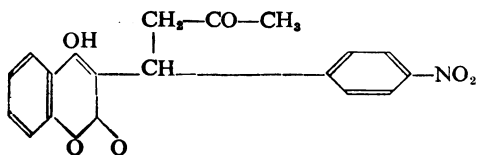


Montigel and Pulver, 1955). It is a coumarin derivative with the following formula:



Nicoumalone: 3-[α -(4'-nitrophenyl)- β -acetylethyl]-4-hydroxy-coumarin.

Like other derivatives of coumarin its main action is to depress factor VII, and later, and to a less extent, prothrombin, though after several weeks of treatment both substances are equally affected (Moeschlin and Schorno, 1955).

It is not cumulative, and rapidly disappears from the body, being excreted unaltered in the urine.

It is of low toxicity in animals (Pratt, 1956), the mouse LD_{50} being 1,470 mg./kg. body weight compared with 270 mg./kg. in the case of dicoumarol. It is practically tasteless and is well tolerated by patients.

In this study no attempt has been made to assess the drug on purely clinical grounds—that is, incidence of deaths among patients with coronary artery disease, or the frequency of spontaneous haemorrhage. This omission has been allowed for two reasons. Firstly, because such statistics are often difficult to interpret and may be misleading (Honey and Truelove, 1957). Secondly, because it seems a reasonable deduction that the clinical results are but a reflection of the stability, or otherwise, of the "prothrombin" level during anti-coagulant therapy. The patient with the "straight line graph" is less likely to suffer the hazards of extending thrombosis or dangerous haemorrhage than his less fortunate neighbour whose tests indicate widely fluctuating "prothrombin" levels from day to day.

Only two cases of severe spontaneous haemorrhage have occurred in this series of patients receiving nicoumalone. In one instance the patient exhibited abnormal sensitivity to the drug, a "prothrombin" activity of less than 10% being recorded after the patient had received a total of only 12 mg. in 48 hours. In the second instance melaena occurred in a patient with a history of probable gastric ulcer. In this case also the "prothrombin" activity was less than 10%.

The results recorded in Table II and in the Graph indicate that a high degree of stability of the "prothrombin" level may be anticipated with the use of nicoumalone. This is likely to be accompanied by an improved prognosis among patients with thrombo-embolic phenomena.

Conclusion and Summary

Nicoumalone, a new coumarin derivative, represents a step forward in the search for the ideal anticoagulant.

The stability of the "prothrombin" levels of 269 patients receiving nicoumalone is compared with the same in 117 patients receiving indema and 242 patients receiving dindevan. In this series the results with nicoumalone are superior to those obtained with the other two drugs.

The properties of this new anticoagulant are briefly reviewed.

My thanks are due to Dr. W. W. Walther for reading the manuscript and for his advice.

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MASS RADIOGRAPHY AND CANCER OF THE LUNG

BY

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During 1955, the last year for which national figures have been published, mass radiography units in England and Wales detected 1,482 cases of cancer of the lung and mediastinum (Ministry of Health, 1957a). National morbidity figures for new cases of cancer of the lung are not available, but the 17,272 deaths from cancer of the lung during that year (Ministry of Health, 1956) suggest that at present mass radiography does not find more than 10% of all new cases of cancer of the lung in England and Wales. It must be added that of the above figures almost half were not detected by conventional routine mass radiography, but at sessions for symptomatic cases referred by general practitioners, a type of service now widely employed by many units. The organization and deployment of the mass radiography units in the Birmingham Region have recently been described by one of us (McDowell, 1958).

The small contribution of the service to the finding of a highly fatal disease, such as carcinoma of the lung, is thought by many to be a major challenge. From the public health viewpoint the problem is, of course, entirely different from that of tuberculosis; the community derives no epidemiological benefit from finding cases of cancer whether they are curable or not, and the results are purely personal. Nevertheless, if it could be shown that mass radiography improves the prognosis for this disease by "early diagnosis" it could be argued that the present mass radiography policy needs revising and that an intensive national campaign for periodical chest x-ray examination of persons in the critical age groups is called for.

