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Acknowledgements—This work was supported by the Swiss League against Cancer.

Eur J Cancer, Vol. 28A, No. 8/9, pp. 1490–1495, 1992.
Printed in Great Britain

0964–1947/92 $5.00 + 0.00

Trends in Cancer Survival in Vaud, Switzerland

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Survival rates from the Vaud Cancer Registry were compared for incident cases registered in 1974–1978 and 1979–1983. No appreciable difference was evident for most major cancer sites: 5-year relative survival rates were 0.21 in 1974–1978 and 0.23 in 1979–1983 for stomach, 0.49 and 0.46 for colon, 0.45 and 0.47 for rectum, 0.04 and 0.03 for pancreas, 0.08 and 0.10 for lung, 0.41 and 0.42 for kidney, 0.21 and 0.13 for brain, and 0.32 and 0.30 for multiple myeloma, respectively. A modest advancement in 5-year relative survival rates was, however, registered for total cancer mortality (non-melanomatous tumours excluded, from 0.41 to 0.43) while, with regard to specific sites, a significant improvement was seen only for cancer of the testis (from 0.73 to 0.88). More than 10% non-significant improvements in survival were recorded for melanomatous skin cancer (from 0.67 to 0.78), thyroid cancer (from 0.73 to 0.85), particularly in females, non-Hodgkin lymphomas (from 0.37 to 0.45), Hodgkin's disease (from 0.61 to 0.78), cancer of the ovary (from 0.28 to 0.32) and the prostate (from 0.44 to 0.52). However, significant declines in survival rates were seen for cancer of the larynx, gallbladder and biliary tract, and for connective tissue neoplasms. A few differences in the modification of relative survival rates according to age (< 60 versus ≥ 60 years) were noted for a few cancer sites. Changes were larger in older patients with respect to cancer of the prostate and thyroid and non-Hodgkin lymphomas (increases) and connective neoplasms (decreases). Conversely, changes in survival were greater or restricted to younger individuals for testis, bladder and leukaemias (improvements) and cancer of the mouth or pharynx (decline), thus suggesting the different play of age-specific biological characteristics of some tumours, in addition to diagnostic improvements and gradual spread of effective cancer treatments to more advanced age groups.
Eur J Cancer, Vol. 28A, No. 8/9, pp. 1490–1495, 1992.

INTRODUCTION

ANALYSIS OF trends in survival is, at least in principle, the most reliable indicator of progress in cancer treatment. It is, however, extremely difficult to assess and interpret changes in survival rates over different calendar periods since they may reflect not only improved treatment and better survival, but also advances in diagnostic procedures and hence anticipation of diagnosis or, probably, broadening of the spectrum of tumours included among malignancies, although not necessarily bound to progress clinically [1–4].

The US National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) Program [5, 6] periodically produces estimates of 5-year survival rates from various cancer sites diagnosed in subsequent calendar periods, but only few population-based figures are available from other sources, particularly from Europe [7–13].

Table 1. Distribution of cases according to cancer site (and corresponding ICD), sex and calendar period*

Cancer site	ICD	Number of cases			
		Males		Females	
		1974–1978	1979–1983	1974–1978	1979–1983
Mouth or pharynx	140–9	312	325	61	98
Oesophagus	150	143	166	39	65
Stomach	151	265	284	170	141
Colon	153	280	370	311	405
Rectum	154	240	286	180	260
Liver	155	49	71	16	21
Gallbladder and biliary tract	156	28	45	63	93
Pancreas	157	101	151	86	109
Larynx	161	106	137	11	11
Trachea, bronchus and lung	162	883	1020	122	166
Bone	170	14	11	8	7
Connective tissue	171	16	12	27	34
Melanomatous skin cancer	172	96	107	130	144
Non-melanomatous skin cancer	173	1057	1454	825	1234
Breast (females)	174	—	—	1211	1372
Cervix uteri	180	—	—	243	194
Corpus uteri	182	—	—	308	313
Ovary	183	—	—	193	210
Prostate	185	585	700	—	—
Testis	186	118	128	—	—
Bladder	188	203	266	63	71
Kidney and renal pelvis	189.0–0.1	91	112	54	72
Brain	191	67	79	58	52
Thyroid	193	18	33	70	86
Non-Hodgkin lymphomas	200,202	81	119	86	108
Hodgkin's disease	201	51	42	34	34
Multiple myeloma	203	54	54	40	41
Leukaemia	204–8	114	133	74	102
Childhood leukaemia (<15 yrs)	204–8	15	8	8	8
Unknown origin	195,199	145	176	143	172
Total, all cancers	140–208	5239	6573	4748	5804

