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PROPORTIONAL MORTALITY AMONG DINGY-CHLORINE
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Brief Summary

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SUMMARY:

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226 lesions. Finally, radiology indicates only a possible and not the actual source of bleeding, and where two lesions are seen endoscopy has the unique value of actually demonstrating the true site of bleeding. Thus radiology should be carried out only when endoscopy has proved negative.

Endoscopy in Relation to Management

The value of early endoscopy in management is that it tells the clinician the site of bleeding and the nature of the underlying lesion. Since acute mucosal lesions often heal rapidly and may be difficult to deal with surgically, while chronic peptic ulcers tend to rebleed and to be amenable to surgery, endoscopic information could allow early decisions on management. However, whether or not this will reduce mortality remains to be evaluated. Other possible benefits from early endoscopy, such as reduction in blood-transfusion and reduced hospital stay, must also be evaluated.

Emergency Endoscopy Services

For the best possible results endoscopy should be carried out within 24 hours of the patient's admission, although there is still a good diagnostic yield up to 48 hours after admission. Early endoscopy involves the endoscopist in much time and effort, and, if adequate facilities with properly trained paramedical

staff are not easily available, it is prohibitively time consuming.

It is inconceivable that a district general hospital with one gastrointestinal consultant trained in endoscopy could provide an adequate service for acutely bleeding patients. Such hospitals planning to develop an endoscopy service should bear the manpower aspects carefully in mind when doing so. Ideally two consultants with the help of middle-grade medical staff trained in endoscopy should be employed in each hospital.

Requests for reprints should be addressed to J. A. H. F.

REFERENCES

1. Memorandum on Future National Needs for Fibre-optic Endoscopy of the Gastrointestinal Tract. British Society for Digestive Endoscopy, 1973.
2. Palmer, E. D. *J. Am. med. Ass.* 1969, 207, 1477.
3. Crook, J. N., Gray, J. W., Nancoy, F. C., Cohn, I. *Ann. Surg.* 1972, 175, 771.
4. Allen, H. M., Block, M. A., Schuman, B. M. *Archs Surg.* 1973, 106, 449.
5. Sugawa, C., Werner, M. H., Hayes, D. F., Lucas, C. E., Walt, A. J. *ibid.* 1973, 107, 133.
6. Katon, R. M., Smith, F. W. *Gastroenterology*, 1973, 65, 728.
7. Cotton, P. B., Rosenberg, M. T., Waldram, R. P. L., Axon, A. T. R. *Br. med. J.* 1973, ii, 505.
8. McGinn, F. P., Wilken, B. J. *J. R. Coll. Surg. Edinb.* 1974, 19, 112.
9. Forrest, J. A. H., Finlayson, N. D. C. *Br. J. Hosp. Med.* (in the press).
10. Dvorakova, H., Jirasek, V., Setka, J. *Urgent Endoscopy of Digestive and Abdominal Diseases*; p. 48. Basel, 1972.
11. Allan, R. N., Dykes, P. W., Toye, D. K. M. *Br. med. J.* 1972, iv, 281.

Public Health

PROPORTIONAL MORTALITY AMONG VINYL-CHLORIDE WORKERS

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Summary In a proportional-mortality analysis of one hundred and sixty-one deceased workers in two plants using vinyl chloride, a 50% excess of deaths due to all cancer was seen. Specific sites of cancer with the greatest excess included liver and biliary tract, lung, and brain. The excess in fatal cancer was seen mainly in men who died before age 60. Also, there was a trend in time in the ratio of observed to expected deaths: since 1970 over twice as many cancer deaths as expected have occurred.

INTRODUCTION

ON Feb. 15, 1974, four fatal cases of angiosarcoma of the liver among men who worked in a polyvinyl-chloride polymerisation plant were reported.¹ We present here a proportional-mortality analysis of all deaths known among workers in that plant. Also included are deaths in men who worked in a plant in which vinyl chloride is produced.

METHODS

Vinyl-chloride monomer is produced at a plant in Calvert City, Kentucky, and is polymerised into polyvinyl chloride at a plant in Louisville. These plants have been in operation since the late 1930s.

