tackle the problem of the medical curriculum, and promote the essential rewriting of textbooks. The whole medical world would be stimulated and benefited. I think that, with the new medical system in Britain based as it is on the soundness of the past, it is possible for this country more than any other to start such an experiment and make it a success.

Conclusion

And who is concerned in originating this worth-while move we are discussing ? Obviously the Royal Colleges, the Postgraduate Federation, and the universities. I know, too, that many important bodies such as the Rockefeller and Nuffield Foundations and Unesco are interested. But surely out of all these our own College seems pre-eminently suited, as it should be, to serve so uniquely useful a purpose in modern medicine. But what a pity it is that the conception of an Academy of British Medicine died stillborn.

I will finish by quoting some stimulating words from Walshe's (1948) Harveian Oration : "This College can, and, if it is to survive as something significant in the intellectual life of medicine, must remain a fountainhead of academic medicine, or true learning : the home wherein a philosophy of medicine finds a permanent abiding-place and disciples eager to learn and teach it." I hope this meeting will show we are imbued with this spirit, this faith, and this endeavour.

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CLINICAL EVALUATION OF EFFECTS OF DRUGS ON MEDICAL STUDENTS AS A TEACHING METHOD

BY

ANDREW WILSON, M.D., Ph.D., F.R.F.P.S.

G. S. CROCKETT, M.A., M.B.

A. N. EXTON-SMITH, M.A., M.B., M.R.C.P.

AND

HANNAH STEINBERG, B.A.

(From the Department of Pharmacology, University College London)

In the past the medical student often first became acquainted with drugs when faced with the laborious task of trying to write and compound prescriptions to the satisfaction of his teachers. He had little first-hand knowledge of the action of drugs, and the clinical evidence of their effects on patients was often confusing and difficult to interpret. The drugs in use to-day are potent and valuable remedies. It is therefore the responsibility of those who train medical students to ensure, as a prerequisite to safe and effective therapy, a sound knowledge of the principles of pharmacological action.

Numerous experimental methods have been devised to demonstrate the action of drugs on isolated tissues and in the intact animal. Such methods provide the fundamental approach, but the criticism has been made that the student often fails to appreciate the connexion between these effects of drugs and their clinical application. The experimental study of the action of drugs on normal man is a logical step in the process of understanding the effects of drugs in disease. For this reason part of the practical course in pharmacology given to preclinical medical students at University College, London, consists in observing the effects of various drugs administered to members of the class. The experimental methods used and the results obtained in a class of approximately 70 students are described below.

The class was held once a week and lasted approximately five hours. The students worked in pairs, each acting in turn as subject and observer ; during the experiment they were housed in cubicles, each cubicle accommodating two pairs of students and one member of staff acting as supervisor. The subjects were all normal healthy male or female medical students. In each experiment the selection of drugs to be studied was at random, and each student drew from a hat a numbered card representing a dose of a particular drug or inert substance the identity of which was not revealed until the experiment was concluded and the observations fully recorded.

Three types of experiment were carried out, in each of which the drugs were administered by a different route, in order to assess the following: (1) the analgesic activity of certain drugs when given subcutaneously ; (2) the effects on voluntary sensory-motor co-ordination during inhalation of mixtures of nitrous oxide and oxygen ; and (3) the effects of drugs, which were taken by mouth, on the performance of three tasks involving rate of voluntary movement, sensory-motor co-ordination, and sustained attention and muscular control respectively.

1. Assessment of Analgesic Activity

Method

Thirty-five subjects were used for estimating the analgesic potency of the following drugs: morphine, 10 and 15 mg., amidone ("physeptone"), 10 and 15 mg., pethidine, 100 and 150 mg., and physiological saline, 2 ml. Thus each dose of each substance was tested on five students.

