Classification According to Symptoms in Order of Prominence

Fullness after meals	22	Flatulence	4
Biliary regurgitation	8	Diarrhoea	4
Faintness related to meals	8	Easy fatigue	2
Nausea	7	Anorexia	2
Non-biliary regurgitation	5	Dysphagia	1

Some of the patients had multiple symptoms, and so the sum of the above figures exceeds the total of cases exhibiting post-operative syndromes.

4. *Persistent Dyspepsia Without Post-operative Syndromes and With no Proved Ulcer.*—There were five such patients (5.6%). These, together with the four cases of persistent dyspepsia occurring with post-vagotomy and gastro-enterostomy syndromes, are here analysed, making a total of nine (10.1%). In one case the symptoms were only those of "heartburn," but in the remainder they were similar to pre-operative symptoms, only in most cases milder. Six were mild, two were moderate, and one was severe. All these patients underwent barium studies apart from two of the mild cases, one being the patient with "heartburn" and the other a patient who has so far failed to attend for his radiological examination. In none of those examined was there any radiological evidence of ulcer recurrence. In view of this and the fact that all were able to work or attend to their household duties, their symptoms have been controlled by medical treatment and they remain under observation.

5. *Further Peptic Ulceration.*—There were 11 cases (12.4%)—eight have been proved at operation, and three have not undergone operation because one refused operation (gastric and duodenal ulceration), one was unfit for operation for other reasons (gastric and duodenal ulceration), and one was pregnant at the time this report was written and was awaiting operation (gastric ulceration). In all these three patients the diagnosis has been made not only on clinical grounds but on the unequivocal demonstration of an active ulcer crater radiologically.

Site of the Peptic Ulceration

Gastro-jejunal	Duodenal	Gastric	Gastric and Duodenal
6	1	1	3

Of these recurrences six occurred in men and five in women. The average duration before recurrence of symptoms was 16 months, the shortest being five months and the longest 26 months.

6. *Miscellaneous.*—One patient remained well for 22 months, when he had a severe melaena. Clinically and radiologically it was probable that he had a gastro-jejunal ulcer. Laparotomy failed to show such an ulcer, but following his gastrectomy, which was performed at this second operation, he has remained well up to date.

The Defaulters

Of the 10 defaulters there was no trace of five from almost immediately after discharge. Of the remaining five one was seen three months after operation with recurrence of pain, but refused treatment, and shortly afterwards left the country; one was seen one year later with recurrence of pain and vomiting, but he is a seaman and has since been untraceable; one was seen one year later and was well, apart from occasional pain and postprandial fullness; and two were seen one year later and were very well.

Summary of Results

Out of 100 cases of vagotomy and gastro-enterostomy for duodenal ulcer there was one post-operative death. Of the remaining 99 cases 10 defaulted and 89 were followed up. The results in these cases are as follows:

Category	No. of Cases	% of Cases Followed up
Excellent	33	37·1
Good	9	10·1
Persistent post-operative syndromes with or without dyspepsia	30	33·7
Persistent dyspepsia alone with unproved recurrence of ulceration	5	5·6
Proved recurrent ulceration	11	12·4
Miscellaneous	1	1·1

Conclusions

A recurrence rate of 12.4% is undeniably very high, particularly as the average duration of follow-up has been only 29 months: further continuation of the follow-up might produce an even higher percentage of recurrences. It is interesting to note that no fewer than eight patients in this series have undergone further operation for peptic ulceration.

Quite apart from the recurrences, there has been a remarkably high incidence of post-operative syndromes that have so far persisted. Admittedly many of these have been mild in nature, but in our experience vagotomy has little to offer in the search for an operation free of sequelae such as the syndromes which may follow partial gastrectomy. Indeed, in six cases the symptoms have been severe and have interfered with the patients' normal work.

