oxygen and ether. After recovery from the operation the patient stated that he had no recollection of the events preceding the operation, and a full amnesia was attained with the small dose.

In cases where there is a possibility of danger it appears to me that if a basal anaesthesia is used a reduced dose should be given which would effect amnesia without causing complete loss of consciousness.

CONCLUSIONS

In prescribing hypnotics it is wise to select one or a combination of the less toxic type of drugs whose action is well known. I have been so impressed by their toxic effects that I never prescribe any of the barbituric acid group of drugs or of the sulphonal group.

These drugs should only be obtained on the prescription from the medical adviser, and the prescription should be retained by the pharmacist and not repeated, except on medical authority and signature. The total quantity ordered on a prescription should be well under a possible fatal dose.

Legislation regarding the sale of poisons is under consideration as a result of the recent Pharmacy and Poisons Act, which was passed this year (1933).

A close co-operation between the medical profession and those practising pharmacy is essential if dangers from hypnotic drugs are to be avoided.

CARBON DIOXIDE THERAPY IN LOBAR PNEUMONIA

BY

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Of recent years increasing attention has been given to the use of carbon dioxide in respiratory conditions. In some ways it is the ideal respiratory stimulant; its chief action is to increase the depth of breathing without accelerating its rate excessively. This result is apparently achieved in two ways: first, by the changes it produces in the pH of the blood, secondly, by the specific effect of the HCO_3^- ion itself. It is therefore to be expected that its value would be tested in many respiratory conditions, in some of which, indeed, its utility has already been fully demonstrated. These include atelectasis, certain forms of asphyxia, and post-operative bronchopneumonia. Its value, however, is still under dispute in lobar pneumonia. This paper is concerned with the latter condition.

Hanson and Calhoun,¹ in a series of early cases treated for short periods by 5 per cent. CO_2 and 95 per cent. O_2 , carefully controlled by repeated x-ray examinations, failed to abort the spread of consolidation. Alison² claimed that the disease could be arrested if treatment were begun in the first thirty-six hours. In his opinion the patients "were more comfortable and appeared to progress better" with CO_2 added than with oxygen only. On the experimental side Henderson³ and others assert that in pneumococcal pneumonia with bronchial obstruction CO_2 prevents the development of the disease. He considers that atelectasis plays an important part in lobar pneumonia. Since hitherto there has been a lack of blood-gas studies in man after CO_2 administration, the following observations attempt to supply some of the missing evidence.

As there is a considerable amount of information about the benefit of O_2 alone, it was considered advisable to study the effects of CO_2 unaided by oxygen. The procedure adopted has been to measure first the rate and depth of respiration. A sample of arterial blood was

then taken from the femoral artery. Approximately 3 per cent. carbon dioxide was administered with a loose face mask, and the examinations of the breathing and the blood were repeated fifteen minutes later. The blood gases were determined by the van Slyke method. There are obvious difficulties in the way of investigations of this sort; for instance, the accuracy of measurements of the tidal air cannot be strict. Any apparatus is apt to disturb a patient with pneumonia, and in particular any resistance to expiration is quickly resented. To obtain the measurements mentioned here a specially devised low resistance mask was employed, which has proved its value in collection of air in dyspnoea.⁴ Some results are shown in the accompanying table.

	Arterial Saturation (Vol. per cent.)		Respiratory Rate per Minute	Litres per Minute Ventilation	Tidal Air in c.cm.
	O_2	CO_2			
1. (a) before CO_2	87	35	41	11.47	280
(b) after (15 minutes later)	88	46	42	15.1	360
2. (a)	91	37.4	31	12.1	390
(b)	92.5	48.2	29	13.75	473
3. (a)	85	32	33	12	365
(b)	85.6	41.5	31	13	420
4. (a)	84	31.4	35	10.4	290
	83.2	43	33	12.05	365

These observations were made during the first five days of lobar pneumonia.

The first point to be noted in the table is that arterial anoxaemia is unrelieved after CO_2 administration in these quantities, in spite of the fact that the depth of the tidal air is considerably increased. This raises the question as to what part shallow breathing plays in the production of anoxaemia.

SHALLOW BREATHING

Haldane, Meakins, and Priestley⁵ have shown that the artificial limitation of the tidal air in normal subjects to about 200 c.cm. resulted in periodic breathing, which was removed by adding oxygen. They also demonstrated that the mixed alveolar air under such conditions may contain a higher pressure of O_2 than would be expected to cause anoxaemia. This they explained by uneven ventilation.

Meakins⁶ investigated the question further in pneumonia by correlating the ventilation with the cyanosis. He considered that the shallow restricted breathing in pneumonia was an important factor in causing the anoxaemia. Since anoxaemia in its turn gradually leads to failure of the respiratory centre and rapid shallow breathing, there is a vicious circle which has to be broken if recovery is to follow. The same observer and Davies⁷ published valuable studies of the tidal air and arterial oxygen in pneumonia. Consecutive examinations of the same patient revealed that, as the cyanosis deepened, the arterial oxygen fell and the breathing became more shallow. In that series of observations there were only two measurements of a tidal air below 200 c.cm.; they occurred on the ninth day, when the patient died. These measurements were associated with respiratory rates of over sixty per minute, which is rare in adults who recover. The lowest tidal air during the first five days in four patients was 220 c.cm. In my experience the breathing of patients with pneumonia during the first few days is often of normal depth or even greater, as the table shows. It must be remembered, also, that when a large part of a lung is solid a given tidal air represents a better ventilation for the remaining lung.

