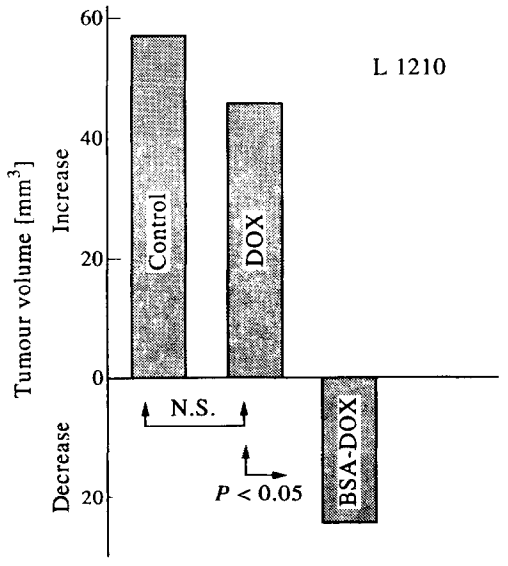

Figure 1. Increase or decrease in tumour volumes (from day 0 to day 4 after treatment) of solid (DOX)-resistant tumours (L1210). After the solid tumours had reached an average diameter of 5 mm, the animals were treated with DOX alone (8 mg/kg) or bovine serum albumin-conjugated DOX (BSA-DOX; equivalent dose of DOX). The control animals were treated with 0.9% NaCl solution. Mean values (changes of tumour volumes during 4 days) of 10 tumours (n = 30 mice).

present investigation, we cannot decide whether circumvention of DOX resistance by albumin-conjugated DOX is due to its effects on resistance mechanisms (e.g. blockage of P-glycoprotein-efflux) or belongs to a more general effect, for example, on membrane permeability.

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Hereditary Breast Cancer in 19 Females and 2 Males: Kindred, P.G. 1940

P. Ghadirian, S. Narod, C. Perret, D.M. Lambert, J. Latreille, F. Letendre, M. Monté and D. Belanger

BREAST CANCER is the most common cancer in women in Québec, with a standardised incidence rate of 70.8/100 000 women [1], and a case-control study showed that 32.6% of breast cancer cases had confirmed positive family history of the same cancer [2]. Hereditary breast cancer is characterised by early onset, bilaterality, multiple primaries, and associations with other cancers [3]. Forms of hereditary breast cancer recognised include site specific breast cancer, breast and ovarian cancer, and breast cancer with associated sarcomas, brain, lung, leukaemia and adrenocortical cancer (Li-Fraumeni syndrome).

Retrospective case-control studies have shown that a family history of breast cancer or any cancer is more common among male cases with breast cancer than controls [4–6]. A prospective population-based case-control study demonstrated that while there was an elevated risk of cancer among first degree relatives of men with breast cancer, there was no such risk among their wives, indicating a genetic, and not a shared environmental risk [7].

The standardised incidence rate of male breast cancer ranges from 0.16/100 000 (Japan) to 1.06/100 000 (Israel), at rates of approximately 1% of those of female breast cancer [8]. Factors which have been associated with male breast cancer include ethnic origin (black), remaining a bachelor, religion (Jewish), exposure to radiation, excessive weight, as well as occupational exposure to phenoxyacids, heat, dust, gasoline, grease, or electromagnetic fields [9]. Endocrine factors seem to play a large role in development of male breast cancer, with serum oestrogens being higher in affected subjects than controls. The effect of (female) hormones is evidenced by several risk factors for the development of male breast cancer, that is, Klinefelter syndrome, use of female hormones and history of orchiectomy [9].