Our inevitable conclusions are that vagotomy and gastro-enterostomy, in our hands, is an unsatisfactory operation for duodenal ulcer. If the operation demands for its greater success a highly specialized technique, we still consider it unsatisfactory: any operation for such a common disorder must stand or fall by the results obtainable in average hands.

We wish to thank Mr. H. H. G. Eastcott and Mr. D. L. P. Farley, who performed many of the operations included in this series and who have assisted us with the follow-up.

SPIROMETRY IN ASSESSMENT OF ANALGESIA AFTER ABDOMINAL SURGERY

A METHOD OF COMPARING ANALGESIC DRUGS*

BY

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Pain is a complex experience, and the comparison of pain-relieving drugs is complex also. Clinical trials of analgesics based on subjective reports are notoriously unreliable unless hedged around with stringent precautions to keep the patient and administrator in ignorance of what is being given. Similarly, estimations of pain-relief based on objective degrees of tranquillity tell us very little, for a patient can be made completely tranquil with drugs which make no pretence of analgesic action. Moreover, procedures such as these are qualitative rather than quantitative.

Hardy, Wolff, and Goodell (1940, 1952) have carried out quantitative comparisons of analgesics in experimental pain, using a machine called the "dolorimeter." This machine inflicts graded thermal burns, and has been the basis of a great deal of sound laboratory work, but for accurate results it must be used on trained subjects under standard conditions. Attempts have been made to equate the pain caused by this machine with naturally occurring pain (Javert and Hardy, 1951), but it is doubtful whether comparisons of such entirely different kinds of pain have any value (Haugen and Livingston, 1953). Ideally, analgesic drugs should be

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compared under the conditions for which they were designed—namely, in the presence of naturally occurring pain.

This paper is concerned with a method of comparison which is essentially related to everyday anaesthetic practice, and which is both objective and quantitative.

Pain in the upper abdomen restricts breathing to a marked degree. In 1927 Churchill and McNeil found that the vital capacity was reduced by 75% in the first twenty-four hours after gall-bladder operations, and by about 40–50% after lower laparotomies. In the same year Head found that pain could reduce the vital capacity to less than one-fifth of the normal value after upper abdominal operations. Modern anaesthesia has not changed this picture in any way.

Post-operative reduction of vital capacity is due to pain, to mechanical interference with the abdominal muscles, and, to a much smaller degree, to the pneumoperitoneum that is sometimes caused by trapping air during closure of the peritoneum in a relaxed patient. But pain is by far the greatest factor in reducing vital capacity (Cleland, 1949). Therefore an important aspect of post-operative analgesia is not only subjective relief of pain, although this is desirable, but also improvement of respiratory function, with the ability to cough and to breathe deeply.

Reduction of vital capacity by abdominal pain is shown most clearly when the pain is uncomplicated by the mechanical interference of operation—for instance, in acute pancreatitis or in acute perforation of a viscus. In these conditions restriction of respiration may be so severe as to cause cyanosis, but if the pain is relieved breathing is relieved also, and the cyanosis disappears. The case shown in Fig. 1 illustrates this point. The patient had already received papaveretum, ¼ gr. (22 mg.), one hour before the first vital-capacity tracing was taken, and he said, "I can breathe much better now since the injection," so one may presume that his vital capacity had been even lower before the opiate was given. Complete subjective relief by a sensory epidural block doubled his vital capacity, and repeated injections up the epidural catheter allowed painless deep breathing and coughing after operation.

Here, then, is an objective method for comparing the efficiency of analgesic agents in patients who have undergone upper abdominal operations. A drug which removes pain effectively will also restore the vital capacity closer to normal than one which does not relieve pain. Comparison of vital capacities after different analgesics will provide a quantitative indication of the amount of pain relief obtained with each drug (see Figs. 2 and 3).