Whenever an active or pensioned employee at these plants dies, a copy of the death certificate is obtained. An abstract of the certificate is made and the certificate is sent to the insurance company. Using these sources, one hundred and sixty-one deceased White males who were employed at one of the two plants were identified. No information was available on workers who left employment before retirement. For all but nineteen a copy of the death certificate was obtained. For the remainder the cause of death as recorded in the company abstract was used. Deaths from 1947 through 1973 were ascertained. Of these deaths, one hundred and thirty-five occurred among Louisville workers and twenty-six were among Calvert City workers.

The distribution of causes-of-death was tabulated using the code on the death certificate. The expected distribution was calculated on the basis of proportional-mortality ratios for United States White males. The observed deaths from all causes were stratified into 5-year age/time-specific groups, and age/time/cause-specific proportional-mortality ratios were multiplied by these numbers to obtain the stratum-specific expected numbers.²

RESULTS

The patterns of mortality among workers in the two plants were similar, so all men were grouped together. As seen in table 1, a 50% excess of deaths due to cancer was observed ($\chi^2=5.7$, $P<0.02$). In addition to the four deaths previously reported,¹ a fifth man who died of angiosarcoma of the liver was identified. Also, there was one cancer of each of the following sites: gallbladder, common bile duct, and

TABLE 1—OBSERVED AND EXPECTED DEATHS IN VINYL-CHLORIDE WORKERS*

I.C.D. no.†	Cause of death	Observed	Expected	Obs./exp.
..	All	161	161.0	1.0
140-205	All cancer	41	27.9	1.5
150-159	Digestive	13	8.3	1.6
155	Liver and biliary tract	8	0.7	11.0
162, 163	Lung	13	7.9	1.6
193	Brain	5	1.2	4.2
200-205	Lymphatic and haematopoietic	5	3.4	1.5
..	Other cancer‡ ..	5	7.1	0.7
330-334	C.N.S. vascular ..	8	9.5	0.8
400-408	Circulatory	66	68.6	1.0
800-998	External	22	24.5	0.9
960-969	Suicide	10	5.3	1.9
..	All other causes§ ..	24	30.5	0.8

* Expected numbers based on age/time/cause-specific proportional-mortality ratios for U.S. White males.

† International Classification of Diseases, seventh revision.

‡ Nasopharynx 1, prostate 1, kidney 1, thyroid 1, undetermined 1.

§ Includes 2 cirrhosis (4.4 expected).

liver (type unspecified). There were five brain tumours—three glioblastoma multiforme and two of unspecified type. There was a 60% excess of cancer of the lung, of the following cell types: bronchogenic (one), anaplastic (one), adenocarcinoma (three), unspecified (eight). There were two unusual other types of cancer—thyroid and nasopharynx.

There was an excess of deaths due to suicide: ten observed and about five expected.

The observed and expected numbers of all cancer according to age and year of death are presented in table II. Excess death due to cancer was seen primarily in men who died before age 60. There was a trend in the observed/expected ratio with year at death. Before 1965 no excess of deaths due to cancer was observed. However, since then there has been an increase in the proportion of death due to cancer, so that since Jan. 1, 1970, death from cancer has occurred twice as frequently as would be expected on the basis of U.S. vital statistics data.

TABLE II—OBSERVED AND EXPECTED DEATHS DUE TO ALL CANCER ACCORDING TO AGE AND YEAR OF DEATH

Characteristic	Category	Observed	Expected	Obs./exp.
Age at death (yr.) ..	< 50	11	7.6	1.4
	50-59	17	8.1	2.1
	60+	13	12.2	1.1
Year of death ..	< 1965	12	11.4	1.1
	1965-69	10	7.3	1.4
	1970+	19	9.2	2.1

DISCUSSION

These data include the original four vinyl-chloride workers who were known to have died with angiosarcoma of the liver. Four other workers with fatal cancer of the liver and biliary system have been identified. In addition, there is a suggestion that at least two other types of cancer—lung and brain—appear with excess frequency in vinyl-chloride workers. It also appears that the relative frequency of all cancers is increasing with time. While no projection may be made with certainty, additional excess cancer among vinyl-chloride workers would seem likely.