In the United States some workers believe mass radiography to be an effective method for finding cases with good chances of operability and survival (Overholt and

Schmidt, 1949; Guiss, 1952; Rigler *et al.*, 1953; Overholt *et al.*, 1955), but other American authors take a rather pessimistic view (Ehler *et al.*, 1954; Boucot and Sokoloff, 1954; McNulty, 1954).

In this country little information about the fate of cancer cases found by mass radiography is available. The allegedly better prognostic chances for such cases have so far been deduced from very small numbers only (Nicholson *et al.*, 1957).

A follow-up study of a large number of cases discovered by mass radiography seemed therefore desirable, and since July, 1955, we have been collecting information about all such cases in the Birmingham Region. The present contribution deals with 238 out of 240 male cases found by six mass radiography units of the Birmingham Regional Hospital Board in the twelve months following July 1, 1955, whose fate had been traced by the Regional Cancer Registry after twelve months.

This paper compares cases found by conventional routine mass radiography and patients referred to the units by general practitioners. The main point of interest is a comparison of resectability rates between these two groups. In the course of the investigation we found much confirmatory evidence of certain aspects of the disease, published by other authors, particularly with regard to age-and-sex distribution, histological types, and smoking habits. In these respects we do not claim to contribute anything new, and relevant data are shown only in their relation to the main subject of interest.

The number of female cases found during the period under review was too small to give useful statistical information, and the paper deals therefore only with men.

Methods of Investigations

Basically all units followed the usual mass radiography procedure and used the 35-mm. film. In addition we recorded on specially designed forms information about area of residence, occupational histories, tobacco habits, principal and first clinical symptoms, the time of first consultation with general practitioners,

and radiographic characteristics. All records were statistically analysed centrally by one of us (K.W.C.).

The methods of further investigations varied slightly from unit to unit. Generally speaking, cases with suspected neoplasms were referred to thoracic surgeons direct, but in a number of cases patients were first seen by chest physicians. A few patients, in whom further investigations established cancer of the lung, were referred from the M.M.R. unit with a preliminary diagnosis other than malignant disease, mostly pneumonitis, post-pneumonic or tuberculous pleural effusion, pulmonary tuberculosis, or progressive massive fibrosis.

Criteria of Diagnosis.—We included in the analysis only such cases where the diagnosis was either established by bronchoscopy, biopsy, cytological or histological examination, or necropsy (established cases), or where in the absence of such evidence two independent sources agreed that the course of the disease left no reasonable doubt about its nature (corroborated cases). The proportion of established to corroborated cases was 4:1, and it seems highly unlikely that this series includes a statistically significant number of misdiagnosed cases.

General Background of Investigation

Tables I and II show the findings of the six units during the calendar year 1956. This period was chosen because age and sex specific information of the number of examinees was easily available from the sample of M.M.R. returns analysed by the Registrar-General. The differences between the actual number of cases found during the year (277) and that of cases under review (240) in no way affect the following argument.

Table I, which includes all men above the age of 15, clearly shows that the number of cases found by each individual unit depended largely on the nature of its work. The Birmingham Static Unit, for instance, which discovered almost half of all cases, examined a high proportion of general-practitioner cases. For all units the case-finding rates for general-practitioner patients was 29 times as great as for volunteers at routine surveys, thus emphasizing the high selection of general-practitioner referrals.

TABLE I.—Cases of Carcinoma of Lung in Men Discovered by Mass Radiography in Birmingham Region in 1956

Unit	General-practitioner Referrals			Routine Surveys			All Men		
	X-rayed	No. of Cases	Rate per 1,000	X-rayed	No. of Cases	Rate per 1,000	X-rayed	No. of Cases	Rate per 1,000
Birmingham static ..	14,190	146	10.3	19,140	3	0.2	33,330	149	4.5
.. mobile ..	2,810	19	6.8	36,460	13	0.4	39,270	32	0.8
Stoke-on-Trent ..	3,200	16	5.0	39,320	14	0.4	42,520	30	0.7
Wolverhampton ..	2,820	20	7.1	27,420	6	0.2	30,240	26	0.9
Dudley ..	2,230	17	7.6	17,970	5	0.3	20,200	22	1.1
Coventry ..	460	5	10.9	33,300	13	0.4	33,760	18	0.5
All units ..	25,710	223	8.7	173,610	54	0.3	199,320	277	1.4

