PUBLIC HEALTH PAST AND PRESENT

Prophylactic oophorectomy: a historical perspective

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Removal of a woman's ovaries (known as bilateral oophorectomy, ovariectomy or, historically, ovariotomy) is undertaken in a number of countries. An estimated 19 000 women aged <60 years had a bilateral prophylactic oophorectomy in the UK in 2003, either as a planned response to an increased specific genetic risk of ovarian or breast cancer or, more frequently, as a prophylactic measure to prevent ovarian cancer. Despite its popularity, however, a full evaluation of the risks, costs and benefits of prophylactic oophorectomy in the absence of genetic markers and at the time of hysterectomy has not yet been undertaken. This paper seeks to provide a historical perspective on current practice by outlining approaches to the ovary in Britain from the 19th century onwards. Historically, ovarian removal has raised many questions about the costs and benefits of surgery. The aim of this article is to highlight the issues, and in so doing, to contribute to a more informed assessment of current practice.

Removal of a woman's ovaries (known as bilateral oophorectomy, ovariectomy or, historically, ovariotomy) is undertaken in a number of countries.[1–4] In a small proportion of cases, the operation is undertaken as part of a planned response to an increased specific genetic risk of ovarian or breast cancer.[5] However, in many other cases, the operation is a prophylactic measure to prevent ovarian cancer in those who are not at genetically increased risk. An estimated 19 000 women aged <60 years had a bilateral prophylactic oophorectomy in the UK in 2003.[6] Prophylactic removal of the colon, the breast and the appendix does occur, but oophorectomy at the time of hysterectomy represents the highest population-based rate of removal of any healthy organ for prophylactic reasons.

This paper seeks to provide a historical perspective on current practice by outlining approaches to the ovary in Britain from the 19th century onwards. This history is part of a larger story about trends in aggressiveness/conservatism in surgery generally, and especially surgery on women, which cannot be analysed within the confines of this article. The aim here is to highlight the issues raised by the surgical removal of ovaries and, in so doing, to contribute to a more informed assessment of current practice.

THE AGE OF THE OVARY

Originally proposed as a radical cure for ovarian disease (mostly benign cysts), ovariotomy was introduced into British gynaecological practice in the early Victorian period, before the era of general anaesthesia and antisepsis. It immediately attracted wide condemnation from the medical profession, as most practitioners did not deem ovarian disease to be serious enough to warrant such a dangerous procedure.[7] Opposition to the practice waned in the last quarter of the 19th century as both operative and postoperative mortality declined. However, there was fresh controversy when its indications were widened to include uterine fibroids, dysmenorrhoea and "menstrual epilepsy", a condition thought to originate from continued ovarian pain during the menstrual period. Popularised by the American gynaecologist Robert Battey (1828–95), who called it "normal ovariotomy" to indicate that the removal of non-cystic ovaries was involved, this procedure met with widespread opposition. Some gynaecologists and a number of lay commentators, feminists especially, objected to "oophorectomy" (the term used in Britain for Battey's operation) on the grounds that it induced sterility, the loss of sexual feeling and the assumption of the masculine characteristics.[7] Many patients also complained of postoperative symptoms resembling those of the menopause (hot flushes, giddiness and headaches), which were often more severe than those occurring around the time of the natural climacteric.

During the 1890s, the success obtained in treating the symptoms of thyroid deficiency with extracts of the thyroid gland raised hopes that the administration of ovarian substance to patients who had undergone oophorectomy might help relieve the menopausal symptoms.[8] Clinicians also began to investigate the possibility of replacing missing ovaries by transplantation. The experiments carried out by Viennese gynaecologists Rudolf Chobrak (1843–1910) and Emil Knauer (1867–1935) on rabbits and guinea pigs showed that the ovary could be transplanted successfully in the same animal, and that in successful transplants it remained functional.[9] Further experimentation by another Viennese gynaecologist, Josef Halban (1849–1931), demonstrated that the ovary controlled the maturation of the reproductive system, suggesting that its influence was mediated by a substance secreted into the circulating blood. By the early 20th century, other experimental evidence indicated that the ovaries were also implicated in the metabolic processes of the body. The withdrawal of ovarian secretion seemed to affect the growth and general nutrition of the organism, leading to changes in lipid and calcium metabolism.[10–12]

This evidence, and the observation that neither ovarian grafting nor the administration of ovarian extracts was entirely successful in reversing the effects of oophorectomy, served to induce a more conservative attitude towards the ovary. As British gynaecologist Louise McIlroy[10] (1874–1968) stated in 1912,

> the ovary is not an organ with the single role of reproduction, but is an essential factor in the maintenance of the equilibrium which exists between the so-called ductless glands or endo-secretory organs. Researches into ovarian function now tend to show that the removal of ovaries for slight pathological affections, or for the alleviation of menstrual derangements, is against the best ultimate interests of the patient, and that total extirpation of the ovaries should not be practised unless these organs are the seat of some severe pathological lesion.