If the vital capacity is measured before operation, and again after operation, when the patient is fully recovered from the anaesthetic and is in pain, we have a measure of the amount of respiratory impairment caused by the pain. Pain impairment becomes less after an analgesic drug is given, and the vital capacity increases in proportion to the

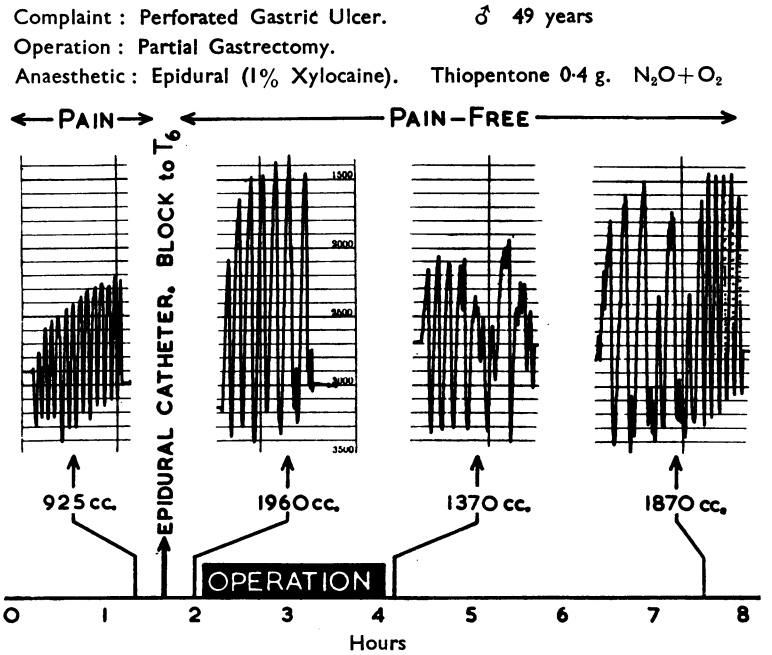

FIG. 1.—Vital capacity records of patient with perforated gastric ulcer, to show effects of pain and regional analgesia.

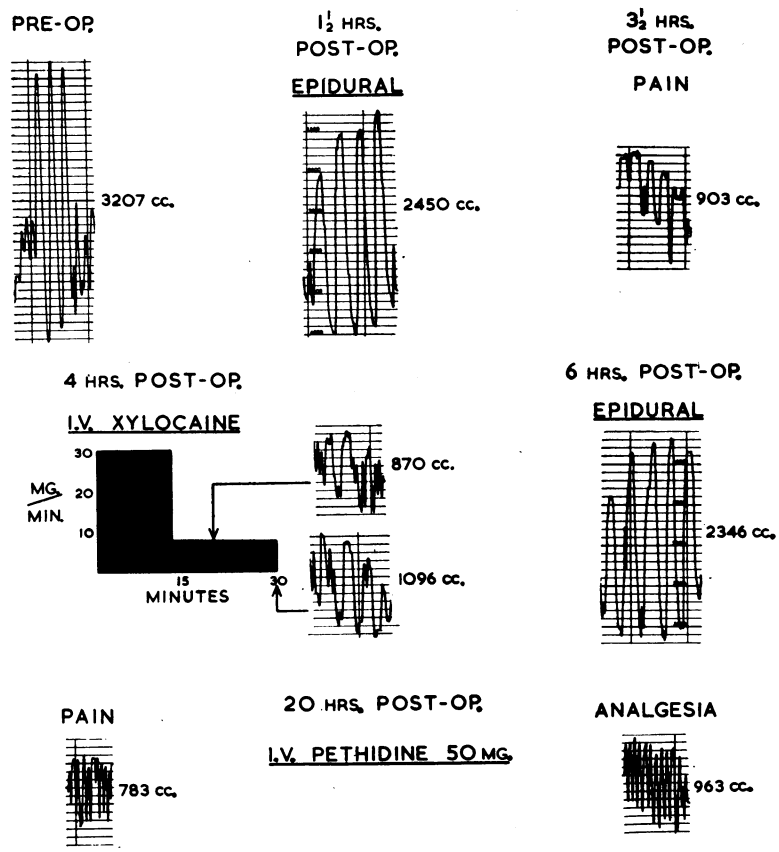

FIG. 2.—Vital capacity tracings from patient aged 30, before and after total gastrectomy (Case 3).

