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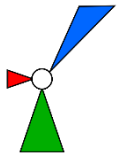
<1070/c>	is given over several days, but not when use is restricted to the period of cardiac surgery. Nonetheless, stroke was observed only in patients in the treatment group in the studies from Philadelphia. The rate of stroke in high-risk cardiac surgery patients receiving aprotinin therapy is lower than would be anticipated. Concerns have also been expressed about the possibility of graft occlusions and increased myocardial ischaemia, especially in patients undergoing myocardial revascularisation. With both lysine analogues and aprotinin, more postoperative myocardial infarctions have been reported in treated patients although the increase is not statistically significant. The effect of lysine analogues on graft patency has not been formally investigated. In low-risk patients there is no effect of aprotinin on graft patency; in high-risk patients there have been reports suggesting graft occlusion in patients receiving the drug. In one study, necropsy was undertaken in about half of the patients who died, and showed graft occlusion only in patients given aprotinin. A surprising observation is that the thrombosed grafts were confined to the patients who received a low dose of aprotinin; graft occlusions were not seen in patients allocated to receive a high dose or placebo. There are several outstanding issues. We need more information about which agent and dose is appropriate for all these compounds, and we also need to know more about their efficacy in reducing the need for donor blood and their safety profile in high-risk procedures. Lysine analogues cost less than SERPINs. With both classes of compounds the challenge is to show that the risk of administration is very low, and certainly less than that of blood products. ONCOLOGY Molecular basis for hormone-related cancer Clinical oncologists have long recognised a group of cancers that respond to hormonal manipulation - eg, tumours of the breast, endometrium, thyroid, and prostate. Tumours of the ovary and testis are likewise hormone-related, although they do not usually respond to hormone therapy. Hormonal factors may also be involved in osteosarcoma and malignant melanoma. The common clinical and epidemiological features of some of these tumours seem to be closely linked at the molecular level. Most cases of ovarian cancer arise on the epithelial surface of the ovary, not in the ovary itself. Many years ago Fathalla proposed that repeated minor trauma to ovarian epithelium caused by ‘incessant ovulation’ increased the risk of cancer. Some epidemiological studies support the Fathalla hypothesis. Ovulation is driven by follicle stimulating hormone. Anything that inhibits ovulation - eg, pregnancy or oral contraception - reduces the risk of ovarian cancer. These findings now have a molecular basis. In cases where a tumour **suppressor gene** is inactivated, repetitive cellular repair may lead to uncontrolled cell division and malignant transformation; a putative tumour **suppressor gene** has been described on
 Key: **Footprint ConEn1** **Footprint ConEn2** **Footprint ConEn3**	**the long arm of chromosome 17**
	. Similar mechanisms may account for other cancers of the reproductive organs. The physiological cycle of incessant ovulation, frequent menstruation, and intermittent breast stimulation is largely wasteful. Cell proliferation is constantly being turned on and off in the target organs. Thus it is hardly surprising that malignant diseases of the breast, ovary, and endometrium all occur more commonly in nulliparous women.

	Moreover, the age-incidence curves for this group of diseases begin to flatten around the time of menopause. A predisposing tumour suppressor gene for breast and ovarian cancer families, BRCA1, has been mapped by linkage analysis on **the long term of chromosome 17**, close to but probably distinct from the region noted in sporadic ovarian cancer. Differentiated thyroid cancer occurs much more commonly in women than in men, largely in the premenopausal years. This feature is thought to be related to the reproductive cycle. The sex difference begins to fade in postmenopausal women and disappears completely in older patients. There is a positive association between thyroid cancer and parity, and an association between breast cancer and thyroid deficiency has likewise been recognised clinically. The fact that the BRCA1 gene for breast cancer is flanked on **the long arm of chromosome 17** by the THRA1 gene for the thyroid hormone receptor may be important in this respect. Moreover, an 80% allele loss has been noted at the THRA1 locus in sporadic breast cancer cases. Osteosarcoma is not usually classified with hormonal cancers, but its onset largely coincides with the final hormonal growth spurt in teenagers. Most tumours are located near the ends of long bones and become apparent around the time of epiphyseal closure. The growth hormone locus has also been mapped on **the long arm of chromosome 17**, at 17q 22-24, close to the BRCA1 gene in breast and ovarian cancer families. The molecular properties of prostate cancer are being intensively investigated. A study in 1982 of Utah Mormons showed clustering of prostate cancer with breast cancer. Ten years later a cohort study in Iceland confirmed that male blood-relatives of women with breast cancer had an excess risk of prostate cancer. The Icelandic report also noted coaggregation between breast cancer and cancers of the prostate, ovary, and endometrium. Some studies have linked the risk of prostate cancer with testosterone concentrations and the degree of sexual activity, but the latter is difficult to measure and reports are inconclusive. An obvious physiological difference between the sexes is that female hormonal concentrations fluctuate throughout the reproductive years whereas male concentrations are relatively constant, declining gradually with age. The absence of intermittent hormonal stimulation in men implies that a similar underlying genetic defect might not give rise to malignant disease until later in life. Thus it is noteworthy that prostate cancer is