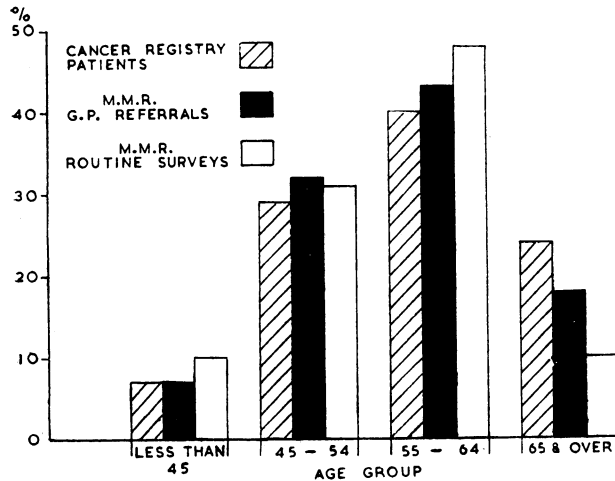
TABLE II.—Age Distribution of Males with Carcinoma of Lung Discovered by M.M.R. Units in Birmingham Region during 1956

Age Group	General-practitioner Referrals			Routine Surveys			All Men		
	No. of Examinees	No. of Cancer Cases	Rate per 1,000	No. of Examinees	No. of Cancer Cases	Rate per 1,000	No. of Examinees	No. of Cancer Cases	Rate per 1,000
< 35	9,860	3	0.3	98,320	1	0.0	108,180	4	0.0
35—	5,390	16	3.0	34,060	3	0.1	39,450	19	0.5
45—	4,850	70	14.4	24,270	15	0.6	29,120	85	2.9
55—	2,080	41	19.7	8,520	15	1.8	10,600	56	5.3
60—	1,780	50	28.1	4,900	9	1.8	6,680	59	8.8
65+	1,720	43	25.0	3,390	11	3.2	5,110	54	10.6
All ages	25,680	223	8.7	173,460	54	0.3	199,140	277	1.4

The age of 180 examinees was not stated.

Results

Age Distribution.—In the Chart comparison is made between the age distribution of the 238 cases in this series and of 824 men suffering from cancer of the lung and registered from all sources with the Regional Cancer



Percentage age distribution of male lung cancer cases. Mass radiography cases and patients registered with the Birmingham Regional Cancer Registry in 1956.

Registry in Birmingham in 1956. It is clear that the age distribution of both our groups is fairly typical for the region as a whole, with the exception of a slight deficiency of mass radiography cases in the oldest age group.

TABLE III.—Current Smoking Habits of Cancer Cases and of Male Population in the Midlands (Percentage Distributions)

Group	Non-smokers	Cigarettes Consumed per Day			Total
		<15	15-24	>24	
G.P. referrals ..	6.4	21.6	43.3	28.7	100.0
Routine surveys ..	7.3	24.4	41.5	26.8	100.0
All cancer cases ..	6.6	22.2	42.9	28.3	100.0
Male population in Midlands ..	29.1	38.5	25.3	7.1	100.0

TABLE IV.—Distribution of Cases According to Predominant Cell Type (Percentage Distributions)

Group	Squamous	Undifferentiated	Adeno-carcinoma	Others	All Cases with Known Type
G.P. referrals ..	62.1	31.1	3.9	2.9	100.0 (103)
Routine surveys ..	51.9	33.3	3.7	11.1	100.0 (27)
Both sources ..	60.0	31.5	3.9	4.6	100.0 (130)

Smoking Habits.—Table III shows the low proportion of non-smokers in both groups of cancer patients. Amounts of tobacco consumed by pipe or “mixed” smokers have been converted into their cigarette equivalents in accordance with the usual formula. The close agreement between smoking habits in these two entirely different groups should be noted if only to emphasize the striking difference in smoking habits between the cancer cases and a cross-section of the male population in the Midlands (Cross *et al.*, 1958) after standardization with respect to age.