* Only invasive tumours considered.
Results from Vaud Cancer Registry, Switzerland, 1974–1983.

The Vaud Cancer Registry has adopted a structured system for monitoring survival since 1974 [11]. This now gives the possibility of comparing 5-year survival rates for cases registered in two subsequent calendar periods, 1974–1978 and 1979–1983.

SUBJECTS AND METHODS

The data included in the present analysis were derived from the Vaud Cancer Registry datafile, which includes data concerning incident cases of malignant neoplasms in the canton (whose population in 1980 was about 530 000 inhabitants) [14, 15]. Information collected by the registry includes general demographic characteristics of the patient (age, sex, municipality of residence), site and histological type of the tumour according to the standard International Classification of Diseases for Oncology (ICD-O) and time of registration. Information on survival was derived from mortality statistics and, for "apparently" non-deceased cases, through an active follow-up based on verification of vital status from registries of current residence. The vital status of each registered case has thus been verified up to June 30, 1989. A total of 22 364 cases, registered between 1974 and 1983 were included in the present study, after exclusion of 1392 cases detected either at autopsy or registered from death certificates alone. Only invasive cancers were considered. Table 1 presents the distribution of cases considered according to cancer site (and corresponding ICD), sex and calendar period.

Survival curves were defined according to the product limit (maximum likelihood, Kaplan and Meier) method [16] for two quinquennial calendar periods (1974–1978 and 1979–1983), sex and age groups (< 60 and ≥ 60 years). Differences in survival were tested using the usual log-rank method [17, 18]. Finally,

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Received 21 Nov. 1991; accepted 21 Nov. 1991.

Table 2. Five-year product-limit crude survival rates from various cancers according to sex and calendar period