Looking back on the development of ovarian surgery from the late 19th century onwards, the Scottish gynaecologist James Hendry (1886–1945) wrote with dismay about the vogue for Battey's operation. ''Little was then known of endocrine glands'', he said in 1936, ''but the steady development of physiological knowledge has carried us far from those barbarous days'' (Hendry,[13] p 610–11).

The standard advice in Britain in the inter-war period was thus that normal ovaries should be preserved in younger women undergoing pelvic surgery. Grafting of ovarian tissue was also advised if the ovaries could not be left in situ, usually because of serious pelvic infection; however, according to James Hendry,[13] in practice, ovarian grafting was rarely undertaken in Britain (p 611). Attitudes to bilateral oophorectomy in perimenopausal and menopausal women were more complex. Some gynaecologists never removed a normal-looking ovary, no matter how old the patient was. The eminent gynaecologist Victor Bonney[14] (1872–1953), for example, declared in 1937 that ''except in malignancy, the surgeon should strive to preserve in the patient's body every atom of undiseased ovarian tissue'' (p 6). Others recommended ovarian removal at hysterectomy, to avoid further surgery if the ovaries subsequently became diseased. In the 1930s, the risk of pelvic adhesions and benign ovarian tumours was usually cited as a justification for prophylactic surgery. By 1940, however, a new anxiety had been added to these concerns: the fear that ovaries left behind might become malignant.

THE AGEING OVARY AND CANCER

In the early 20th century, gynaecologists and surgeons had little interest in ovarian cancer. The attention of the profession and of the public health authorities was focused on the prevention and treatment of cervical cancer, the leading cause of female death from cancer in women since the mid-1800s.[15] However, during the late 1930s, almost overnight, gynaecologists discovered the menace of ovarian carcinoma in the ageing woman, and even those who had previously supported ovarian conservation began to advocate the removal of healthy ovaries as a cancer prevention strategy.

The problem with ovarian cancer was not so much its incidence, but its insidiousness. As Harry Sturgeon Crossen, an American gynaecologist practising in St Louis, Missouri, argued in 1942, in dealing with ovarian carcinoma gynaecologists were confronted with ''a form of creeping death'' that defied early detection. Crossen had been an advocate of conservative surgery of the ovaries and uterus, but he had changed his mind after experiencing 12 cases of ovarian carcinoma over a period of 13 years. The numbers involved were admittedly very small, but if one multiplied them by the number of gynaecologists in practice and added the number of patients who were misdiagnosed each year, Crossen[16] reasoned, one got some idea of the magnitude and importance of the problem.

What could be done to stop the ''silent killer''? Crossen suggested adopting the methods already applied in the control of cervical cancer: periodic examination and surgical removal of potentially cancerous tissue. Operations for the repair and amputation of the cervix had been controversially introduced in the late 19th century on the grounds that chronic infection and damage to the tissues during childbirth were risk factors for cervical cancer.[17] In older women, ovarian removal during abdominal surgery could serve a similar prophylactic purpose: ''the involuting ovaries have fulfilled their reproductive and endocrine function. They are no longer an important part of the economy but vestigial structures which carry a special tendency to cancer'', Crossen[16] claimed (p 1487).

With the refashioning of the ageing ovary into a public health threat, the prophylactic removal of the female gonads began to gain momentum. From about 1940 onwards, prophylactic oophorectomy gradually became more common in older women undergoing hysterectomy for benign conditions, with American commentator describing the postmenopausal ovaries as ''withered husks'' that would exert a danger to women if not removed. The shift in outlook in Britain can be gauged through successive editions of Bonney's classic *Textbook of gynaecological surgery*. As late as 1952, the book argued that conservation of the ovaries was the wisest course to pursue, even in perimenopausal and postmenopausal women (Bonney,[18] p 240). The subsequent edition, revised and updated by London gynaecologists Douglas Macleod and John Howkins in 1964, still recommended conservation of healthy ovarian tissue in premenopausal women, but it now sanctioned bilateral oophorectomy in women aged ⩾45 years. After this age, it was argued, ''the nuisance value of the ovary as a site for neoplasm in our opinion outweighs its value and usefulness''(Macleod and Howkins,[19] p 471).