effectiveness of the drug. A perfect analgesic will restore the vital capacity to normal, or nearly normal, whereas an ineffectual drug will make no difference. If the amount of restoration of vital capacity is expressed as a percentage of the impairment caused by pain we arrive at a quantitative basis for comparing different drugs in the same, and also in different, patients. This percentage restoration of vital capacity (V.C.) may be called the respiratory restoration factor (R.R.F.) of the drug, and is a measure of its analgesic effectiveness (see Fig. 4). The R.R.F. is calculated thus :

$$\text{R.R.F.} = \frac{\text{Analgesic V.C.} - \text{Pain V.C.}}{\text{Pre-operative V.C.} - \text{Pain V.C.}} \times 100$$

The R.R.F. for any one drug will inevitably vary from patient to patient within a fairly wide range, but by carrying out serial readings in a sufficiently large number of cases it is possible to calculate the mean and standard deviation for the R.R.F. of each drug, and thus arrive at a reasonably significant comparison.

I have attempted to illustrate this method by comparing the R.R.F.s of three different types of post-operative analgesia in a group of 20 patients, using : (1) regional analgesia obtained by epidural spinal block, with an indwelling epidural catheter ; (2) systemic analgesia with (*a*) pethidine, and (*b*) methadone ("amidone") ; (3) systemic analgesia, using a local analgesic drug (lignocaine hydrochloride ; "xylocaine") by the intravenous route.

Method

In order to obtain an R.R.F. parameter wide enough for reasonable accuracy it is necessary to choose patients who are likely to suffer a deep depression of vital capacity in the first 48 hours after operation ; in practice, this means confining the series to upper abdominal operations and, possibly, simple thoracotomies. The day before operation the patient is instructed how to use the spirometer, and his co-operation is enlisted by pointing out the similarity between vital-capacity tests and the deep-breathing exercises he has already received from the physiotherapist.

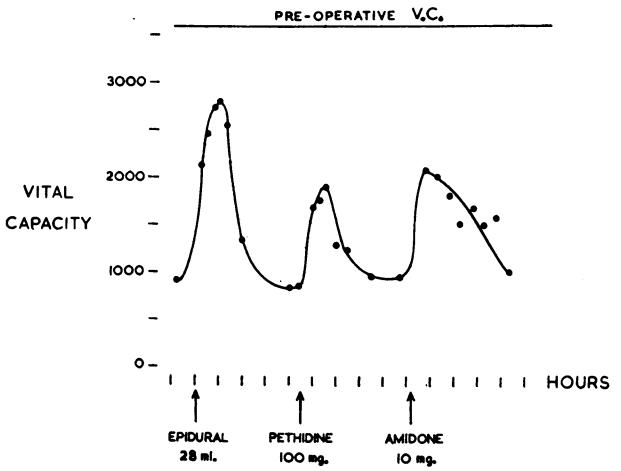

FIG. 3.—Serial vital capacity figures following total gastrectomy (Case 12).

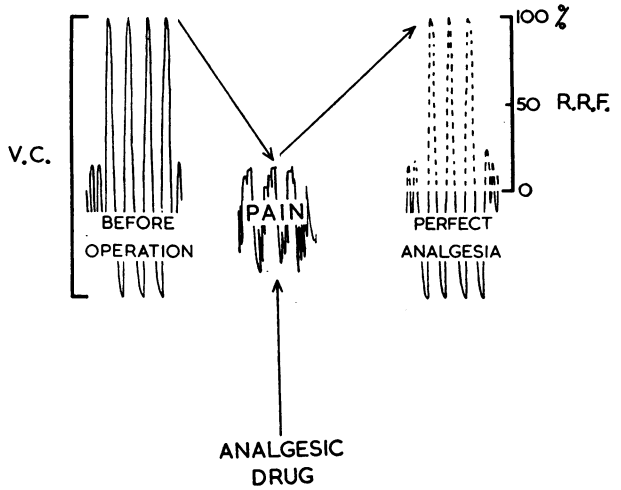

FIG. 4.—The respiratory restoration factor (see text).

