and uses this fact among others to indite cervical lacerations as a factor in cervical carcinoma. In the discussion following this paper, McKelvey objected that the recognized low incidence of cervical carcinoma in the Jewish race still remained to be explained. Weiner *et al.* (1951) indicated that cervical carcinoma in Jewish women is becoming more common, and suggest that the Mosaic laws, which would tend to lessen the incidence of chronic cervicitis, are not now observed as rigidly as formerly. They, however, quote Davidsohn as believing that the difference in incidence of cervical carcinoma may be due to the practice of circumcision, a theory which is supported by the demonstration of the carcinogenic action of smegma.

Ovarian oestrogens have been suspected as a factor in carcinogenesis, and genuine carcinoma of the cervix has been produced in mice by Gardener, Li, and others (Novak, 1951). Ayre (1947) suggests that cervical carcinoma may be due to an abnormal response to cervical infection associated with excessive oestrogen, the latter being due to failure of a liver damaged by vitamin deficiency to inactivate oestrogen. Of interest in this connexion is the fact that Brunelli (1935) showed that in rabbits oestrogen in the blood becomes concentrated and fixed in inflamed tissues. Ayre's suggestions are criticized by Greene and Peckham (1947),

who point out that the previously accepted fact that vitamin-B deficiency, as such, decreases the inactivation of oestrogens by the liver has been shown to be untenable. Drill and Pfeiffer (1946) have shown that "the effect of acute vitamin-B-complex deficiency in producing a failure of the liver to inactivate oestrone seems to be due to the concomitant inanition."

If we may assume that cervical carcinoma is comparatively infrequent in the better-nourished members of a community, then there must be some factor or factors which lessen its occurrence in this group. Alternatively, in the undernourished group there must be some factor or factors which tend to cause this lesion. As cancer is an active condition it would seem more logical to suppose that poor economic conditions in some way produce this disease. Our present knowledge would suggest that cervical carcinoma may be produced in the poorer economic class by some unknown hormonal imbalance or by an unsatisfactory reaction, associated with poverty, to irritative lesions of the cervix.

Summary

Figures are given for the relative incidence of endometrial and cervical carcinoma as seen in a selected population.

These figures are at variance with the incidence usually accepted, and it is suggested that the incidence of the various forms of uterine cancer vary with the socio-economic group.

The possible implications of these findings are briefly discussed.

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The National Research Development Corporation exists primarily to develop and exploit in the public interest inventions (including medical ones) resulting from public research. It also has other powers. In June this year the Corporation's borrowing powers come to an end, and if the Corporation is to continue its normal activities new legislation will be necessary. The chance is therefore taken in the annual report for 1952-3, published recently, to review the results of the Corporation's first four years of trading. Starting in 1950 with costs of a little over £20,000 and a return by way of royalties of less than 1%, by 1953 the accounts showed 23% earnings on operating costs of £120,000. Several of the inventions being developed by the Corporation have a direct bearing on medicine. The pilot scale production of hecogenin from sisal juice in East Africa provides a starting material for the synthesis of cortisone. Prototypes of the Burns analgesic inhaler, designed for trileone and other volatile analgesics, have been prepared for clinical trial. The Corporation has underwritten the costs of the initial manufacture of an aural microscope and chick sexer. Other projects range from large electronic digital computers ("electronic brains") to a new machine for liquefying atmospheric gases.

DIABETES INSIPIDUS ASSOCIATED WITH PULMONARY DISEASE

BY

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Spillane (1952) described four cases in which diabetes insipidus was associated with pulmonary disease. The case here reported falls into the same category and exhibits diabetes insipidus and lung lesions as the only discoverable abnormalities.

Case Report

A housewife aged 57 was first seen in January, 1952, having been referred for further investigation after attending a mass x-ray session. She had suffered from increasing dyspnoea on exertion for about four years, with morning cough and the expectoration of a small amount of yellowish sputum. For several years she had passed large amounts of pale urine at frequent intervals during the day and night. She was also troubled by excessive thirst and said that she could drink a pint of soda-water at a time and still be thirsty. Her sleep rhythm was unchanged and there was no somnolence by day.

Before her present illness she had been healthy and had when younger often cycled 50 miles (80 km.) a day without distress. Until seven years previously she had worked as a waitress in addition to looking after her home, but she had had to discontinue this in order to look after her husband, who was becoming severely disabled owing to post-encephalitic Parkinsonism. She had had pneumonia on three occasions, at the ages of 23, 29, and 37; erysipelas at 14; and scarlet fever in childhood. There was no history of skin disease.

She was the second oldest of a family of 13 of whom five of six brothers had died in infancy, the other being killed in adult life. Of her six sisters, five were healthy and one had died 48 years previously, the cause of death being unknown. The patient had had two children, both of whom were healthy; her son was 34 and her daughter 28.

Examination revealed a rather pale middle-aged woman, weighing 134 lb. (60.8 kg.), an excellent witness, though inclined to make light of her complaints. Her skin was somewhat dry and wrinkled but otherwise showed no abnormality. No lymphatic glands were palpable and there was no enlargement of the salivary glands. Venous congestion, ankle oedema, and finger-clubbing were not present. She was somewhat dyspnoeic at rest, but no other clinical abnormalities were detected in the chest or heart. The blood pressure was 150/100. The abdomen showed no abnormality and the liver and spleen were not palpable. The optic disks were normal and neurological examination was negative.

Further investigation showed that she passed 12 to 16 pints (6.8 to 9.1 litres) of urine daily and drank roughly equal amounts. The specific gravity of the urine was in the neighbourhood of 1005; there was no glycosuria or albuminuria and no casts were present. X-ray films of the chest showed a mixture of reticulation and miliary mottling throughout both lung fields without enlargement of the hilar lymph nodes. No cysts were detected and there was no pneumothorax. X-ray films of the hands, feet, and skull showed no bony abnormalities. The pituitary fossa was radiologically normal.

Sputum tests for tubercle bacilli were repeatedly negative. The Mantoux test was positive to 1:1,000 O.T. Blood examination showed: Hb, 66% (9.8 g.%); erythrocytes, 5,000,000. The E.S.R. was 12 mm. in the first hour (Wintrobe). The blood Wassermann and Kahn reactions were negative and the glucose-tolerance curve was normal. The