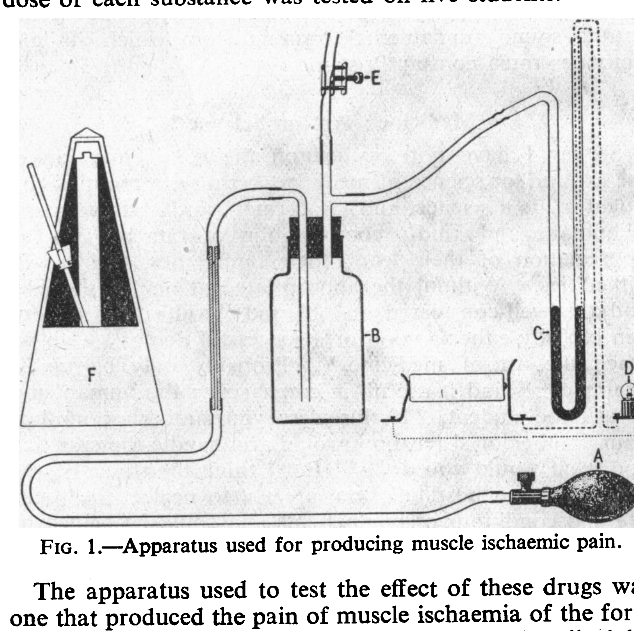

FIG. 1.—Apparatus used for producing muscle ischaemic pain.

The apparatus used to test the effect of these drugs was one that produced the pain of muscle ischaemia of the forearm in a manner resembling that originally described by Lewis, Pickering, and Rothschild (1931) and later modified by Harrison and Bigelow (1943).

The subject lay on a couch and a sphygmomanometer cuff was placed on each upper arm. Muscle ischaemia was produced by inflating the cuff to 160 mm. Hg, and the subject contracted the muscles of the corresponding forearm by squeezing the rubber bulb (A) shown in Fig. 1. The contraction of this bulb forced air into the bottle (B) and thus displaced the mercury in the U-tube (C). When the mercury was displaced sufficiently it completed an electric circuit and lit the lamp (D). To enable the apparatus to be adjusted for subjects with different strengths of grip the resistance to pressure could be modified by means of the variable leak (E) on the T-tube. The frequency of squeezing was determined by a metronome (F) set at 90 beats a minute.

Before each estimation the subject's arm was raised and gently stroked to empty the veins. The cuff was rapidly inflated to 160 mm. Hg and the arm lowered; simultaneously the subject began to squeeze the bulb, in time to the metronome, with enough pressure to light the lamp. The observer noted (1) the time of onset of pain, and (2) the time of onset of "exhaustion," which was determined by the failure of the subject to light the lamp in six consecutive attempts. When the exhaustion point was reached the cuff was deflated and the estimation was repeated on the other arm. The whole procedure was repeated every 15 minutes.

After three or four estimations on each arm the analgesic drug was given subcutaneously and observations were continued at 15-minute intervals for two to three hours. The observer also recorded changes in respiration, pulse rate, and the appearance of the skin; any sensations reported by the subject were also noted.

Results

The typical effects of one of the drugs on an individual subject are shown in Fig. 2. The times of onset of pain and of "exhaustion" were measured in seconds, and a curve for each has been plotted. The first three readings indicate the normal performance; after the drug was injected there was an increasing delay in the onset of pain and a decrease in the time before "exhaustion" occurred.