THE IMPACT OF MODERN HORMONAL THERAPY

What role did the discovery of diethylstilboestrol, a synthetic compound that reproduced the effects of the natural oestrogens, play in the post-war rise of prophylactic oophorectomy? After its discovery in 1938, the new substance was immediately put to the test in women previously treated with natural oestrone.[20] Stilboestrol proved an effective means of relieving the menopausal syndrome. It was also cheaper, more powerful and easier to administer than natural hormonal preparations. But its initial impact on the practice of oophorectomy was less marked than may be supposed. General acceptance of hormonal therapy was prevented by complaints of disagreeable side effects, from nausea and skin rashes to psychosis and liver damage.[20–23] There was also some concern that the wider availability of hormonal preparations would lead to misuse. Contraception, abortion and addiction were all mentioned as potential problems.[24]

In addition, by the mid-1930s, there was considerable anxiety about the likely carcinogenic effects of both natural and synthetic oestrogens. As early as 1933, researchers J W Cook and E C Dodds, just on the verge of producing synthetic oestrogens, had noted that the chemicals which possessed oestrogenic properties also contained carcinogenic constituents.[25] In addition, the experiments conducted by French biologist Antoine Lacassagne (1884–1971) in the 1930s suggested that oestrone injections, if repeated over a period of several months, could produce breast cancer in mice. This research caused some justifiable alarm among medical practitioners.[26] British researchers quickly moved to quell the anxiety, arguing that the mice in which cancer had been induced belonged to susceptible strains.[27–29] A leading article in the *Lancet* for March 1940 observed that the evidence about the carcinogenic effects of long-term oestrogen therapy was still inconclusive, but it also stated that oestrogens should not be given to women who had already breast or cervical cancer.[24]

By the 1950s, there were renewed concerns about the metabolic effects of oophorectomy and fresh doubts about the efficacy of hormonal therapy. In 1953, biochemist D P Barr[30] suggested that natural oestrogens played a part in lipid metabolism, and that their removal increased the tendency to atherosclerosis. This research was confirmed in 1959 by Oliver and Boyd, who argued that all premenopausal oophorectomised women should receive hormonal therapy until about the age of 50 years. They added that ''a case could even be made for administering small doses of oestrogens for a number of years to all menopausal women''(Oliver and Boyd,[31] p 694). However, as an editorial in the *Lancet* argued in 1959, it was still unclear whether the effects of oophorectomy could be reversed by the administration of synthetic hormonal preparations. Conservation of healthy ovaries still seemed the best plan.[32]

As the debate intensified in the late 1950s, gynaecologists sought to quantify the risks and benefits of bilateral

oophorectomy. Norman Jeffcoate, the Liverpool gynaecologist, observed in 1957 that the risk of a woman developing ovarian cancer was variously reckoned at 1:3000 to 1:5000; hence, one gynaecologist could prevent only one case of ovarian cancer at the expense of ''5000 surgical menopauses''. As a senior gynaecologist, he found that ''advancing years and widening experience cultivate increasing respect for the torments which the artificial menopause, or even the knowledge that the ovaries have been removed, may bring.''(Jeffcoate,[33] p 667). Even assuming that the physiological effects of oophorectomy could be reversed, the decision to remove the ovaries needed to encompass the cultural significance of the sex glands. On this point, London obstetrician William Nixon[34] wryly observed in 1960 that ''a woman has an emotional attachment to her uterus and ovaries and it is unfortunate that her gonads, unlike the testicles, are not in an extracorporeal pouch secure from unnecessary extirpation''.

THEN AND NOW

Although the debate continued, prophylactic oophorectomy rates steadily increased in the latter part of the 20th century in the UK, the US and many other countries. An age-related policy was widely suggested and accepted, so that prophylactic oophorectomy was more or less routinely undertaken at the time of hysterectomy, in women aged >45 years. Prophylactic oophorectomy certainly became more common as the availability of hormone replacement therapy grew, but the main justification for the operation continued to be the prevention of ovarian cancer.

Recent research suggests that there is almost certainly a place for oophorectomy. There is a clear-cut case for the intervention in the small proportion of women in the population who have an identified increased genetic risk of breast and ovarian cancer.[35] For most other women, however, the benefits of prophylactic ooohorectomy are far from clear.

The practice of bilateral prophylactic ovarian removal as an addition to hysterectomy for women without a genetically increased risk of ovarian cancer may now be waning. Newer, less invasive methods of treating menorrhagia and fibroids have become more widespread. As none of these newer interventions allow easy access to the ovaries, the practicability and therefore the likelihood of these organs being removed prophylactically as part of another procedure is lessened. Prophylactic ovarian removal may soon come to be seen as a historically interesting, but now outdated response to the combination of a ready availability of hormone replacement therapy coupled with an unfocused response to the threat of ovarian cancer.

What this paper adds

- Ovarian removal has been a controversial issue ever since the introduction of the practice in the middle of the 19th century.
- Medical attitudes to the operation have been shaped by changing beliefs about the natural history of the ovary, and by concerns over the risks and benefits of exogenous hormonal preparations.
- The development of prophylactic oophorectomy raises broader questions about the modern tendency to regard treatment as cancer prevention.

Policy implications

- For healthcare funders to consider whether prophylactic oophorectomy should be undertaken routinely.
- For practitioners and patients to consider choices to be made at the time of oophorectomy.

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