CASE REPORT

A large, rural dwelling family was identified through a study of nutrition and breast cancer in the Montreal region. The proband indicated an extensive family history of breast cancer,

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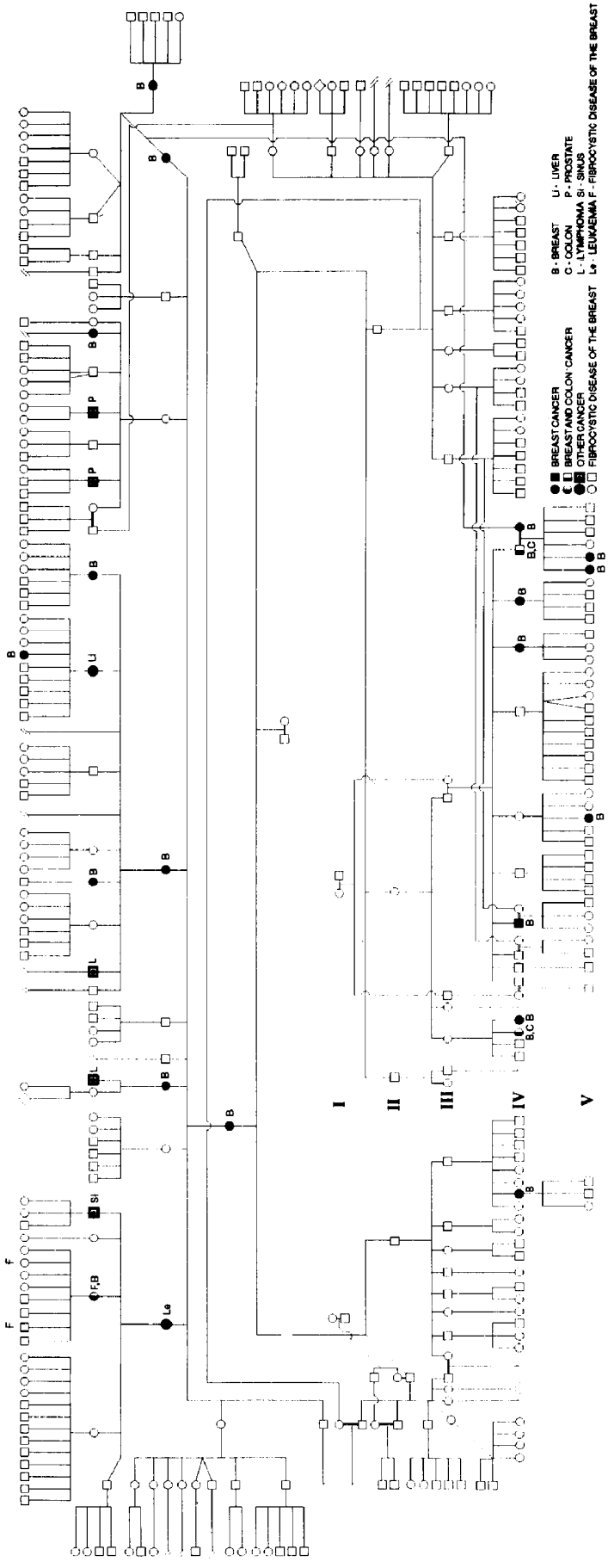
B - BREAST
C - COLON
L - LYMPHOMA
Le - LEUKAEMIA
Li - LIVER
P - PROSTATE
Si - SINUS
F - FIBROCYSTIC DISEASE OF THE BREAST
BREAST CANCER
BREAST AND COLON CANCER
OTHER CANCER
FIBROCYSTIC DISEASE OF THE BREAST
I
II
III
IV
V

Figure 1.