Histological Cell Type.—A histological diagnosis became available in 130 (55%) of all cases, which is slightly lower than the histological confirmation rate (62%) reported by Bignall (1958a) in a larger series from two London hospitals. In Table IV we attempted

to group these cases on the lines suggested by Hinson (1958). This was possible in all but six cases, which are shown as “others.” The group of “undifferentiated neoplasms” includes the oat-cell type. The table suggests a close similarity of the histological pattern in both groups, although the numbers of routine survey cases are rather small. Because of the lack of uniform reporting on histological specimens and of the different pathological material used in other investigations, comparisons with results elsewhere are difficult. Approximately 60% of our histological reports were based on resection specimens, and the proportion of types in this series is very similar to the distribution of cell types in resection specimens reported from two neighbouring regions (Nicholson *et al.*, 1957; Gifford and Waddington, 1957).

Twelve Months' Survival, Irrespective of Treatment.—Twelve months after attendance at the M.M.R. units 69 general-practitioner cases and 24 routine cases were still alive. The first-year survival rate of the latter group (50%), therefore, considerably exceeded that of the general-practitioner cases (36%), although the difference between the two rates was not statistically significant. The survival experience for both groups together (39%) was slightly higher than that of patients at two London hospitals (30%) reported by Bignall (1958b). Bignall's results are, however, not strictly comparable with this series, as his survival rates were calculated from first attendance at hospitals, which is not the same as first attendance for x-ray examination.

Resectability

Of all cases from both groups, 33% had a pneumonectomy or lobectomy (Table V). The rate was higher in the routine survey group (44%) than among general-practitioner patients (30%). The precise number of purely palliative resections (Abbey Smith, 1957) is not known, but is likely to have been small. It cannot have improved the resectability rates for routine survey cases, as the proportion of lobectomies in this group was much higher than for general-practitioner patients. We attach some importance to the high proportion of lobectomies in the routine survey cases, in view of the significance of this operation not only with regard to survival but also to post-operative disability (Bignall and Moon, 1955; Belcher, 1956; Cleland, 1958a).

Because of the many varying factors, to mention only different selection of cases by different surgeons, a true comparison of resectability rates between various

TABLE V.—Resectability of M.M.R. Cases

Group	Total No. of Cases	Pneumonectomies		Lobectomies		All Resections	
		No.	% of Total	No.	% of Total	No.	% of Total
G.P. referrals ..	190	41	21.6	16	8.4	57	30.0
Routine surveys ..	48	8	16.7	13	27.1	21	43.8
Total ..	238	49	20.6	29	12.2	78	32.8

TABLE VI.—Deaths Within 2-Months and 12-Months Survival After Resection

Group	Total No. of Cases	Patients Dying within 2 Months	Patients Alive 12 Months after Operation
G.P. referrals ..	57	4 (7.0%)	35 (61.4%)
Routine surveys ..	21	3 (14.3%)	10 (47.6%)
Total ..	78	7 (9.0%)	45 (57.7%)

TABLE VII.—Resectability by Age

Group	Under 45 Years			45-54 Years			55-64 Years			65 Years and Over			All Ages		
	All Cases	Resections		All Cases	Resections		All Cases	Resections		All Cases	Resections		All Cases	Resections	
		No.	%		No.	%		No.	%		No.	%		No.	%
G.P. referrals	14	3	21.4	60	27	45.0	82	25	30.5	34	2	5.9	190	57	30.0
Routine surveys	5	1	20.0	15	6	40.0	23	12	52.2	5	2	40.0	48	21	43.8
Total	19	4	21.1	75	33	44.0	105	37	35.2	39	4	10.3	238	78	32.8

thoracic centres is notoriously hazardous. We were interested to find that the resectability rates not only of our routine survey cases but also of general-practitioner patients were substantially higher than the corresponding rates of 19% for 748 male and female cancer cases diagnosed at the Birmingham United Hospitals in 1952 (United Birmingham Hospitals, 1954). The resectability rate reported from two London hospitals (Bignall, 1958c) was 23%, which is slightly lower than that for our general-practitioner patients and appreciably lower than for our routine survey cases.