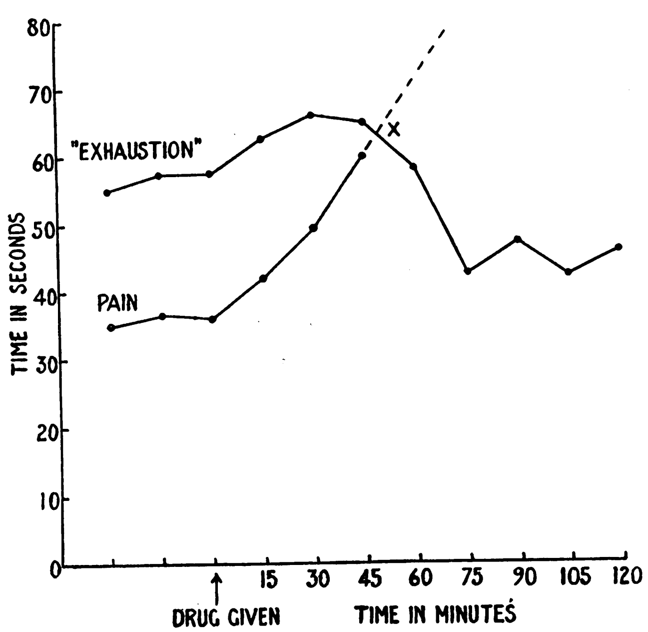

FIG. 2.—The typical effects of an analgesic drug on the time of onset of "exhaustion" and of pain. At about the time indicated by X the subject failed to compress the bulb for long enough to produce pain before the onset of "exhaustion."

This method of assessing pain is limited by the fact that the time of onset of pain cannot be measured when it is preceded by the onset of "exhaustion." For example, at the point X the subject ceased to contract his hand effectively, and useful estimations of the time of onset of pain could not be made unless and until pain occurred again *before* the onset of "exhaustion."

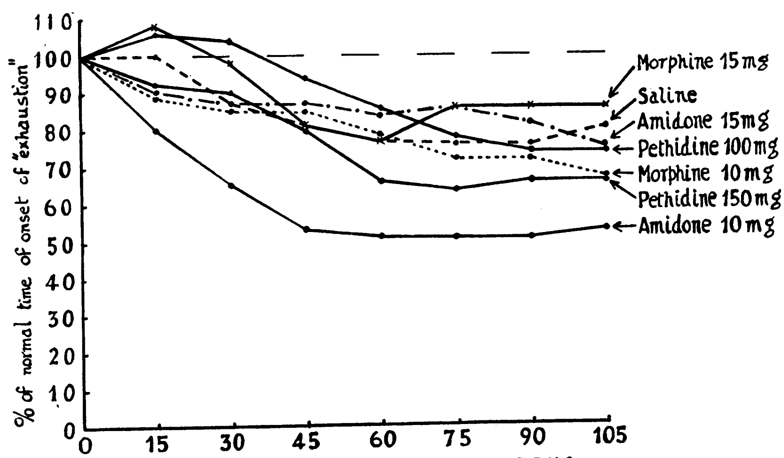

FIG. 3.—The effects of analgesic drugs on the time of onset of "exhaustion." Each curve represents the average results from five subjects.

Average curves (five subjects) of the percentage decrease in time before onset of "exhaustion" with each drug are shown in Fig. 3. In comparison with the relatively slight effect of the other drugs it is surprising to note that with amidone in the smaller dose of 10 mg. "exhaustion" occurred earliest of all.

The difference between the mean values for all "exhaustion" times for saline and amidone, 10 mg., was tested for the "significance of trend differences" (Lindquist, 1947). The F-ratio thus obtained was 2.37 (d.f. $n_1=7$, $n_2=56$, $0.05>P>0.01$). The difference in trend between the two curves is therefore significant. It is evident from inspection of the graph that significant differences are not to be expected in the case of the other drugs. We find it difficult to advance an explanation for this singular effect of 10 mg. of amidone, which was also observed in a previous class. This anomaly might be further investigated.

It was not possible, for the reasons already described, to construct complete average curves of the effect of the analgesic drugs on the time of onset of pain. However, if the drug had no analgesic effect, pain would have been expected to occur well before the onset of exhaustion, as in the case of saline. Since with all drugs except amidone, 10 mg., the onset

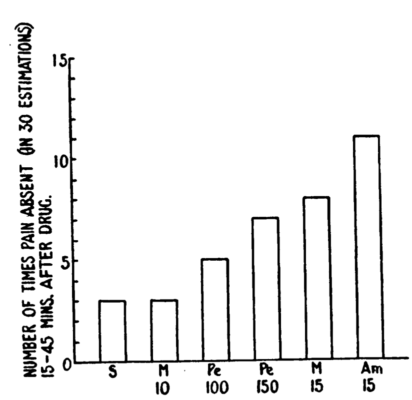

FIG. 4.—Diagrammatic representation of the comparative potencies of the analgesic drugs, assessed by the number of times pain was absent when the subjects were tested during the period 15 to 45 minutes after injection of the drug. S = saline, M = morphine, Pe = pethidine, Am = amidone. The number beneath each drug indicates the dose in mg.