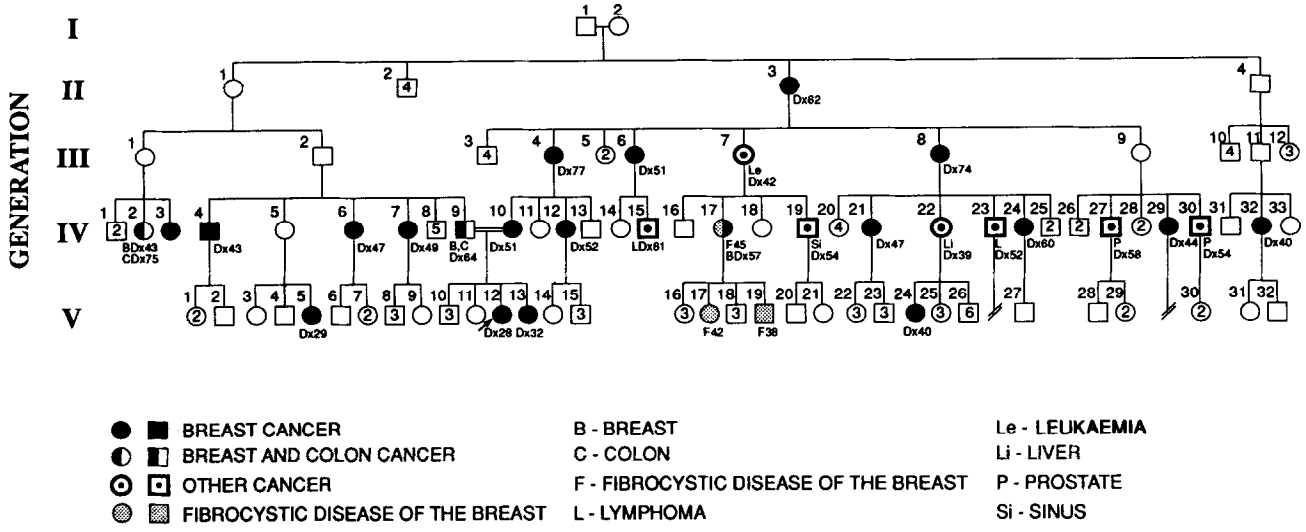

Figure 2.

including breast cancer in both parents. Other affected relatives included two paternal aunts and two uncles, as well as a maternal aunt, grandmother and great-grandmother. The parents of the proband were related, having a common set of great-grandparents. A thorough investigation of the extended family (Figure 1) revealed a large family of over 350 people containing 19 female and 2 male cases of breast cancer and 9 individuals with other cancers (2 lymphomas, 2 colon, 2 prostate, 1 leukaemia, 1 sinus and 1 liver cancer). Two other individuals (one male, one female) had benign breast disease. No record of Klinefelter syndrome was seen in hospital charts for either of the men with breast cancer. Figure 2 shows the pedigree of affected individuals in detail. The pattern of cancer in this family suggests a genetic predisposition to cancer, segregating in an autosomal dominant manner. The gene causing familial breast cancer in this family is incompletely penetrant because of female obligate carriers III-1 and IV-5, who reached the age of 70 years without becoming affected.

The age of diagnosis of breast cancer is decreasing with generation. The earliest age of onset for each generation was II:62; III:51; IV:40; V:28 years (in generation V, ages ranged from 28 to 40 years). Causes of anticipation could be gene expansion as the cause of the cancer phenotype [10], increased awareness and surveillance in successive generations of the family, or an increasing environmental burden over the past century acting to cause a more rapid cancer progression and shorter latent period [11].

The consanguineous marriage of the proband's parents (IV-9 and IV-10), who are both affected with breast cancer and presumably have the causal gene, raises the possibility that the proband and her siblings (V-10 to V-13) may be homozygotes for the gene defect. Of additional interest is the progression of fibrocystic disease in individual IV-17. Two of her children now have fibrocystic breast disease.

DNA analysis of blood of members of the family will hopefully reveal the genetic cause of breast cancer in this family.

Families with hereditary male breast cancer show similar characteristics to families with hereditary female breast cancer. Similar to female breast cancer [12], the relative risk of breast cancer to relatives of men with breast cancer increases with the number of affected relatives and an early age of diagnosis (before 45 years) [13]. Bishop and Gardner, in a lengthy study of several pedigrees, have identified a family (Kindred 107), similar to our family (Kindred, P.G. 1940) with 29 female and 2 male cases of breast cancer [14, 15]. A recent review of the literature reported that eight of 13 studies of familial male breast cancer had a positive family history of other cancers, and six out of those studies reported female breast cancer in the families [5]. The study of Kozak and associates describes family members with diverse cancers including lymphoma, leukaemia, prostate cancer and female breast cancer. LaRaja and associates have documented three siblings with breast cancer (2 males, 1 female) occurring at an early age, with ages of diagnosis being 36 years for the sister and 41 and 61 years for the brothers, together with breast cancer also present in the paternal grandmother [16]. Evenson and colleagues documented two families with 3 affected males in each (age of diagnosis 47–78 years), and daughters with fibrocystic breast disease [4].

