etc.—may be a major factor responsible for the alarming increase of lung cancer in South Africa and Britain, and presumably elsewhere.

Summary

Analysis of the 1947–56 male lung cancer deaths in South Africa by age, country of birth, and place of residence has shown that among those dying aged 45 to 64 (but not among those dying aged 65 and over) British immigrants have had much higher lung cancer mortality rates than Union-born men or immigrants from other countries. Further, among all three categories in South Africa—Union-born men, British male immigrants, and male immigrants from other countries—the lung cancer mortality rates have increased approximately with the level of urbanization and industrialization. Neither the differences between the lung cancer mortality rates of these three groups nor the urban/rural gradient can be attributed to differences in smoking habits. Instead, both would seem to have been due to the exposure of the men concerned to different degrees of atmospheric pollution. The excess lung cancer mortality among British immigrants aged 45–64 would seem to have been due to their exposure in Britain to some form of atmospheric pollution to which those emigrating before 1910 had not been subject. The urban/rural lung cancer mortality gradient in South Africa would appear to reflect the increasing atmospheric pollution that is encountered in passing from rural areas to areas of increasing industrialization.

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In his Annual Report for 1958 on Industrial Health, published on July 29, the Chief Inspector of Factories refers to the constant watch that is kept on health problems which may have their origin anywhere in industry. In the main, this is done by the Medical Branch in conjunction with the general inspectorate and other specialist branches; additional information is obtained from members of the medical professions specializing in industrial health. But, the Chief Inspector feels, "There are members of the medical profession outside this specialized field who could add to the available knowledge on health hazards by reporting to the Medical Branch cases of interest coming to their notice in which occupational factors may be involved." This is the second occasion on which a separate report on industrial health has been published. As before, it reviews the events of the year, and describes significant cases of industrial diseases, poisoning, and gassing. Special chapters deal with occupational cancer, and with a survey on medical supervision which was carried out in more than 200 factories. (H.M.S.O., Cmd. 811, price 3s. 6d. net.)

RESULTS OF SURGICAL TREATMENT OF CANCER OF THE STOMACH

BY

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In the Soviet Union the treatment of cancer of the stomach is one of the most vital problems of oncology, for it is the commonest malignant tumour, constituting about 30% of all malignant growths. So far surgery has been the only method of treatment. The names of A. G. Savinich, E. L. Beresov, B. V. Petrovsky, and V. I. Kazansky have been especially associated with the surgical treatment of cancer of the stomach in the Soviet Union, but many problems remain unsolved. Late results of the treatment are very unsatisfactory.

The experience in our clinic is very small, but a critical review of the late results of treatment allows certain conclusions to be drawn. During the period 1952 to December 1, 1958, 722 cases of cancer of the stomach were treated (Trapeznikov, 1957)—451 underwent radical operations (Table I), 254 had non-radical operations (laparotomy, palliative anastomosis, gastrostomy), and in 17 other operations were performed. The resectability rate was 62.4%.

In 66 of the 298 resections of the lower part of the stomach the so-called combined operation was performed (with resection of the adjacent organs). This was also done in 56 of the 123 patients submitted to total gastrectomy. The resections of the lower part of

TABLE I

	No. of Cases	Died After Operation
Partial resection of lower part ..	298	20 (6.7%)
"upper" ..	30	10 (33.3%)
Total gastrectomy ..	123	27 (21.9%)
Total ..	451	57 (12.6%)

the stomach were of the Polya-Reichel type, but in a number of cases anastomosis was performed according to Finsterer (13 patients) and Billroth I (21 patients). As a rule gastrectomy was completed by the construction of an anastomosis between the oesophagus and the jejunum on a long loop, with an interintestinal anastomosis by the method of Braun (1892–3). Under favourable anatomical conditions (with a mobile duodenum and a long end of the abdominal oesophagus) anastomosis was performed between the oesophagus and the duodenum (23 patients). Gastrectomy was preferably done through the abdominal approach, but when the tumour infiltrated the oesophagus a left thoracic approach was employed. A follow-up was made in 440 (97.5%) of the 451 patients on whom radical operations had been performed, and 33% of the patients survived for five or more years after the operation. This figure is similar to that obtained by other authors (Berkson, Walters, Gray, and Priestley, 1952).

A number of questions arise. First, whether extension of the operation to include resection of the adjacent organs improves the results. In our clinic the

indications for the performance of the combined operation were: (1) local penetration of the tumour into the pancreas; (2) penetration of the growth into the liver, or the presence of a single metastasis in the left lobe; (3) local penetration into the mesocolon or into the colon; and (4) metastasis into the hilum of the spleen. The more extensive operation might be thought to carry a higher mortality. Table II, however, shows that the post-operative mortality after the combined operation increases only insignificantly, while, on the other hand, some patients with a seemingly hopeless prognosis lived for five years or more. Similar results were obtained in the group of patients who were subjected to total gastrectomy.

