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LAWYERS' WORK PRODUCT
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October 31, 1983

Dr. William Gaffey
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Dear Bill:

I am sure that you have seen the enclosed. Do you consider this as unique or are there other such reports which implicate working in a chlorophenol-producing and/or -using plant with lymphomata?

I would like you thoughts on this if you have the time.

Thanks for your help on this.

Very truly yours,

WEINBERG CONSULTING GROUP Inc.
Myron S. Weinberg, Ph.D.

MSW/vh

Enclosure

extremities (10%), unspecified debility (3%), and speech troubles (2%). Combinations of disabilities were common. There was considerable variation between the assessment made by the G.P., the district nursing services, and the geriatric department regarding the incidence of these types of disabilities. The numbers cited correspond to the assessment made by the geriatric department.

Two-thirds of the referred pensioners wished for, or at least contemplated, a change of accommodation. Requests for allocation of accommodation in nursing-homes were met in about 50% of the cases, whereas only 23% of the requests for sheltered housing were met. After assessment, treatment and provision of necessary services and improvements in living conditions it was decided, in 51% of cases, that the referred pensioner could and should remain at home.

Almost all of the pensioners had been referred because of imminent or established breakdown in their ability to cope independently in their own homes. The figures demonstrate that geriatric assessment and consequent action help many elderly people to continue independent living outside institutions —and such assessments reduce (by half) the need for institutional care for frail elderly people.

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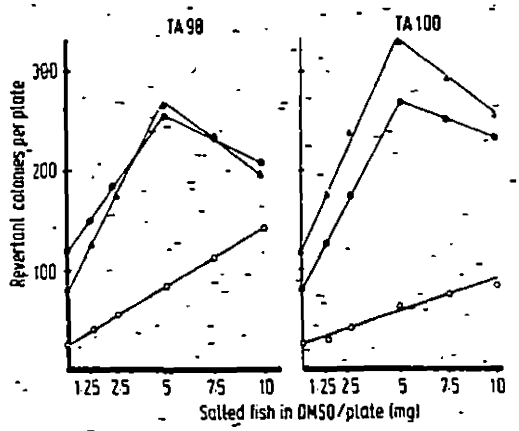
SALTED FISH AND NASOPHARYNGEAL CARCINOMA IN SOUTHERN CHINESE

SIR,—The unusually high incidence of nasopharyngeal carcinoma (N.P.C.) in southern Chinese both in and outside China has been known for over fifty years and is thus likely to be the product of a traditional environment peculiar to southern Chinese. The age-specific incidence curves for southern Chinese of both sexes rises steeply after the age of 19–24 years. Ho,[1-3] has suggested that the ætiology involves an interaction between a genetically determined susceptibility, early infection by the ubiquitous Epstein-Barr virus (E.B.V.), and consumption of a traditional preserved food by southern Chinese from early childhood. Salted fish, a traditional food frequently consumed during weaning and post-weaning periods, contains a variety of volatile nitrosamines,[4-6] compounds which induce tumours in the nasal cavities and/or nasopharyngeal tube in animals.[7-10] Carcinomas appeared in the nasal cavity and maxillary sinus of 4 of 22 albino rats fed salted fish for 12–24 months (ref. 11 and unpublished).

We have applied the Ames mutagenicity test[12] using the TA100 and TA98 strains of *Salmonella typhimurium* and mammalian microsomal (S-9 mix) activation to extracts of salted fish and to the urine of albino rats which had consumed such fish. Salted-fish extracts were prepared by mincing and suspension in dimethylsulphoxide (2 ml/g of fish) with vigorous shaking for 24 h and centrifugation at 10 000 rev/min for 10 min at room temperature. The Ames test was done with the supernatants.

Urine samples were collected for 72 h from 4 pairs of fish-consuming rats and 4 pairs of controls (matched for sex, age and body-weight). The test animals were fed daily with steamed cooked salted fish and fresh water, whereas the control rats were given fresh water and animal chow salted to the concentration found in the salted fish. Pooled urine from each pair of rats was concentrated about a 100-fold,[13] dissolved in 4 ml dimethylsulphoxide, and subjected to the Ames test.



Mutagenic activity of extracts of salted fish.
o bacteria without S-9 mix; ● bacteria with S-9 mix; Δ bacteria with S-9 mix and Yahagi's[14] procedure.

Mutagenic activity for both TA100 and TA98 was found in all the salted-fish preparations tested and all showed a dose-responsive curve (see figure). Since TA100 and TA98 detect different mutagens, there was probably more than one mutagen in the preparations tested. In most cases mutagenic activity was enhanced by liver microsomal activation, and in some cases also by preincubating the bacteria with S-9 mix at 25°C for 20 min before the test.[14] This procedure causes selective enhancement of the activity of N-nitroso compounds, suggesting that some of the mutagens in the samples tested are N-nitroso compounds.

Mutagenic activity was also found in urine from the experimental rats with a dose-response relationship.

Our findings may explain the induction of carcinoma in rats fed with salted fish[16] and the high incidence of N.P.C. in southern Chinese, although one must be cautious in extrapolating events in animals, especially under experimental conditions, to the human situation.