An analysis using proportional-mortality ratios does not take into account the absolute risk of dying in the population being studied. Thus, it is possible that the mortality-rate in the vinyl-chloride workers is less than that of the United States population. For example, the mortality in White steelworkers was 86% of that expected² and in White cotton textile workers 79% of that expected.¹ However, even if each of the observed/expected ratios in table II were multiplied by 0.8 (80%) an excess of cancer, especially of the liver and biliary tract and brain, would prevail. Further, the increase with time in the ratio for all cancers would still be observed, since each of the observed/expected ratios in table II would be multiplied by 0.8.

Another theoretical objection to a proportional-mortality analysis is that a high ratio of observed to expected deaths may be due either to an excess of one cause of death or a deficit of another cause of death. Based on the data in table I, it seems most likely that the high ratio for cancer reflects an excess of cancer, since the ratios for each of the four major categories other than cancer are all in the range of 0.8-1.0.

It will be several years before a final conclusion can be made with respect to the carcinogenic potential of vinyl chloride. Since any harmful effect in an individual may require many years of exposure, we believe that current exposure must be controlled.

Requests for reprints should be addressed to R. R. M.

REFERENCES

1. Creech, J., Johnson, M. N., Block, B. *Morbidity Mortality*, 1974, 23, 49.
2. Monson, R. R. *Computers biomed. Res.* (in the press).
3. Lloyd, J. W., Cusick, A. J. *Occup. Med.* 1969, 11, 299.
4. Henderson, V., Enterline, P. C. *ibid.* 1973, 15, 717.

Packaging for Safety

HOSPITAL admissions of children with suspected accidental poisoning by medicines: are not on the increase, and death of the child is a very unlikely result of such incidents. All the same, the work-load involved, the unpleasant nature of the treatment, and the worry to parents justify a hard look at any proposal to make medicines safer. A working-group of the Medicines Commission has just reported on the packaging aspects of this question.* The working-group opposes the compulsory introduction of reclosable child-proof containers and comes down in favour of a stepwise introduction of non-reclosable containers, where potentially dangerous tablets and capsules are packed in individual units in strip or blister packs. Among the objections to the reclosable containers comes one from the Department's lawyers; under the draft British Standard such containers would need to be tested on children who would have to be taught how to open them to see if they were capable of repeating the operation. If a child so tutored poisoned himself the testers might be held liable. But the D.H.S.S. legal division adds a further objection: "the position in law is that no parent or guardian of a child of tender years is entitled to give consent to any procedure which is not for the benefit of the child." Medical research workers have long feared that this was so, but has the Department, now the commissioner of much clinical research, stated this publicly before?

* Medicines Commission. Report on the Presentation of Medicines in Relation to Child Safety. Obtainable from the D.H.S.S., 31 Finsbury Square, London EC2A 1PP.

cranial aneurysms during the time from initial haemorrhage until surgical treatment.^{1,2}

A year ago we adopted a regimen of 4 g. E.A.C.A. 4-hourly in such patients, but it was our clinical impression that there was little change in the rebleeding-rate and several haemorrhages recurred on the night before operation. The E.A.C.A. blood level falls steadily over the 2 or 3 hours after intravenous administration, implying that there may be a "rebound phenomenon" by 4 hours.³

The dosage regimen of E.A.C.A. was therefore changed to 3 g. 2-hourly. Since using this higher dosage five patients out of nine have had a second subarachnoid haemorrhage before they could be treated surgically (see accompanying table).

RESULTS OF HIGHER-DOSE REGIMEN OF E.A.C.A. IN PATIENTS WITH SUBARACHNOID HAEMORRHAGE

Sex	Age (yr.)	Site of aneurysm	Spasm	Grade on admission	Re-bleed	Final grade
M	42	Middle cerebral artery	-	I	?	II
F	49	Anterior communicating artery	+	I	+	Dead
F	49	Posterior communicating artery	+	II	3+	Dead
F	41	Posterior communicating artery	-	I	+	III
M	50	Posterior communicating artery	-	I	-	I
M	37	Multiple	-	I	+	I
F	48	Multiple	-	I	+	Dead
F	66	Posterior communicating artery	+	II	-	II
F	36	Multiple	-	I	-	I

Grade I = fully oriented and no signs.