Secondly, an improvement in the late results can undoubtedly be obtained by means of modern surgical techniques and by the extension of the indications for total gastrectomy. This question has repeatedly been discussed in the literature. As early as 1930 Professor Sapozkov advocated complete removal of the stomach in all cases of cancer. However, his idea was not popular in our country, because the operation had a high mortality at that time. Total gastrectomy for all cases has since been revived by Pack *et al.* (1947), Sweet (1953), McNeer *et al.* (1956), and Nakayama (1956). Besides complete resection of the stomach, they removed the spleen in all cases and performed a partial resection of the pancreas. This facilitated an easier excision of the retroperitoneal metastases. Their experience in this respect is limited, but their preliminary published data show that the late results improve, though not very much. It would seem reasonable to extend the indications for total gastrectomy to include cases of cancer localized to the body of the stomach and to the infiltrating forms arising in the antrum.

From an analysis of our late results we concluded that in 30% of cases death was due to recurrence of the growth in the stump of the stomach (Table III). It is clear that approximately one-half of the patients died after a partial resection of the stomach as a result of recurrence of the growth. In cases of cancer arising in the antrum the recurrence rate was about 20%. McNeer *et al.* stated that about 50% of the recurrences are observed in the stump of the stomach. He based his conclusions on the material of Memorial Center for Cancer, New York.

Our material shows that recurrence was most frequent in patients who had undergone partial resection of the stomach for an infiltrated form of cancer. It seems likely that some of the patients might have been saved from recurrence of the malignant

TABLE IV

Partial Resection		Total Gastrectomy	
Alive	Dead	Alive	Dead
115 (41.3%)	163 (58.7%)	25 (25.1%)	71 (74.9%)

growth if they had undergone total instead of partial gastrectomy. Table IV shows that the late results of total gastrectomy were much worse than those of partial resection of the stomach. This is because total gastrectomy was usually performed in cases with growths involving the whole of the stomach, or in cases with growths in the upper part of that organ. Thus, out of 123 cases of total gastrectomy and 30 cases of resection of the cardia, the growth arose in the proximal part of the stomach or involved the whole stomach in 120, and was of distal origin in only 33 cases. Resection of the cardia carried the same risks as total gastrectomy.

Thus judicious extension of the indications for total gastrectomy in the infiltrating forms of growths of the distal part, and in the tumours of the body of the stomach, will undoubtedly lead to a reduction in the number of recurrences, and will therefore improve the late results of treatment.

The desirability of removing the spleen and of resecting the pancreas in every case was questionable. This method was proposed by Longmire (1947) and improved by McNeer, Nakayama, and others. It is extremely difficult to remove all the metastases, and the method was not favourably received in the Soviet Union. Moreover, Moore, Sandberg, and Schubarg (1958) and Cole, Watne, Roberts, and McGrew (1958) in the U.S.A., and others, have proved that, in about 30% of patients who have undergone the so-called radical operations, malignant cells can be demonstrated in the blood stream and in smears from the operation wounds. Evidently a more rational approach would be to combine surgical treatment with chemotherapy by means of growth-inhibiting agents.

The clinic of the Institute worked out an additional programme of chemotherapy combined with surgical treatment. In 1958 this method was tried on 30 patients who received one of two kinds of biological alkylating agents—sarcosylsin (Perevodchikova and Blokhin, 1958; Blokhin, Perevodchikova, and Trapeznikov, 1958) or thiotepa. During 1959 this method will be applied to 1,000 patients suffering from cancer of the stomach. This programme is very similar to the one approved by the Pan-American Oncological Congress in 1957 with regard to thiotepa. Our aim is to obtain information on the therapeutic value of the two drugs given as an adjunct to surgery. The late results will be compared with those in a control group.

The drugs are administered as follows: (1) sarcosylsin (*p*-di(2-chloroethyl)amino-DL-phenylalanine) is given three times. The first dose of 40 mg. is injected during the operation (20 mg. is injected into a tributary of the portal vein, and 20 mg. into the peritoneal cavity through a catheter before closing the last suture on the aponeurosis). The second dose (40 mg.) is given intravenously two days after operation, and the third dose (40 mg.) three days later. (2) Thiotepa (triethylene thiophosphoramide) is given three times; the first dose is 0.4 mg./kg. of body weight. One-half is injected into a tributary of the portal vein, the second half into the peritoneal cavity. The second and the third doses are

TABLE II

	No. of Cases	Died After Operation	Alive 3 to 5 Years
Ordinary resection	232	15 (6.4%)	100 (43.1%)
Resection combined with removal of neighbouring organs	66	5 (7.5%)	15 (21.2%)

TABLE III

Site of Tumour	No. of Resections	Alive	Causes of Death		
			Recurrence	Metastases	Unknown
Antrum	187	85	22	60	20
Body of stomach	91	30	26	25	10
Total	278	115	48	85	30

introduced intravenously on the first and second days after the operation, and each contains 0.2 mg./kg. of body weight. Regular estimation of leucocyte and platelet counts are performed. After discharge the patients are seen in the out-patient department every three months and examined for signs of recurrence.