Vital capacities are all taken in the supine position with one or two pillows, using a Benedict–Roth recording spirometer containing air, and a facepiece. The soda-lime tower is removed in order to reduce resistance to a minimum, and the spirometer is flushed out with air after each recording. A recording takes about one minute, and so one may ignore the respiratory stimulating effects of carbon dioxide accumulating in such short periods, because the CO_2 is diluted to negligible proportions by the large volume of air in the spirometer. With the facepiece firmly applied, the patient takes two normal breaths and then breathes in and out as deeply as possible four times in succession while receiving vigorous encouragement. The vital capacity is taken as the average of the three best expirations.

Premedication is light, or omitted altogether, and general anaesthesia is minimal, a sleep dose of thiopentone or hexobarbitone and nitrous oxide and oxygen being used. Relaxation is obtained with either an intravenous relaxant, in which case artificial respiration is carried out, or by means of a regional nerve block. When the effects of general and regional anaesthesia have worn off and the patient complains of pain, serial vital capacity recordings are started at intervals of 15–30 minutes, and two similar values obtained as a baseline for the "pain vital capacity."

The first analgesic procedure is then carried out, and serial spirometer recordings are taken until the vital capacity has risen to a zenith, and finally returned to its nadir as analgesia recedes. A second pain baseline is then obtained and the next procedure under test carried out. Two or more drugs or procedures may be tested in a series in this way.

For post-operative epidural analgesia a critically differential block is required, giving good relief of pain but the minimum of muscular paralysis. It was found that 0.8% xylocaine was best for this purpose. In order to keep the period of investigation within reasonable limits it was desirable that the epidural block should come to a peak and then wear off as quickly as possible, and therefore no long-acting drug such as cinchocaine was mixed with the xylocaine, and no adrenaline was added.

Pethidine was given in an approximate dosage of 1.4 mg. per kg. body weight, and amidone in one-tenth of this dosage. Both drugs were given intravenously.

Intravenous xylocaine was administered in the following way. A 0.5% solution was dripped in at a rate of about 2.5 ml. a minute until the patient became sleepy or confused. Signs of cerebral depression were taken to indicate saturation with the drug, and the drip was then slowed until a total of 400–500 mg. had been given in about 40–60 minutes. Serial vital-capacity readings were taken throughout this period, and following it for a further 30 minutes. In this way dosage was related to the observed central depressive effects of the drug, rather than to body weight, in order to be quite certain that a saturating dose had been given. Moreover, by continuing readings after the drip was stopped any evidence of analgesia without depression would be recorded.

Since the pain baseline may fluctuate slightly during the period of eight to sixteen hours when recordings are taken, the R.R.F. for each procedure is always calculated from the level of the "pain vital capacity" immediately preceding it. As a further precaution against errors arising from alterations in pain intensity, the order for the different analgesic procedures was varied from case to case.

Results

Curves for R.R.F.s calculated from serial vital capacities are shown in Fig. 5, and the figure for maximum vital