Cancer site	Males		Females		Total	
	1974–1978	1979–1983	1974–1978	1979–1983	1974–1978	1979–1983
Mouth or pharynx	0.31 (0.03)	0.26 (0.02)	0.43 (0.06)	0.39 (0.05)	0.33 (0.02)	0.29 (0.02)
Oesophagus	0.06 (0.02)	0.04 (0.02)	0.05 (0.04)	0.08 (0.03)	0.06 (0.02)	0.05 (0.01)
Stomach	0.16 (0.02)	0.15 (0.02)	0.19 (0.03)	0.23 (0.04)	0.17 (0.02)	0.18 (0.02)
Colon	0.38 (0.03)	0.33 (0.02)	0.41 (0.03)	0.40 (0.02)	0.40 (0.02)	0.37 (0.02)
Rectum	0.30 (0.03)	0.38 (0.03)†	0.45 (0.04)	0.39 (0.03)	0.37 (0.02)	0.38 (0.02)
Liver	0.02* (0.02)	0.03* (0.02)	0.19* (0.10)	0.05* (0.05)	0.05* (0.03)	0.02* (0.02)
Gallbladder and biliary tract	0.11* (0.06)	0.07* (0.04)	0.12* (0.04)	0.03* (0.02)†	0.12 (0.03)	0.04 (0.02)‡
Pancreas	0.03* (0.02)	0.01* (0.01)	0.03* (0.02)	0.06* (0.02)	0.03 (0.01)	0.03 (0.01)
Larynx	0.57 (0.05)	0.48 (0.04)†	0.64 (0.15)	0.55 (0.15)	0.58 (0.05)	0.48 (0.04)†
Trachea, bronchus and lung	0.07 (0.01)	0.08 (0.01)	0.09 (0.03)	0.11 (0.02)	0.07 (0.01)	0.08 (0.01)
Bone	0.43 (0.13)	0.52 (0.16)	0.75 (0.15)	0.57 (0.19)	0.55 (0.11)	0.55 (0.12)
Connective tissue	0.41 (0.13)	0.39 (0.15)	0.66 (0.09)	0.38 (0.08)‡	0.57 (0.08)	0.38 (0.07)†
Melanomatous skin cancers	0.55 (0.05)	0.66 (0.05)	0.65 (0.04)	0.72 (0.04)	0.61 (0.03)	0.70 (0.03)
Non-melanomatous skin cancers	0.75 (0.01)	0.75 (0.01)	0.81 (0.01)	0.82 (0.01)	0.78 (0.01)	0.78 (0.01)
Breast (females)	— —	— —	0.60 (0.01)	0.64 (0.01)	— —	— —
Cervix uteri	— —	— —	0.60 (0.03)	0.57 (0.04)	— —	— —
Corpus uteri	— —	— —	0.65 (0.03)	0.67 (0.03)	— —	— —
Ovary	— —	— —	0.25 (0.03)	0.29 (0.03)	— —	— —
Prostate	0.32 (0.02)	0.37 (0.02)	— —	— —	— —	— —
Testis	0.72 (0.04)	0.85 (0.03)†	— —	— —	— —	— —
Bladder	0.25 (0.03)	0.28 (0.03)	0.25 (0.05)	0.27 (0.05)	0.25 (0.03)	0.28 (0.02)
Kidney and renal pelvis	0.36 (0.05)	0.34 (0.05)	0.35 (0.07)	0.40 (0.06)	0.36 (0.06)	0.37 (0.04)
Brain	0.21 (0.05)	0.09 (0.03)	0.19 (0.05)	0.17 (0.05)	0.20 (0.04)	0.12 (0.03)
Thyroid	0.60 (0.12)	0.63 (0.08)	0.68 (0.06)	0.84 (0.04)‡	0.67 (0.05)	0.78 (0.04)†
Non-Hodgkin lymphomas	0.35 (0.05)	0.35 (0.04)	0.29 (0.05)	0.41 (0.05)†	0.32 (0.04)	0.38 (0.03)
Hodgkin's disease	0.52 (0.07)	0.76 (0.07)‡	0.69 (0.08)	0.68 (0.08)	0.59 (0.06)	0.73 (0.05)
Multiple myeloma	0.21 (0.06)	0.25 (0.06)	0.34 (0.07)	0.25 (0.07)	0.27 (0.05)	0.25 (0.04)
Leukaemia	0.21 (0.04)	0.27 (0.04)	0.27 (0.05)	0.26 (0.04)	0.24 (0.03)	0.27 (0.03)
Childhood leukaemia (<15 yrs)	0.33 (0.12)	0.63 (0.17)	0.38* (0.17)	0.75 (0.15)	0.35 (0.10)	0.69 (0.12)
Unknown origin	0.15 (0.03)	0.07 (0.02)	0.12 (0.03)	0.07 (0.02)	0.14 (0.02)	0.07 (0.01)‡
Total, all cancers	0.35 (0.01)	0.38 (0.01)‡	0.52 (0.01)	0.53 (0.01)	0.43 (0.00)	0.45 (0.00)‡
Total, skin non-melanoma excluded	0.25 (0.01)	0.27 (0.01)	0.45 (0.01)	0.45 (0.01)	0.35 (0.00)	0.36 (0.00)

Crude survival rates (S.E.).
* Estimates based on less than 5 cases at the beginning of the interval.
† $P < 0.10$.
‡ $P < 0.05$.
Results from Vaud Cancer Registry, 1974–1983.

relative survival rates [19] were computed, after allowance for the general lifetables of the canton [15].