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Correction

At what age do sunburn episodes play a crucial role for the development of malignant melanoma—This paper by J. Westerdahl, H. Olsson and C. Ingvar was published in the *European Journal of Cancer*, Vol. 30A, No. 11, pp. 1647–1654, 1994. A number of errors appeared in Tables 2–4. The corrected tables are printed in full below.

Table 2. Relative risk of malignant melanoma in a matched case–control study of malignant melanoma in southern Sweden between 1988 *and* 1990, *according to painful sunburn in different age groups*

Factor	Category	Cases	Controls	RR* (95% CI)	RR† (95% CI)	Test for trend (*P*-value)
Number of sunburns before age 15 years	Never	143	259	1.0‡	1.0‡	
	1–5 times	149	224	1.4 (1.0–1.9)	1.0 (0.6–1.5)	
	>5 times	47	65	1.6 (1.0–2.6)	1.0 (0.5–2.1)	>0.05
Number of sunburns from age 15–19 years	Never	108	209	1.0‡	1.0‡	
	1–5 times	213	312	1.4 (1.0–1.9)	1.3 (0.8–2.0)	
	> 5 times	46	65	1.6 (1.0–2.5)	0.9 (0.4–2.1)	>0.05
Number of sunrburns after age 19 years	Never	123	254	1.0‡	1.0‡	
	1–5 times	205	296	1.5 (1.1–2.1)	1.6 (1.1–2.4)	
	>5 times	48	58	1.9 (1.2–3.1)	2.2 (1.1–4.1)	0.004

*Crude relative risk. †Adjusted for raised naevi, red hair colour and blond/fair hair colour. ‡Reference category.

Table 3. Relative risk of malignant melanoma in southern Sweden between 1988 *and* 1990, *according to painful sunburn in different age groups, after exclusion of all persons who had sunburned before age* 15 *years*

Factor	Category	Cases	Controls	RR* (95% CI)	RR† (95% CI)	Test for trend (*P*-value)
Number of sunburns from age 15–19 years	Never	90	185	1.0‡	1.0‡	
	1–5 times	80	111	1.3 (0.8–2.1)	1.0 (0.6–1.8)	
	>5 times	8	65	1.2 (0.2–6.6)	0.3 (0.04–3.0)	>0.05
Number of sunburns after age 19 years	Never	81	188	1.0‡	1.0‡	
	1–5 times	87	129	1.2 (0.7–2.1)	1.5 (0.8–2.9)	
	> 5 times	18	13	2.8 (1.0–7.8)	6.8 (1.6–29)	0.001

*Crude relative risk. †Adjusted for raised naevi, red hair colour and blond/fair hair colour. ‡Reference category.

Table 4. Relative risk of malignant melanoma in southern Sweden between 1988 *and* 1990, *according to painful sunburn in different age groups, excluding individuals who had sunburned more than five times after age* 19 *years*

Factor	Category	Cases	Controls	RR* (95% CI)	RR† (95% CI)	Test for trend (*P*-value)
Number of sunburns before age 15 years	Never	130	251	1.0‡	1.0‡	
	1–5 times	143	210	1.6 (1.1–2.3)	1.2 (0.8–1.9)	
	>5 times	23	34	1.8 (0.9–3.5)	1.1 (0.5–2.7)	>0.05
Number of sunburns from age 15–19 years	Never	101	204	1.0‡	1.0‡	
	1–5 times	202	259	1.6 (1.1–2.2)	1.6 (1.0–2.4)	
	> 5 times	18	31	1.5 (0.8–3.0)	1.0 (0.4–2.7)	>0.05

*Crude relative risk. †Adjusted for raised naevi, red hair colour and blond/fair hair colour. ‡Reference category.