TABLE I.—*Vital Capacities and R.R.F.s in 20 Cases*

Case No.	Operation	Pre-Op. V.C.	Pain V.C.	Analgesia							
				Epidural		Pethidine		Amidone		I.V. Xylocaine	
				V.C.	R.R.F.	V.C.	R.R.F.	V.C.	R.R.F.	V.C.	R.R.F.
1	Partial gastrectomy ..	3,850	1,420	3,300	77·3	1,940	21·4				
2	,, ,, ..	2,560	1,110	1,970	59·3	1,095	−1·0				
3	Total ,, ..	3,205	905	2,470	68·0					1,096	8·2
4	Cholecystectomy ..	2,110	540 (before pethidine) 600 (,, amidone and xylocaine)	2,040	95·5	760	14·0	1,240	42·4	1,623	67·8
5	,, ..	1,300	860	1,470	138·5						
6	,, ..	2,660	1,425	2,850	115			1,595	13·8		
7	Partial gastrectomy ..	2,850	960	2,190	65·1			1,380	22·2		
8	,, ,, ..	3,660	1,700	3,380	85·5			2,400	35·6		
9	,, ,, ..	2,040	840	1,450	50·8	880	3·3	950	9·2		
10	Cholecystectomy ..	2,360	775 (before epidural) 900 (,, amidone) 850 (,, I.V. xylocaine)	1,960	73·5			1,030	11·9	1,090	15·9
11	Partial gastrectomy ..	2,630	1,070 (,, pethidine) 880 (,, amidone)			1,460	25·0	1,423	31·1		
12	Total ,, ..	3,580	950 (,, epidural and pethidine) 1,000 (,, amidone)	2,756	68·6	1,920	36·9	2,063	41·2		
13	Gastrostomy	3,060	1,660	3,453	136·5	2,070	29·3	3,080	101·4	2,186	37·5
14	Partial gastrectomy ..	3,000	1,000			963	−2·0	2,283	64·2	1,400	20·0
15	Cholecystectomy ..	2,446	1,000	1,896	62·0	1,070	4·8	1,433	30·0	1,300	20·8
16	Upper laparotomy ..	3,270	800	2,450	67·0	970	6·9	1,616	33·0	1,076	11·1
17	Partial gastrectomy ..	1,150	365 (before epidural and amidone) 450 (,, pethidine and I.V. xylocaine)	990	79·5	540	12·8	583	27·8	500	7·0
18	Cholecystectomy ..	2,500	1,100	2,703	114·5						
19	Partial gastrectomy ..	1,890	650 (before epidural and amidone) 510 (,, pethidine and I.V. xylocaine)	1,560	73·5	650	10·2	1,066	33·6	750	17·4
20	Upper laparotomy colostomy	770	380	816	111·8						

Each vital-capacity measurement is the average of the three largest in a series of four or five readings.

capacities and R.R.F.s in each case is shown in Table I, with the means and standard deviation in Table II.

It will be observed that in five cases the post-operative vital capacity under epidural block exceeded the pre-operative vital capacity by a significant amount. Four of these patients had signs of some degree of left-sided cardiac strain and pulmonary congestion. In patients with pulmonary congestion ventilation is improved and the vital capacity may increase by 20 to 30% following a moderate fall of systemic blood pressure caused by ganglionic or spinal blockade (Bromage, 1954, 1955), and this is probably the cause of the raised R.R.F. in these cases. Restoration of respiration beyond 100% clearly does not indicate a more than perfect analgesia, but merely an increased intrathoracic air space, and so these R.R.F.s have been reduced to 100% in calculating the mean epidural R.R.F.

R.R.F.s below the baseline in Fig. 5 occurred during periods of depression, when the drugs had made the patients too sleepy to co-operate fully in vital-capacity tests.