RESULTS

Table 2 gives the 5-year crude survival rates from each cancer site and sex diagnosed in two subsequent calendar periods (1974–1978 and 1979–1983). No appreciable difference was evident for most cancer sites. For instance, the 5-year crude survival was 0.17 in 1974–1978 and 0.18 in 1979–1983 for stomach, 0.40 and 0.37 for colon, 0.37 and 0.38 for rectum, 0.03 in both periods for pancreas, 0.07 and 0.08 for lung, 0.25 and 0.28 for bladder and 0.27 and 0.25 for multiple myeloma (Table 2). Only survival rates for testicular cancer improved significantly (from 0.72 to 0.85) and some non-significant increase in survival rates were observed for skin melanoma (from 0.61 to 0.70), breast (from 0.60 to 0.64), ovary (from 0.25 to 0.29), prostate (from 0.32 to 0.37), thyroid (from 0.67 to 0.78), non-Hodgkin lymphomas (from 0.32 to 0.38), Hodgkin's disease (from 0.59 to 0.73) and total leukaemias (from 0.24 to 0.27).

Survival rates, however, declined from 0.12 to 0.04 for cancer of the gallbladder and biliary tract, from 0.57 to 0.38 for connective neoplasms and from 0.20 to 0.12 for brain neoplasms. Also the combination of cancer of upper aero-digestive tract (i.e. mouth pharynx, oesophagus and larynx) showed a significant decrease in survival among males (from 0.31 to 0.26). 5-year survival for all cancer sites (non-melanomatous skin cancers excluded) and sexes combined was 0.35 in 1974–1978 and 0.36 in 1979–1983.

Although overall and in a few specific sites (i.e. most tumours of the digestive tract, melanomatous skin cancer and thyroid cancer), female survival rates were more favourable than the corresponding male rates, changes over calendar periods were consistent in both sexes. The decline in 5-year survival rate for connective neoplasms and the increase for thyroid cancer were, however, virtually restricted to females, whereas improvement for Hodgkin's disease was more marked in males.

Corresponding figures are presented in Table 3 in terms of relative survival rates, i.e. after correction for general mortality of the Vaud population. Relative rates were higher, but the pattern of changes is similar to that observed for crude survival rates, although a slight increase was noted for total cancer (from 0.41 to 0.43).

Table 3. Five-year relative survival rates from various cancers according to sex and calendar period

	Males		Females		Total	
Cancer site	1974–1978	1979–1983	1974–1978	1979–1983	1974–1978	1979–1983
Mouth or pharynx	0.35	0.30	0.50	0.44	0.38	0.33
Oesophagus	0.08	0.05	0.06	0.10	0.07	0.07
Stomach	0.20	0.19	0.23	0.29	0.21	0.23
Colon	0.48	0.42	0.49	0.50	0.49	0.46
Rectum	0.39	0.48	0.52	0.46	0.45	0.47
Liver	N/A*	0.04†	0.22†	N/A	0.05†	0.03†
Gallbladder and biliary tract	0.15	0.09	0.15	0.04	0.15	0.06
Pancreas	0.04	0.01	0.04	0.06	0.04	0.03
Larynx	0.66	0.55	0.70	0.60	0.67	0.56
Trachea, bronchus and lung	0.08	0.09	0.10	0.13	0.08	0.10
Bone	0.45	0.58	0.79	0.65	0.57	0.61
Connective tissue	0.54	0.49	0.72	0.42	0.66	0.44
Melanomatous skin cancer	0.61	0.75	0.71	0.80	0.67	0.78
Non-melanomatous skin cancer	0.94	0.94	0.96	0.97	0.95	0.96
Breast (female)	—	—	0.67	0.71	—	—
Cervix uteri	—	—	0.65	0.62	—	—
Corpus uteri	—	—	0.72	0.76	—	—
Ovary	—	—	0.28	0.32	—	—
Prostate	0.44	0.52	—	—	—	—
Testis	0.73	0.88	—	—	—	—
Bladder	0.31	0.35	0.30	0.33	0.31	0.35
Kidney and renal pelvis	0.42	0.40	0.39	0.45	0.41	0.42
Brain	0.23	0.10	0.20	0.18	0.21	0.13
Thyroid	0.68	0.72	0.75	0.90	0.73	0.85
Non-Hodgkin lymphomas	0.40	0.42	0.34	0.47	0.37	0.45
Hodgkin's disease	0.55	0.81	0.71	0.72	0.61	0.78
Multiple myeloma	0.25	0.31	0.40	0.29	0.32	0.30
Leukaemia	0.25	0.32	0.30	0.30	0.27	0.31
Unknown origin	0.18	0.10	0.14	0.09	0.16	0.09
Total, all cancers	0.43	0.47	0.59	0.62	0.51	0.54
Total, skin non-melanoma excluded	0.31	0.34	0.51	0.52	0.41	0.43