Of the resected cases in both groups, 58% were alive 12 months after operation (Table VI). The number of resected routine cases is rather small, and no importance can therefore be attached to the higher survival rates of general-practitioner patients. The proportion of deaths within the first two months after operation (9%) was very similar to that reported by Cleland (1958b) for male patients at the Brompton Hospital between 1944 and 1955.

Factors Affecting Resectability

Age.—The very similar age distribution of cases in both our groups is shown in the Chart. The numerical excess of men over 65 years old in the general-practitioner group is, however, important, as in this age group only 4 out of 39 men were considered suitable for surgery (Table VII). This poor resectability rate lowered the proportion of resections for the group of general-practitioner patients as a whole. In the age group 55-64 years the proportion of routinely examined men who were resected was much higher than that for general-practitioner cases. The low resection rates for men below the age of 45 should be noted.

Histological Type.—The resectability rates for 124 cases of the squamous, undifferentiated, and adenocarcinoma types of neoplasm are shown in Table VIII.

TABLE VIII.—Resectability by Histological Type

Group	Squamous			Adenocarcinoma			Undifferentiated		
	No. of Cases	Resected		No. of Cases	Resected		No. of Cases	Resected	
		No.	%		No.	%		No.	%
G.P. referrals	64	39	60.9	4	2	50.0	32	11	34.4
Routine surveys	14	8	57.1	1	1	100.0	9	7	77.8
Total	78	47	60.3	5	3	60.0	41	18	43.9

In accordance with common experience (Bignall, 1958d; Nicholson *et al.*, 1957) squamous neoplasms proved generally to be more resectable than the undifferentiated tumours. As the numbers in each subgroup of the routine survey cases are small, comparison between the two groups is difficult, but it is worth pointing out that the proportion of squamous-cell tumours in

the routine survey group was smaller than among general-practitioner cases (Table IV).

Diagnostic and Therapeutic Delays

Ideally the prognostic significance of early or late diagnosis and treatment should be measured from the onset of first warning symptoms specifically related to the disease. The average duration of symptoms before diagnosis is usually given as four to six months (Taylor and Waterhouse, 1950; Brooks *et al.*, 1951; Thomas, 1952; Nicholson *et al.*, 1957); but, like Bignall (1958e), we have good reason to believe that the histories collected in this respect from our patients were in many instances very inaccurate and too unreliable for statistical evaluation.

Well-remembered incidents such as haemoptysis were present in only 19% of all cases and a febrile attack in only 8%. The main symptoms were cough and dyspnoea—36% and 34% respectively—and usually not even an approximate date could be recorded for the onset or change in character of these symptoms, which are common afflictions in the male population of this highly industrialized and air-polluted area, where approximately 70% of men are cigarette smokers (Cross *et al.*, 1958).

For most general-practitioner referrals we were, however, able to measure with reasonable accuracy the period between the patients' first visit to their doctors and their attendance at the M.M.R. unit. These "general-practitioner-x-ray intervals" are shown in Table IX.

TABLE IX.—Resectability According to Interval Between Consulting G.P. and X-ray Examination

Interval between G.P. Consultation and X-ray Examination	No. of Patients	% of Total	% Resected
Less than 1 month	68	35.8	22.1
1-2 months	62	32.6	29.0
3-4 "	23	12.1	43.5
5 months and over	12	6.3	(16.7)
Not recorded	25	13.2	
Total	190	100.0	

In recent years the controversial question of gross delay in diagnosis and treatment of lung cancers has often been raised in the medical press (Lutwyche, 1956; Thompson, 1957; d'Abreu and Taylor, 1957), and we believe it important to point out that at least two-thirds of general-practitioner cases were referred to us for x-ray examination within the first two months of consultation with their doctors and more than one-third within the first month. It is possible that the easy and direct access to chest x-ray facilities open to general practitioners in the Birmingham Region at M.M.R. units contributed to the early referrals of cases for x-ray examination.