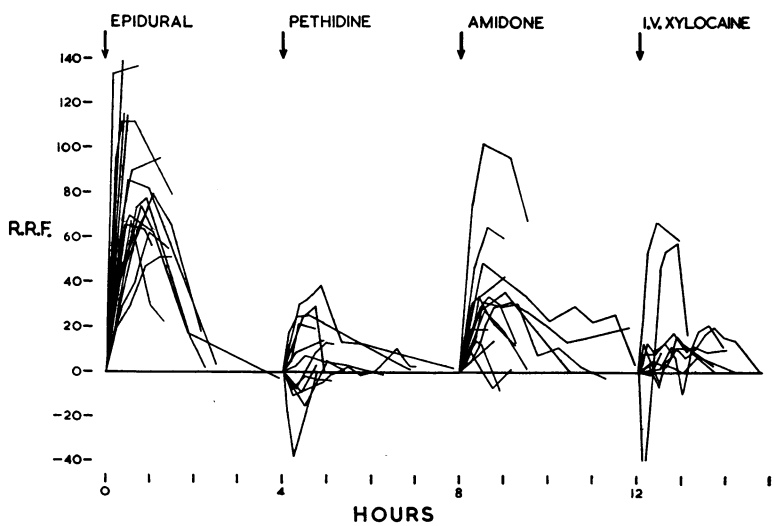

FIG. 5.—Serial R.R.F.s calculated from serial vital capacity tracings in 20 patients after upper abdominal operations.

TABLE II.—*Comparison of Maximum Respiratory Restoration Factors*

Procedure	No. of Observations	Mean R.R.F.	S.D. of Mean R.R.F. (corrected $\sqrt{\frac{n}{n-1}}$)
Epidural	17	80·2	16·4
Pethidine	12	13·5	12·3
Amidone	14	35·4	24·2
I.V. xylocaine	9	22·8	19·1

Discussion

The central problem of pain relief is to obtain analgesia without the depression which may unfortunately accompany it. If the object is merely relief of pain, regardless of other considerations such as depression, then there is no problem. But if we think in terms of function we must strive for purity of analgesia, with the minimum of functional depression. This investigation is directed to showing the resultant of these two opposing forces—the positive and negative aspects of pain relief.

As might be expected, regional nerve block, as illustrated by epidural blockade in this series, is paramount in the quality of analgesia produced. Restoration of respiration is not perfect for a number of reasons. The block must be very high to include afferent impulses from the diaphragm, and Cases 3 and 12 complained bitterly of shoulder-tip pain at the end of inspiration when all other pain was abolished. Also, for 100% restoration of vital capacity the block must differentiate perfectly between motor and sensory nerve fibres, for any degree of motor block will diminish intercostal activity in the analgesic segments, and, since patients differ in their sensitivity to analgesic drugs, it is unlikely that a perfectly differential block can be performed every time. The optimum concentration of xylocaine seems to lie between 0.7 and 1%, with 0.8% as the mean, and this latter concentration was used in most cases.

In the same way that a depressant concentration of regional analgesic produces a low R.R.F., so also systemic analgesics with a central depressant overlay result in a poor ventilatory performance. Pethidine and intravenous xylocaine have this disadvantage, which is shown clearly when contrasted with the relative purity of action of amidone. Local analgesics administered systemically can be effective if the speed of infusion is carefully regulated (Gordon, 1943 ; McLachlin, 1945), but the margin between effective analgesia and depression is narrow, and a drip rate that suddenly accelerates can rapidly lead to profound depression and dangerous convulsions. This lability in the balance between depression and analgesia is shown by the jagged peaks and valleys of the xylocaine series in Fig. 5. It would seem illogical to use local analgesics by the systemic route, unless the superior quality of analgesia provided were such as to warrant the close supervision required. This series shows no evidence of such superiority.

Clearly, the spirometric method of comparison would have to be modified if used for analgesic drugs having a direct respiratory stimulating effect of their own, for otherwise an abnormally high R.R.F. would be obtained, unrelated to the analgesia produced (something akin to the improvement of respiration found in the epidural series). This source of error could be eliminated by carrying out control vital capacities with a test dose of the drug before operation. The improvement of vital capacity that occurred following epidural block in patients with pulmonary congestion suggests that greater accuracy would be obtained by employing only patients with normal cardio-respiratory function in this type of investigation.