* Probability not assessable.

† Estimates based on less than 5 cases at the beginning of the interval.

Results from Vaud Cancer Registry, Switzerland, 1974–1983.

Relative survival rates were further considered in Table 4 according to two separate age groups (< 60 vs. ≥ 60 years). Survival was generally higher in the younger age groups, but trends over calendar periods were not more favourable in the young for most major sites, including cancers of digestive and respiratory tract, skin cancer and female tumours. A few differences in the modification of relative survival rates over the calendar periods were, however, noted between the two age groups. Changes were larger in older patients as concerns cancer of the prostate and thyroid and non-Hodgkin lymphoma (increases) and connective neoplasms (decrease). Changes in survival were greater or restricted to younger individuals for testis, bladder and leukaemias (improvements) and combined cancers of the upper aero-digestive tract (decline).

DISCUSSION

This study is essentially descriptive in nature, but it offers useful documentation since it is one of the few European population-based series allowing comparison of cancer survival in subsequent calendar periods.

Survival increases were seen for a few relatively rare neoplasms such as testicular cancer (which became the most favourable cancer from a prognostic viewpoint), skin melanoma, thyroid cancer, particularly in females, Hodgkin's disease, non-Hodgkin lymphoma and childhood leukaemia. Also, most female cancers (i.e. breast, corpus uteri, and ovary), and cancer of the prostate and bladder showed increases of a few percentage points.

Less favourable findings have, however, also emerged: not only did 5-year survival rates of a few rare neoplasms such as cancer of the gallbladder and biliary tract, connective neoplasms and brain tumours decrease, but a certain decline was apparent also for tumours of the upper aero-digestive tract, a group which accounts for nearly 10% of male cancer incidence in the registry area [15]. Further, the present data are clearly not reassuring for a number of other major sites, including lung, stomach, liver, pancreas, kidney and brain, for which there was no evidence of appreciable advancements in survival between the mid-1970s and the early 1980s, at least on a population level.

Only survival trends for all cancers together, and a few selected sites such as colo-rectum and childhood neoplasms have been published in the scientific literature from European countries such as Sweden or Britain [7, 20]. In Sweden, for instance, survival from all cancers increased from 34 to 47% in males and from 48 to 57% in females between 1960–1964 and 1980–1984, but these figures do not even take into account the changed distribution across cancer sites [7]. Thus, of further

Table 4. Five-year relative survival rates from various cancers according to age at diagnosis and calendar period