The "x-ray-resection" intervals are shown in Table X. Only 18% of all cases were operated on within the

TABLE X.—Interval Between X-ray Examination and Resection

Interval between X-ray Examination and Resection	No.	% of Total
Less than 1 month	14	17.9
1- month	38	48.7
2- months	13	16.7
3-	6	7.7
5 months and over	7	9.0
Total	78	100.0

first month after x-ray examination, but 67% within the first two months. As the patients were under our control for only three or four days, the time between miniature and full-size films, we do not feel in a position to comment on the reasons for delay in treatment. Obviously very complex and often unavoidable causes contribute to this delay, to mention only the reluctance of patients to accept thoracotomy. Generally we feel that the figures in Table X give no cause for dissatisfaction. Furthermore, taking the "general-practitioner-x-ray" interval as an index of delay, the data in Table IX do not show a direct relation between early referral and increased resectability. In fact, the highest resectability rates were found in men who were referred three to four months after consulting their doctors, and the rates for patients referred within the first month were much lower. This seems to confirm the findings of others (Bignall and Moon, 1955; Gifford and Waddington, 1957) that the duration of symptoms is not a reliable prognostic factor and that patients with long histories may fare better than those with very short ones.

Asymptomatic Cases

A case was classified asymptomatic if, after careful inquiries, neither the director of the M.M.R. unit nor the thoracic surgeon or chest physician to whom the patient was referred elicited significant symptoms in the man's history. There were only seven such cases, or 15% of the routine survey group. Naturally all the general-practitioner referrals had symptoms. These findings are in accordance with those of Boucot and Sokoloff (1954), who found only seven truly asymptomatic cases out of 77 discovered at mass radiography surveys in the United States. Of our seven cases, three had lobectomies and a fourth had a pneumonectomy.

The radiographic manifestations of "silent" cancers of the lung have been described as small peripheral coin lesions, small areas of atelectasis, obstructive localized emphysema, or linear atelectasis (Rigler *et al.*, 1953). Kerley (1958) believes that the chances of successful surgical removal of neoplasms presenting as small peripheral shadows are good.

We consider it important to stress that in this small group of seven silent tumours five cases presented with increased hilar shadows or opacities close to the pulmonary roots, one with a pleural effusion, and one with a large peripheral ring shadow. The smallest shadow was 2 by 2 in. (5 by 5 cm.) on a 12- by 15-in. (30- by 38-cm.) film. Small peripheral coin shadows were therefore entirely absent in this group.

Discussion and Conclusions

Statistical evidence of the small chances of influencing the course of lung cancer (Bignall, 1958f) is indeed overwhelming. On the other hand, Ellman's (1952) statement that "mass x-ray examination of the chest offers the best known single means of detecting, as

rapidly and economically as possible, significant intrathoracic lesions in presumably healthy subjects" is now generally accepted.

The present series is to our knowledge the largest analysis of lung cancer cases found by mass radiography in this country, but we cannot claim that this contribution gives a clear-cut answer to the question of the value of mass radiography in the detection of this disease. We are also aware that a follow-up period of twelve months is short; but the investigation is continuing, and in future we hope to present data of survival after subsequent periods. Because of the widely accepted belief that early diagnosis can increase the chances of surgery (Bignall, 1958f) and diminish the number of those who arrive at thoracic surgeons only in the last stage of their illness (d'Abreu and Taylor, 1957), an analysis of resectability in cancer patients found by mass radiography seems to us important at the present time.

On the positive side we found a higher resectability rate in cases found at routine surveys as compared with cases referred by general practitioners because of symptoms. The difference, however, is small and not statistically significant. In a number of cases the fate of the patient was governed by factors of age, histology, acceptance, or refusal of operation—factors which are little or not at all related to early diagnosis. The 12-months-survival rate, irrespective of treatment, was higher for routine survey cases than for general-practitioner patients. This proves that other factors than resectability played an important part in prognosis.

The relatively large proportion of lobectomies in the routine survey group is encouraging, and it also seems that the resection rates for general-practitioner cases were higher than those for patients referred to the United Birmingham Hospitals from other sources.

On the negative side the most disturbing finding, to our minds, was the very small number of truly "silent" lesions, a strong reminder of the difficulties of early radiological diagnosis of lung cancer. Although we believe that since the inception of this investigation our threshold of suspicion has been raised, we do not know how many shadows due to cancer were missed during the period under review. Also, the number of men who attended our surveys, in whom the disease was already established but would not have shown on films of any size, is an unknown factor.