of exhaustion did not differ significantly from that following the injection of saline, it is possible to assess the analgesic effect of the drug in terms of the number of times when pain failed to occur by the time "exhaustion" had set in. A block diagram (Fig. 4) has been constructed on this principle for each dose of each drug, from the results of estimations carried out at 15, 30, and 45 minutes after the injection of the drug. The height of each block may be regarded as an indication of the relative analgesic potency of the different drugs. Our experiments fail to distinguish between the effects of saline and those of 10 mg. of morphine, and the greatest analgesic activity was observed with 15 mg. of morphine and 15 mg. of amidone. Moreover, reference to Fig. 3 suggests that these two drugs in doses of 15 mg. produce the least effect on "exhaustion." In the choice of drug to be used clinically analgesic potency combined with minimum effect on "exhaustion" is obviously a factor to be taken into consideration.

Incidence of Subjective Effects

The numbers of subjects who reported side-effects are shown in Table I. Drowsiness and "muzziness" occurred in nearly three-quarters, and nausea and vomiting in more than half of the group. In one-fifth of the subjects the respiratory rate fell below 15 a minute.

TABLE I.—*Incidence of Subjective Effects in 30 Subjects Given Analgesic Drugs*

Subjective Effects	No. Showing Effects
Drowsiness and muzziness	23 (77%)
Dizziness	22 (73%)
Nausea (without vomiting, 8; with vomiting, 10)	18 (60%)
Sweating, pallor, and flushing	11 (37%)
Dryness of mouth	11 (37%)
Respiration below 15/min.	6 (20%)

With amidone, 15 mg., and morphine, 15 mg., nausea and vomiting, or dizziness, occurred more often than with pethidine, 100 and 150 mg., or amidone, 10 mg. These effects are particularly apt to begin when the subject assumes an upright position at the end of the experiment.

2. Effect of Gas Mixtures on Voluntary Sensory-motor Co-ordination

Method

This experiment was designed to show the effect of different mixtures of nitrous oxide and oxygen on a task involving sensory-motor co-ordination.

The gas mixtures were measured by rotameter type flowmeters (estimated accuracy within 2%) and delivered to a large reservoir bag of 3½ gallons (15.9 litres) capacity which was connected to an R.A.F. oxygen mask. This type of mask incorporates a small microphone by means of which the subject can communicate with the experimenter. All gas mixtures delivered to the mask were perfumed by inserting into the circuit a filter paper impregnated with lavender oil.

For the test of sensory-motor co-ordination we used a tubular apparatus with a hole at the top just large enough to admit small steel ball-bearings, which were inserted with a pair of forceps. (This apparatus resembles the R-V manual dexterity test developed by the National Institute of Industrial Psychology.) The subject's performance was measured by the average time taken to insert 25 ball-bearings.

Every subject first practised the task in sets, each of which consisted of four consecutive trials, until his performance did not improve further; this usually involved four to five sets. The average score of the last set was then taken as the subject's normal performance and was compared with his performance while inhaling the gas. The normal performance ranged from 41 to 56 seconds, the average being about 50 seconds.

Each subject, according to the card which he drew, was then given 40% nitrous oxide in oxygen, or 50% nitrous oxide in oxygen, or oxygen only. The subjects were told that they would be unable to distinguish between the gas mixtures and the oxygen on the basis of smell or taste.

After inhaling the gas for 1½ minutes at rest, the average performance on four trials of the ball-bearing test was again assessed during continuous inhalation of the gas mixture. Most subjects continued the experiment for six to eight minutes.

After the experiment they were asked to describe subjective effects noted during inhalation; any signs observed by the experimenter were also recorded.

Results

The mean scores on the ball-bearing test are shown in Table II. It will be seen that only a proportion of those subjects who received nitrous oxide mixtures were able to complete the experiment. Several pulled off the mask; two, whose scores have not been included, completed the test only after continuous prodding and encouragement from the demonstrators; and seven lost consciousness.