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FAMILIAL AND SPORADIC HODGKIN'S DISEASE ASSOCIATED WITH OCCUPATIONAL WOOD EXPOSURE

SIR,—The aggregation of Hodgkin's disease in communities and families has suggested the influence of environmental risk factors, particularly of an infectious nature.[1] Evidence implicating industrial or chemical agents has been scarce, although an excess risk has been reported among woodworkers[2,3] and organic chemists.[4]

An occupational exposure may have contributed to a fami-

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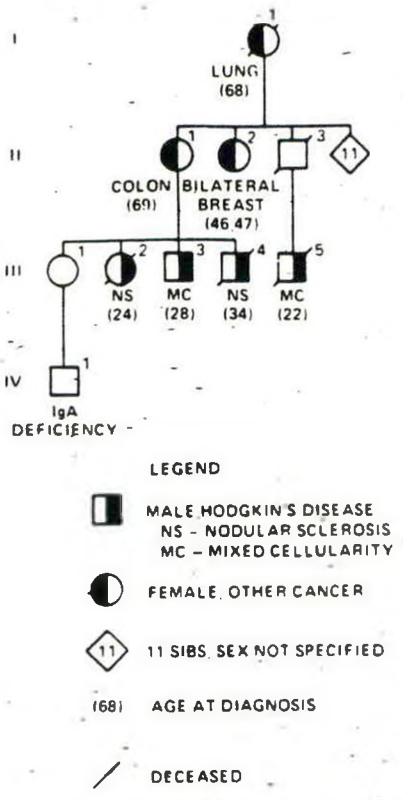

Pedigree of a familial Hodgkin's disease kindred (N.C.I. Epidemiology Branch no. 323).

lial occurrence of Hodgkin's disease affecting three sibs and a first cousin (see figure). All cancers reported were histologically verified. Except for one child with isolated IgA deficiency (IV-1), detailed laboratory investigation of family members showed no abnormalities of immune function, chromosome structure, or Epstein-Barr virus titre. Two brothers with Hodgkin's disease (III-3, 4) had been employed by a fence-installation company for 15 and 12 years, respectively, and worked primarily with cedar wood products immersed in a fungicide/insecticide solution, pentachlorophenol (P.C.P.). The brothers prepared and applied the preservative solution by hand, without protective clothing, and the one sib still employed at the time of study had high levels of P.C.P. in the serum (1299 p.p.b.) and urine (90 p.p.b.). There were no similar exposures in the remaining two familial cases. Hodgkin's disease (nodular-sclerosis type) also developed in an unrelated 31-year-old employee of the same company (average number of workers 15).

Since a positive association between woodworking and Hodgkin's disease has not been consistently observed, we examined the occupational statements on death certificates in North Carolina counties with a significant proportion of the population employed in furniture manufacturing and lumbering. In an earlier study,[5] this approach was used to confirm the relationship between nasal cancer and woodworking previously reported in the U.K. Between 1956 and 1974, there were 167 deaths from Hodgkin's disease among white males. To each case, two control certificates chosen from other causes of death were matched by sex, race, county of death, age, and year of death. An excess risk was found only among occupational groups with wood and paper exposure. Matched triplet analysis revealed a relative risk of 1·4 (95% confidence interval 0·8–2·3). The major difference occurred for carpentry and lumbering, with a relative risk of 4·2 (95% confidence interval 1·4–12·5).

Reports of Hodgkin's disease among workers in the wood industry have stimulated interest in various physical properties of wood.[6,7] In the family under study, there was conspicuous exposure to chemical preservatives, notably P.C.P., which is extensively used in the lumber and wood industry (1969 world production $2{\cdot}1\times10^6$ kg). However, only two of the four family members with Hodgkin's disease were occupationally exposed, suggesting the interplay between genetic and environmental determinants, as illustrated by the susceptibility to radiogenic cancers among persons with xeroderma pigmentosum, bilateral retinoblastoma, or the basal-cell nævus syndrome.[8] However, P.C.P. easily escapes from the workplace into the general environment,[9,10] especially water supplies, and is present in the urine of occupationally exposed and "normal" individuals.[11] P.C.P. is not known to be carcinogenic, but data are limited and commercial preparations usually contain structurally related compounds, like dioxin, which is carcinogenic in rodents.[12] Since P.C.P. is applied to lumber at many stages in its processing, beginning at the sawmill, unrecognised exposure may occur among many wood-utilising occupational groups. Thus, it may be that the association between occupational wood exposure and Hodgkin's disease (and perhaps nasal cancer) is related to the use of particular chemical preservatives.

We thank Dr Lyle Wong of the Hawaii Epidemiologic Studies Program for P.C.P. determinations on patient III-3.

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CHROMOSOMAL DAMAGE AND HAIR DYES

SIR,—Having been asked by a U.S. Congressional committee to evaluate the quality of certain epidemiological studies of the possible carcinogenicity of hair dyes I read the July 15 paper by Dr Kirkland and colleagues (p. 124). For teaching physicians about research methodology and biostatistics this report could be used as a "museum of pathology", displaying a plethora of violations of fundamental scientific principles.

(1) The study cannot be reproduced because the procedure used to obtain the two groups under investigation is not described, except for a statement that they were "volunteers".

(2) In most such studies the number of controls equals (and often exceeds) the number of cases. Kirkland et al. do not explain why they compared 36 controls and 60 hair tinters.

(3) Having designed a study to test a hypothesis about the effects of hair dyes on tinters and non-tinters Kirkland et al. analysed the data and found no difference in the two groups. They then defined a new hypothesis, and, using the same data, constructed new sets of cases and controls. The results of this post hoc act of hypothesis generation are presented and interpreted as though they emerged from a valid act of hypothesis testing.

(4) The authors examined 100 cells in all of 96 people. I would expect the results to be expressed in terms of damaged people, but all the data are shown only for the 9600 cells counted. 132 chromatid breaks in 2800 cells of a group of 28 subjects (mean 0·047 breaks per cell) does not tell us whether 2 subjects each had 66 breaks and 26 had no breaks or whether the 28 subjects all had 4 or 5 breaks. Furthermore, the subsequent statistical analyses are improperly conducted as

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