We agree with Kerley (1958) that part of the failure to detect a larger number of silent cancers may be due to radiographic technique, and that very small peripheral lesions are often not distinct enough on the 35-mm. film to be noted even by very experienced observers. It also seems reasonable that, in any surveys concerned with the early detection of cancer, dual independent reading is an essential prerequisite.

At present, both cancer of the lung and active tuberculosis are found predominantly in men above the age of 35, and it is on these age groups that the main effort of mass radiography should be concentrated.

In our opinion, regional hospital boards should implement, with a sense of urgency, the recent circular of the Ministry of Health (1957b) which called for an increase in static mass radiography facilities. The recommended use of the 100-mm. camera unit, with its larger film format and superior quality of film, would make interpretation easier and more reliable. Dual

reading, which has proved to be impracticable in conventional mobile mass radiography, would present relatively little difficulty at static units with 100-mm. cut films. It is obvious that even a large number of these static units would be unable to deal with the periodical routine x-ray examination of all men in the critical age groups, but general practitioners could help by sending for chest x-ray examination all men over 35, irrespective of the reasons for visiting their surgeries.

In the meantime, it would be wrong in our opinion to engage in any form of propaganda that suggests that at present routine mass radiography is a certain means of detecting "early cancer," and attention should not be deflected from the much more important preventive aspects of the present situation.

Summary

A series of 238 cases of cancer of the lung in men found by mass radiography in the Midlands are reviewed. Comparisons are made between cases found by conventional routine mass radiography and patients referred to the units by general practitioners.

The 12-months-survival rates irrespective of treatment and the resection rates were higher for routine survey cases than for general-practitioner referrals. A larger proportion of routine survey cases had a lobectomy than general-practitioner patients. Various aspects and reasons for these differences are discussed.

Symptomatic cases were referred by general practitioners generally without undue delay, and the majority of resections were carried out within the first two months after x-ray examination.

The very small number of truly asymptomatic cases and the absence of small peripheral shadows in this series are discussed in their relation to future mass radiography policy.

The installation of more 100-mm. x-ray units to deal with a larger number of general-practitioner referrals, particularly of men in the critical age groups, is suggested.

ADDENDUM: Second-year Survival Rates.—Since this paper was written a second-year follow-up report has been obtained on all but three patients (two general-practitioner referrals and one routine survey case) of the 238 in the series. Assuming all three had died, there were 38 general-practitioner referrals and 12 routine survey cases alive two years after the date of x-ray examination. Hence the second-year survival rates regardless of treatment for the two survey groups were respectively: G.P. referrals, 20%; routine survey cases, 25%. The rate for all patients was 21%. Of the 57 general-practitioner cases and 21 routine survey patients resected, 25 and 8 respectively were alive two years after the date of operation. Hence the second-year survival rates for the two groups of patients were respectively 44% and 38%, and for both groups combined 42%.

We are indebted to the chest physicians and thoracic surgeons in the region for their full co-operation in providing information of patients referred to them. We are grateful to Miss J. M. Levi, of the Birmingham Regional Cancer Registry, for obtaining follow-up details of our patients; to Mrs. M. Sheldon and Miss A. Holdsworth for clerical assistance, and to Miss J. Yates for help with processing of the material.

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KALA-AZAR OF UNUSUAL DURATION, ASSOCIATED WITH AGAMMAGLOBULINAEMIA

BY

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The case here reported is of extraordinary duration in that over ten years must have elapsed between the last possible date of infection with *Leishmania donovani* and ultimate diagnosis. It is of further interest because the serum gamma-globulin was abnormally low, and because the patient finally developed secondary amyloidosis.

Case Report

An unmarried Pole aged 31 was admitted to the Royal Hampshire County Hospital, in the care of Dr. W. D. Brinton, in November, 1956, with the following history. He was born in 1925, and had lived and worked on the family farm near Cracow until taken to Austria in 1941, where he worked on farms near Klagenfurt for nearly four years. In 1945 he went to Italy, where he lived for 18 months in camps in the Bologna region; he mentioned Monte Prandone and San Giuliano particularly, and Budrio, a town of some size, ten miles (16 km.) east of Bologna. In the autumn

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