TABLE II.—*Effect of Gas Mixtures on Ball-bearing Test*

	O_2		N_2O 40%		N_2O 50%	
	Before	During	Before	During	Before	During
No. of subjects who attempted experiment	10		10		15	
No. of subjects who completed experiment satisfactorily	10		7		5	
Mean scores (seconds)	49·0	54·9	50·3	76·0	50·8	96·2
Standard deviations of mean scores	±6·4	±7·4	±4·5	±17·7	±3·1	±16·6
Mean % decrease of speed under gas		11		52		89

The mean scores of the three groups of subjects before inhalation—that is, their normal performances—are practically identical. The mean scores during inhalation of the different gas mixtures all show an increase in the time taken, equivalent to a decrease in speed: 11% with oxygen, 52% with the 40% nitrous oxide mixture, and 89% with the 50% nitrous oxide mixture.

Analysis of variance has been applied to the differences in score of the three groups, and has shown the results to be highly significant ($F=16.2, [n_1=2, n_2=19]$; for $P=0.001$, $F=10.16$—that is, with the given degrees of freedom, one would expect an F-ratio as great or greater than 10.16 to arise less than once in a thousand times.)

The general trend of the quantitative results was very much what one would expect: the higher the dose, the less efficient the performance. The deterioration of performance under oxygen should also be noted. The difference from the normal of 11% may seem small, but it is consistent and statistically significant ($t=4.47$, [d.f.=9], $0.01>P>0.001$). Some of this might be attributable to discomfort caused by wearing the mask, but it seems likely that psychological factors such as suggestion and expectation were also involved. This was confirmed by some of the reports given by the subjects, and by the fact that occasionally a subject showed quite marked symptoms with oxygen alone. For instance, one student, after inhaling oxygen for one minute, told the demonstrator that he was sure that it was nitrous oxide, and subsequently described his experiences in great detail as "typical nitrous oxide symptoms," such as giggling, talkativeness, difficulty in concentrating, and "twitchings."

The wide range of individual responses, especially under the higher drug concentration, is also noteworthy. One subject, for example, was no more inefficient under 50% nitrous oxide than another who received only oxygen, while, as has already been pointed out, seven others lost consciousness and could not complete the test at all.

Subjective Effects

The most commonly reported subjective effect was a general "muzziness," variously described as feeling vague, dreamy, or "being distant." One subject reported, "I've just had the most frightening dream about relativity I have ever had." Sporadic chuckling was quite frequent, though it decreased noticeably when no appreciative audience was present. Pleasant symptoms were often indicated by comments such as "Enjoyed the experience," "Was sorry to take the mask off," or "Nice giggly feeling." Several subjects described changes in time sense, asserting that time during inhalation seemed to drag and a few minutes appeared like several hours. One subject under 40% nitrous oxide persisted in dropping imaginary ball-bearings into the apparatus long after the experiment was over. These various symptoms, however, were usually of short duration.

3. Effects of Other Drugs which Stimulate or Depress the Central Nervous System

Methods

This experiment consisted of three types of tests, which were used to demonstrate the effects of drugs which stimulate or depress the central nervous system. The drugs were given by mouth and were selected as previously described, so that five students each received one of the following: amphetamine sulphate, 15 or 25 mg.; "seconal," 3 or 4½ gr. (0.2 or 0.3 g.); cyclobarbitone, 3 or 4½ gr.; tablets or capsules of lactose as control.

The tests used were: (*a*) The ball-bearing test (already described). (*b*) The tapping test, which was used to measure the speed and consistency of voluntary motor movement. The apparatus consisted of a morse key connected to an electric numeral counter, and the performances were scored as the number of taps which were recorded during a standard period of continuous tapping for three minutes. (*c*) A disk-dotting machine of the McDougall–Schuster type was used to test sustained voluntary attention and muscular control (Smith, Culpin, and Farmer, 1927). The performance was scored as the total number of dots aimed at and hit before five consecutive misses were recorded.