	Age group			
	< 60 years		≥ 60 years	
Cancer site	1974–1978	1979–1983	1974–1978	1979–1983
Mouth or pharynx	0.46	0.34	0.31	0.33
Oesophagus	0.07	0.06	0.07	0.07
Stomach	0.34	0.33	0.18	0.19
Colon	0.61	0.52	0.45	0.45
Rectum	0.55	0.53	0.42	0.45
Liver	0.10	0.07	0.03	0.02
Gallbladder and biliary tract	0.24	0.11	0.13	0.04
Pancreas	0.06	0.04	0.03	0.03
Larynx	0.69	0.57	0.65	0.54
Trachea, bronchus and lung	0.13	0.14	0.06	0.08
Bone	0.62	0.66	0.30	0.34
Connective tissue	0.55	0.62	0.73	0.29
Melanomatous skin cancer	0.72	0.87	0.60	0.68
Non-melanomatous skin cancer	0.97	0.99	0.94	0.94
Breast (female)	0.67	0.73	0.67	0.69
Cervix uteri	0.74	0.76	0.52	0.49
Corpus uteri	0.83	0.86	0.64	0.71
Ovary	0.37	0.43	0.19	0.24
Prostate	0.39	0.41	0.44	0.53
Testis	0.74	0.92	0.63	0.36
Bladder	0.39	0.50	0.28	0.31
Kidney and renal pelvis	0.49	0.52	0.36	0.36
Brain	0.29	0.20	0.10	N/A*
Thyroid	0.91	0.96	0.50	0.69
Non-Hodgkin lymphomas	0.48	0.53	0.28	0.41
Hodgkin's disease	0.68	0.86	0.24	0.51
Multiple myeloma	0.57	0.41	0.24	0.28
Leukaemia	0.29	0.47	0.26	0.20
Unknown origin	0.22	0.11	0.14	0.09
Total, all cancers	0.57	0.62	0.47	0.50
Total, skin non-melanoma excluded	0.50	0.53	0.35	0.37

* Probability not assessable.
Results from Vaud Cancer Registry, Switzerland, 1974–1983.

interest with these European data is the possibility of comparison with larger American data sets, such as the National Cancer Institute's Program [5].

When the changes in relative 5-year survival rates in this study are compared to those published by the SEER Program for the calendar period of 1974–1976 and 1981–1985 [6], three main groups of cancers can be identified. A first group, including a few cancer sites with unfavourable prognosis such as pancreas and lung, behave rather similarly concerning both lack of changes across different calendar periods and survival rate in the most recent quinquennium. A second group, chiefly including cancer sites where recent advances in treatment have or are likely to have occurred (i.e. testis, breast, corpus uteri, all lymphomas and leukaemia), while still showing a substantial superiority of US rates, seem to be moving toward an increasing similarity in relative 5-year survival rates. Finally, the third group includes total cancer mortality and a miscellanea of tumours where the gap between Switzerland and the US is very wide and may even be broadening across the calendar periods under study. This includes tumours of the upper aero-digestive tract and a few sites, like colo-rectum and bladder, for whom both intensive search of early tumours and inclusion in incidence cancer rates of non-invasive lesions of doubtful malignant potential may be more frequent in the USA than in Europe [21].

Cancer patients live longer if better diagnostics and treatments are developed, and this generally occurs to a different extent and/or at different times in middle-aged adults and in the elderly. Thus, a rather complex picture emerges from a comparison of variation in relative survival rates at different ages. Aside from tumours with intrinsic variations in prognosis according to patients' ages (i.e. testicular cancer and leukaemia, on account of more favourable distribution by histological sub-type in the relatively young, and prostatic cancer, possibly on account of weaker hormonal stimulation in the elderly) [22], the substantial increases of a few formerly very low survival rates in older individuals suggest the gradual spread to this age group of more sophisticated diagnostic tools (thyroid) or effective multiple cancer therapies (non-Hodgkin lymphoma and Hodgkin's disease). Overall, however, it is clear that some moderate improvement in survival involves individuals above 60 approximately as much as those below this age, with the regrettable exception of cancer of the cervix uteri whose 5-year survival rates in Vaud, as well as in the SEER data, remain poor and reflect well the low coverage attained by Pap-smear screening programs in elderly women in both countries [23–25].