Lastly, it must be emphasized that the results of this method of comparison, based upon wound pain, may not be applicable to other types of pain. The method is deliberately designed to measure relief of pain in an inherently painful situation, whereas many analgesics act by removing the painful situation and not by dulling the pain. For example, a correctly applied Thomas's splint relieves the pain of a fractured femoral shaft, and the methonium drugs (although innocent of any essential analgesic action) may yet be most effective in the pain of acute pancreatitis (Davies *et al.*, 1953; Pyke, 1953). Similarly, although pethidine scores poorly in this series, it may be very valuable in pain from smooth-muscle spasm, such as ureteric colic, for then relief of pain is partly due to a direct antispasmodic action.

Summary

There is a need for comparing analgesic drugs quantitatively under clinical conditions. A quantitative method is described, based on vital capacity measurements. After an upper abdominal operation breathing is restricted by pain ; analgesic drugs are assessed by the amount they restore the vital capacity towards normal.

The method is illustrated by comparing four analgesic procedures in 20 patients.

This investigation was carried out with the aid of equipment purchased by the Research Fund of the Association of Anaesthetists of Great Britain and Ireland.

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UVEOPAROTID SARCOIDOSIS WITH CEREBRAL INVOLVEMENT

A CASE REPORT

BY

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Heerfordt (1909) first indicated that the nervous system might be affected in sarcoidosis, and since then the occurrence of neurological complications has been widely affirmed. The attack is recognized to be usually upon cranial or peripheral nerves, and sarcoid of the brain or spinal cord is a distinct rarity. The following case of a man personally observed at intervals for over twenty years, and only recently dead, is therefore of interest, for he had a cerebral lesion at one stage of his illness. This presented as a slowly growing intracranial tumour which was surgically removed some 13 years ago.

Case Report

The patient, a van driver, was first seen when aged 24 as an out-patient in the ophthalmic department of the Cumberland Infirmary, Carlisle, on November 3, 1934. He complained that the sight in his right eye had begun to fail early in June that year, and the left eye six weeks later. In August he had developed bilateral parotid swellings, first on the right and three weeks later on the left, which had persisted since, and in October he had noticed a transient swelling on the left shin. On questioning it appeared that he had had an attack of left-sided chest pain, with shortness of breath, for some weeks in April and May, 1934, and a similar episode in 1931. There were no other significant points in the previous medical or family history.

On examination both eyes showed ciliary injection, fine keratic precipitates, a number of small pale nodules in the iris (eight in the right, four in the left : Fig. 1), and many posterior synechiae. The fundus was obscured by vitreous opacities. His visual acuity was less than 6/60. Both parotid glands and the right submaxillary gland were enlarged and hard. No other abnormal physical signs were found.

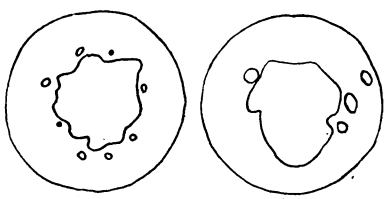

FIG. 1.—Showing relative size and position of iris nodules.

The patient was admitted to the ward under the care of Dr. T. McL. Galloway, the results of whose special investigations were as follows:—chest *x*-ray examination: hilar glands enlarged bilaterally, lung fields clear ; tuberculin tests : negative at 1/10,000, 1/1,000, and 1/100 ; blood W.R. negative ; full blood count: red cells, 6,150,000 ; Hb, 125% ; white cells, 4,700, normal differential count ; urine: no albumin or sugar, no casts or cells, no tubercle bacilli ; B.P., 138/80 ; no cough, no pyrexia. When discharged from hospital on January 30, 1935, the parotid swellings had subsided, the ciliary injection and the iritic nodules had gone, though some keratic precipitates and many vitreous opacities remained. Radiologically the hilar masses were still present, but were thought to have decreased somewhat in size. The diagnosis was chronic uveoparotitis.

The patient was seen at intervals during 1935 and once in 1936. The ocular signs regressed further, but he continued to complain of shortness of breath on exertion and easy tiring. Early in 1940 he had severe headaches ; these increased in severity, and in consequence he had to stop