Two of these tests were chosen by each subject, who practised the tests until consistency in performance was attained, the last score being taken as his normal performance. The drug was then given with a draught of water; the tasks were repeated at intervals of 15 minutes for two to three hours.

Results

Average curves have been plotted showing the effect of several of the drugs on the performance of the tapping test. These are shown in Fig. 5 as the percentage increase

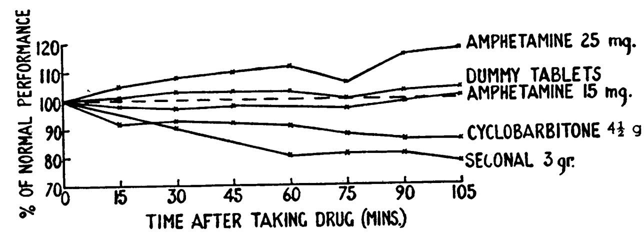

FIG. 5.—The effects on the performance of the tapping test after administration by mouth of amphetamine sulphate, cyclobarbitone, and seconal. Dummy tablets containing lactose were used as controls.

or decrease of normal performance. On the whole the dotting test provided the most sensitive index of the action of the various drugs.

We were unable to obtain sufficient records for statistical analysis of the effects of all the drugs on the three different tests. It was possible, however, to average the maximum responses for two doses of each of the sedative drugs on the tapping test, of which Fig. 6 is a diagrammatic representation. Although this gives no information about the time of onset or of maintenance of the maximum effect, it illustrates to the student one method of assessing the nature of and the quantitative differences in the effect of drugs. It is not intended to suggest that this is an ideal method for testing hypnotic drugs—the best way to do this is by observing their power to produce sleep. This they often did in the course of the experiment, but the conditions in the class were not quiet and consistent enough to make this effect a valid criterion.

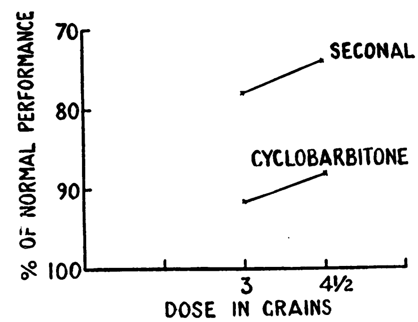

FIG. 6.—Comparative effects of seconal and of cyclobarbitone on the performance of the tapping test. The results are expressed as the maximum percentage decrease in performance for each drug given in doses of 3 and 4½ gr.

Discussion

It might be asked, "What does the medical student learn from this method of teaching pharmacology?" It is well to point out, of course, that these experiments are only part of the practical course in pharmacology and are, moreover, preceded and followed by systematic lectures on the subject, so that the student is able to appreciate the general nature of the action of drugs. We consider that the outstanding advantage of this part of the practical class is that the student experiences at first hand the effects of certain drugs and learns to assess some of the qualitative and quantitative changes produced. By comparing his own experiences with those of the other members of the class, he begins to appreciate the individual variation in response to the same dose and drug. In addition, different methods of administering drugs are illustrated.

The importance of control observations and the influence of suggestion are illustrated by studying the effects of inert substances. This provides a valuable basis for the appreciation of the function of the "placebo" in therapeutic practice. The undesirable side-effects of drugs are also demonstrated, and the student learns that these effects must be taken into consideration in the choice of a drug for a particular purpose.

On the whole there was little disturbance of the normal routine of the student; the overall incidence of subjective effects in the class is shown in Table III. With the exception of five students, all the members of the class were

Table III.—*Total Incidence of Subjective Effects in 70* Subjects Performing Experiments 1 and 3*

Subjective Effects	No. Showing Effects
Nausea (without vomiting, 8; with vomiting, 13) ..	21 (30%)
Dizziness	33 (47%)
Other minor symptoms	39 (56%)
Sleep the following night:	
Sounder than usual	20 (29%)
Less sound than usual	13 (18%)
Same as usual	37 (53%)
Spent night in hospital	5 (7%)

* This number includes 11 who received dummy tablets or saline injections.

conducted safely and without incident to their home or lodgings by one or more persons not under the influence of any drug. Because of persistent vomiting or dizziness, or because the journey home involved a long period of travel, five students were accommodated overnight in hospital. For them it was an interesting experience, and they had all fully recovered by the next morning. There was little disturbance of sleep, except with those who had taken amphetamine, and this also served to illustrate the action of that drug.