In conclusion, although it is important to bear in mind a few limitations of the present study (i.e. a relatively low statistical power and the adoption of survival rates in two adjacent quinquennia), a few findings are of interest. Among these, are the persisting favourable trends in the cure rates of cancer of the testis, melanomatous skin cancer, thyroid cancer, childhood leukaemia, Hodgkin's disease and non-Hodgkin lymphoma, especially above age 60. More modest, yet encouraging, findings emerge concerning survival of hormone-dependent tumour sites (including prostate, breast, ovary and corpus uteri). These positive results only marginally affected overall cancer survival statistics, since there were no tangible improvements for most major cancer sites, including a few noeplasms such as colo-rectum and cervix uteri, where there would have been scope for advances, and even some unexpected decline in the survival rate of a few sites, most notably cancers of the upper aero-digestive tract.

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Acknowledgements—The staff of the Vaud Cancer Registry includes Ms G. Kaufmann, Ms N. Puenzieux, Mrs N. Menoud and Mrs G. Descombaz, to whom most of its results and accomplishments are due. We thank the Swiss League against Cancer, Bern for support.

Eur J Cancer, Vol. 28A, No. 8/9, pp. 1495–1500, 1992.
Printed in Great Britain

0964–1947/92 $5.00 + 0.00

Features Articles

Are Tumours Immortal?

Alasdair C. Stamps, Barry A. Gusterson and Michael J. O'Hare

INTRODUCTION

NORMAL MAMMALIAN CELLS in culture exhibit a finite proliferative lifespan before entering a state of irreversible and degenerative growth arrest known as senescence [1,2]. Occasionally, however, a cell escapes from senescence, acquiring apparently unlimited proliferative capacity and giving rise to what is termed an immortal cell line. The widely held notion that all tumours are immortal *in vivo* cannot, however, be rigorously tested by culture. Not only are many tumour cell types difficult to propagate *in vitro*, but the system itself may select for immortalising events occurring after introduction into culture. Thus, whether the equivalent of *in vitro* immortalisation of normal cells is an obligate event in multistep oncogenesis [3–5] cannot be directly answered in this manner. An understanding of the molecular mechanism of immortalisation of normal human cells *in vitro* will supply a genetic definition which can then be tested in the context of tumorigenesis.

SENESCENCE AND GROWTH CONTROL IN NORMAL CELLS

There is good evidence that *in vitro* senescence results from the expression of a biological programme that also operates *in vivo*. Correlations of declining cellular proliferation with age have been made in various tissues in mice [6] and in human epidermis [7]. Phenotypically senescent fibroblasts are also found in ageing hamsters [8]. Serially transplanted normal murine mammary glands exhibit a finite proliferative capacity, as do bone marrow stem cells [9]. The division potential of an individual culture of primary cells appears to be fixed and independent of their chronological age; thus, cells may be maintained in a quiescent, i.e. non-dividing, state for some time and then induced to divide without altering the final division number at senescence [10, 11]. Comparative studies of cell structural protein expression and hormonal responsiveness of cells *in vitro* with ageing tissues *in vivo* have identified a number of morphological and biochemical changes that are common to the two situations [12–16], further supporting the view that senescence *in vitro* reflects an *in vivo* phenomenon. Several groups have also demonstrated an inverse relationship between donor age and proliferative potential *in vitro* [17–20].

THE GENETIC BASIS OF CELLULAR MORTALITY

A number of lines of evidence point to a genetic basis for the mortal phenotype of normal cells. Somatic cell hybrids between primary and immortal cells, or between senescent and "young" fibroblasts, predominantly senesce [21, 22]. Transfer of human chromosome fragment 1q23–25 to immortal hamster fibroblasts induces senescent growth arrest [23, 24]. Thus, senescent potential is dominant over immortality. Cell fusions between disparate immortal human cell lines have shown that there are four

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Revised 13 Feb. 1992; accepted 19 Feb. 1992