Grade II = confused or neurological signs.

Grade III = chronic vegetative state.

We have lately seen a case of extensive muscle necrosis in an obstetric patient on the lower-dose regimen. Thromboembolic complications during E.A.C.A. therapy have been reported, including peripheral gangrene; thrombosis in the coronary, gastrointestinal, and glomerular vessels; and pulmonary embolism from deep-vein thrombosis.^{4,5} Cerebral angiographic changes resembling arteritis or intravascular thrombosis have been reported in three of seven patients receiving E.A.C.A.⁶

Although we realise that the number of patients involved is too small for statistical analysis, the benefits of E.A.C.A. therapy in subarachnoid haemorrhage from ruptured intracranial aneurysm do not seem to justify the potential risks, and we feel deterred from proceeding with a therapeutic trial. We would, therefore, be interested to hear of the experiences of others.

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1. Mullen, S., Dawley, I. *J. Neurosurg.* 1968, 28, 21.
2. Ransohoff, J., Goodgold, A., Benjamin, M. V. *ibid.* 1972, 36, 525.
3. Patterson, R. H., Harper, P. *ibid.* 1971, 34, 365.
4. Charyton, C., Pantilo, D. *New Engl. J. Med.* 1969, 280, 1102.
5. Naeve, R. L. *Blood*, 1962, 19, 694.
6. Sonntag, V. K. H., Stein, B. M. *J. Neurosurg.* 1974, 40, 480.

PROPORTIONAL MORTALITY AMONG VINYL-CHLORIDE WORKERS

SIR,—As indicated by Purchase and Williamson (Sept. 7, p. 591) it is desirable in studies of mortality and proportional mortality to compare disease-rates in a study group with those from a similar community. However, tabulations of deaths in the United States are not available in sufficient detail by age, time, sex, race, and cause to permit county-specific or, for many diseases, State-specific comparisons.

A recent publication is an invaluable aid in assessing the degree of bias likely to be introduced by using national data.¹ Average annual age-adjusted cancer-mortality rates per 100,000 for White males in Jefferson County, Kentucky, where Louisville is situated, compared with rates for the United States (in parentheses) are: biliary passages and liver 5.5 (5.2), primary and secondary trachea, bronchus, and lung 43.9 (38.0), brain and other parts of central nervous system 4.5 (4.4), all malignant neoplasms 184.0 (174.0). Also, mortality in 1960 for all causes for Kentucky White males is similar to that for United States White males²—973.6 (956.2). There is no indication in these data that use of proportional mortality for United States White males could account for the observed/expected ratios reported in our paper (Aug. 17, p. 397).

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1. Mason, T. J., McKay, F. W. *U.S. Cancer Mortality by County: 1950-69.* Department of Health, Education and Welfare Publication no. (N.I.H.) 74-615. Washington, 1974.
2. Grove, R. D., Hetzel, A. M. *Vital Statistics Rates in the United States; 1940-60.* Public Health Service publication no. 1677. Washington, 1968.

Obituary

ARTHUR HENRY DOUTHWAITE

M.D.Lond., F.R.C.P.

Dr A. H. Douthwaite, consulting physician emeritus to Guy's Hospital, London, died on Sept. 24 at the age of 78.



He was born in China and educated at Bristol Grammar School, the University of Bristol, University College London, and Guy's Hospital. He was a civilian prisoner-of-war in Ruhleben, Germany, from 1914 to 1918, and he entered Guy's in 1919, qualifying in 1921. In 1922 he became M.R.C.P. and was appointed medical registrar at Guy's. Ill-health led him to leave London and work in general practice in Worthing for a few years, but he returned to Guy's as assistant physician in 1927. He remained at Guy's until his retirement as senior physician in 1965. His published work included

R&S 110791