Although it was clearly understood that attendance at the class was optional, all students eagerly participated and co-operated well in the arrangements necessary for the conduct of the experiments. Indeed, many of them welcomed the opportunity later of acting as subjects in further research on the action of drugs on man.

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According to *Time* magazine Dr. Willard Cole Rappleye, dean of the faculty of medicine at Columbia University, is reported to have said recently: "Medicine is becoming a social as well as a biological science. We would rather have a student with intellect . . . and a rounded capacity for life than one whose only view of humanity was gained as he passed from one laboratory to another. So-called 'premedical' education should be abolished in the colleges. . . . There is no such thing as 'premedical' education nor should students in colleges who plan to enter professional schools be regarded as premedical or predental students. [College] education is not 'pre' anything, but should be devoted to the objective of providing as broad a cultural education as the institution can provide. It should be a preparation not for medicine or dentistry or public health, but for life."

SOME MECHANICAL AIDS TO INSTRUCTION

BY

ROBERT OLLERENSHAW, B.M., D.M.R.D., F.I.B.P. F.R.P.S.

AND

PETER HANSELL, M.R.C.S., F.I.B.P., F.R.P.S.

(From the Departments of Medical Photography, Manchester Royal Infirmary and Westminster Hospital)

Over the last two decades there has been a very marked shift of emphasis in instructional method from the aural to the visual. The two are, of course, complementary and neither can readily stand alone, but perhaps one of the greatest positive experiences emerging from the war was the wide realization of the great efficiency of the eye compared with the ear as a receptor of instruction. The Army Bureau of Current Affairs (ABCA) succinctly modernized the old Chinese proverb "One picture is worth a thousand words" to "One in the eye is worth two on the ear."

The newer methods of teaching are undoubtedly of very great value. Yet they often run the risk of being "oversold" by their enthusiastic backers and of falling into disrepute for failing to do what they were never meant to do. They are "aids" to instruction, not instruction in themselves; they must never be used as a form of escape for the lazy teacher. To use these mechanical methods correctly requires more, not less, effort than the preparation of a lecture of the traditional type.

School-teachers have been quick to realize the value of the new methods, and many of the more enlightened local education authorities have set aside substantial resources to provide the material; to date most medical schools have lagged sadly, and the few that are progressing are often more impeded than helped by ill-informed enthusiasm. There is a widespread tendency to say, "Let's make a film of this, or a filmstrip of that," without consideration of the limitations or suitability of the media, or without proper understanding of the audience for which the

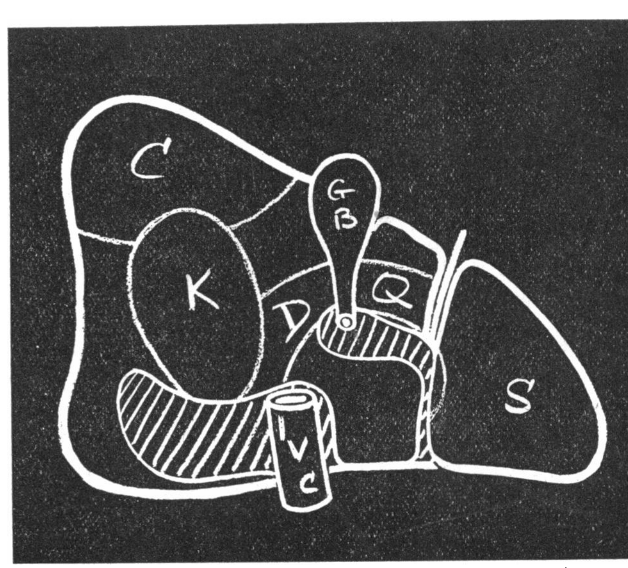

Fig. 1.—The simple type of drawing suited to the chalkboard.