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USE OF PREMIXED PETHIDINE AND ANTAGONISTS IN OBSTETRICAL ANALGESIA

WITH SPECIAL REFERENCE TO CASES IN WHICH LEVALLORPHAN WAS USED

BY

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The introduction into clinical practice of the two specific opiate antagonists nalorphine (*n*-allyl derivative of morphine) and levallorphan (*n*-allyl derivative of levorphan) has opened up a new field in the relief of pain by morphine and all the drugs related to morphine. The main effect of these antagonists is to correct the respiratory depression which inevitably follows the administration of opiates. When pethidine is used in obstetrics the main hazard is that the baby will be depressed at birth by the drug administered to the mother, will fail to breathe immediately, will become asphyxiated, and will require resuscitation. If the baby is also suffering from shock due to some obstetric abnormality or to operative birth under general anaesthesia, the additional effect of the pethidine in its body might endanger its life.

The antagonists can be used to prevent respiratory depression occurring when an opiate is given, or to correct or relieve existing respiratory depression already caused by opiates. In obstetrics there are thus three possible ways in which they can be used (Baker, 1957).

1. A single adult dose is given to the mother a sufficient time before the baby is born for the drug to enter the baby's respiratory centre and antagonize the effects of pethidine or other opiates the mother has

received. This was tried successfully by Eckenhoff *et al.* (1953), using a dose of 10 mg. of nalorphine to the mother. The difficulties arising from this method are that the exact time that the baby will be born is not known and that the time the drug takes to cross the placenta and enter the baby's brain is also not known. Thus an intravenous dose to the mother is usual.

2. A small dose can be given to the baby after birth if it fails to breathe in a reasonable time. This has also been reported on (Eckenhoff *et al.*, 1953; Paterson and Prescott, 1954). For a reasonably rapid effect the drug must be injected into the umbilical vein or the heart, to which procedure there are some objections.

3. The antagonist may be premixed with the opiate at each dose given to the mother in labour. This would appear to be the method of choice, as the other two methods require the presence of a doctor, whereas the mixture can be used by midwives without any special supervision. The correct mixture of the two drugs (called the ratio) is probably the least amount of the antagonist which, when mixed with a dose of the opiate, will, as near as possible, prevent respiratory depression. Much work has been done by others (Cullen and Santos, 1954, 1955; Eckenhoff *et al.*, 1955; Foldes *et al.*, 1955; Gaard, 1955; Baker, 1957) and myself (Bullough, 1957, 1958a, 1958b, 1959) in trying to find the correct ratios of antagonists and opiates. It is not known whether the antagonists cross the placental barrier at the same rate as the opiates; research on this point remains to be carried out.

This paper describes the effects of pethidine and mixtures of pethidine with nalorphine and levallorphan, used to relieve pain in childbirth over the past five years in the maternity unit at the West Hill Hospital, Dartford. This is a busy unit in which 1,200 to 1,400 babies are born annually.

In 1954 I introduced the use of premixed pethidine and nalorphine for the relief of pain in childbirth at Dartford, with the full co-operation of the obstetric staff, to whom my thanks are due. So far as I know, this unit was the first to employ premixed pethidine and antagonists in obstetrical analgesia. The first report on the use of such mixtures came from this unit in 1956* and was published later (Baker, 1957). After a pilot series of 75 mothers who received individual doses of pethidine 100 mg. premixed with nalorphine 5 mg., three series of cases were compared (see Table I). Series A: the mothers received pethidine 100 mg. in the customary way. Series B: nalorphine 2 mg. was added to each dose of pethidine. Series C: nalorphine 5 mg. was added to each dose of pethidine.

As a result of this trial it was tentatively concluded that the use of the mixture of pethidine 100 mg. and nalorphine 5 mg. provided more effective analgesia than pethidine alone, as it could be used in larger quantities without interfering with labour and without increasing the incidence of neonatal asphyxia (which was actually reduced). After this trial all mothers received the mixture as a routine for two years, so that over 2,000 mothers were treated in this way. Details of 1,000 of these await publication.

In 1957 it was decided to substitute the newer drug, levallorphan, in place of nalorphine, and compare the results. At that time the correct ratio of these two drugs was thought to lie between 1 and 2 mg. of

*A paper read at the Royal College of Surgeons to the Association of Anaesthetists of Great Britain and Ireland.