When air ventilation is adequate, CO_2 in the quantities here given evidently cannot raise the alveolar O_2 enough to be reflected in the arterial blood. Even with maximum ventilation with air in the normal subject (breathing 60 litres per minute and 1 litre per breath), it has not been found possible to raise the alveolar O_2 from its normal 100 mm. to above 120 mm. Even this rise would be quite inadequate in treating the anoxaemia of pneumonia. The actual increase of ventilation brought about by the use of CO_2 in pneumonia is far inferior to this. In severe cases of pneumonia with much anoxaemia, as the disease progresses the breathing becomes more shallow. It is not possible to measure the effect of this on the alveolar O_2 of a patient with pneumonia, but the effect of gradual

diminution of the tidal air on the normal alveolar oxygen pressure is shown in the figure. The subject was given an oxygen-rich mixture to breathe in order to avoid any oxygen lack. The breathing was timed at a given rate and the depth was left to regulate itself automatically.

It will be noted that the alveolar O_2 actually rises as the tidal air falls. When the tidal air is at about 230 c.c.m., the alveolar O_2 begins to return towards its original level. Even when the tidal air is 200 c.c.m. and the rate sixty per minute (which may well be termed rapid shallow breathing) the mixed alveolar O_2 is not below the figure at which it began during quiet breathing. On breathing air at the rate of seventy-two respirations per minute and at a depth of only 128 c.c.m. the average alveolar O_2 was 91 mm. Such breathing is far more rapid and shallow than ever occurs in lobar pneumonia in the adult, and yet the mixed alveolar O_2 is but little below the average normal 100 mm.

It is possible that uneven ventilation of alveoli may explain such high O_2 figures, in spite of such a low tidal air, as was shown in the experiments of Haldane on normal subjects; but in the anoxaemia of pneumonia, when there is some alveolar obstruction to the passage of O_2 , there is more chance of compensatory oxygenation in some of the overventilated areas than there is in the anoxaemia of artificially limited breathing. Uneven ventilation is quite inadequate to explain the experiments of Uyeno.⁸ This observer, by heating from 35° to 39°, increased a cat's respiration from sixteen per minute to 240: the depth was reduced from 16.7 c.c.m. to 2.7 c.c.m. The minute-volume of the heart stayed at the same level, and the arterial O_2 saturation changed only from 99 per cent. saturation to 92 per cent. These observations tend to minimize the importance usually attributed to shallow breathing in the causation of anoxaemia, and help to explain why CO_2 as given here fails to relieve the condition.

Before leaving the question of the effect of CO_2 on arterial O_2 saturation, there is one more point to be made. If areas of lung collapse played an important part in the causation of anoxaemia in lobar pneumonia, it would be expected that an increase in the tidal air would improve

the oxygenation of the blood by preventing venous short circuits. These observations appear to show that this is not the case.

ACTION OF CO_2 ON THE O_2 DISSOCIATION CURVE

It is well known that CO_2 alters the shape of the O_2 dissociation curve of haemoglobin, but it is difficult to assess the practical importance of this shift to the right. Theoretically it means that the tissues obtain their O_2 more readily. It also means that O_2 is picked up less readily in the lungs. This latter factor would tend to prevent a rise in alveolar O_2 pressure from having the expected result on the arterial O_2 saturation. But on the whole it is probable that changes in CO_2 tension of the order here considered play a part of minor importance in pneumonia with regard to the carriage of O_2 by haemoglobin.

ARTERIAL CO_2

It will have been noted from the table that the arterial CO_2 is low in pneumonia. This provides confirmation of Meakins's original observations. The explanation would seem to be that the increased ventilation has "washed out" the gas, as is well known to occur with overbreathing. This might be due to central or peripheral causes, but we have still much to learn in this connexion about lung reflexes, such as the Hering-Breuer reflex, in pathological states.⁹

Whatever the mode of production there is some evidence that a reduction of arterial CO_2 may have in itself serious effects and its removal therefore bring benefit. Thus Yandell Henderson¹⁰ has dealt in a series of papers with the circulatory failure which results from acapnia or acarbia, as he now terms it. Dale and Evans¹¹ have shown that the fall of arterial pressure after severe overventilation is due to depression of the vasomotor centres of the bulb and the spinal cord brought about by removal of free CO_2 , and not to changes in the hydrogen-ion concentration in the blood ("alkalosis"). On the other hand, CO_2 has a direct vaso-dilator action on capillaries. In lobar pneumonia, however, there are other factors influencing the blood pressure, so that the part played by CO_2 lack of itself cannot be analysed at present except by measuring the effect of its administration. One thing is clear: whatever ill effects may be demonstrated as due to acapnia, this state can be removed very rapidly by the addition of small quantities of CO_2 .

CLINICAL EFFECTS

Pain

The increased respiratory effort brought about by CO_2 is apt to distress a patient unless it is kept within narrow limits. Reference to the table shows that CO_2 in sufficient quantity to augment the tidal air by 100 c.c.m. or less will raise the arterial CO_2 by 10 volumes per cent. in a few minutes. Such an increase in depth does not apparently cause much discomfort. In cases of thoracic pain the use of CO_2 would, of course, be contraindicated unless opiates were given at the same time. The use of CO_2 after morphine is helpful in avoiding excessive depression of the respiratory centre.

Blood Pressure

Clinically, the effect of CO_2 on the blood pressure in some cases is very noticeable. A rise of about 20 mm. Hg in systolic pressure was observed. The pulse became fuller. The explanation of this is probably a mechanical one from an increased venous return rather than from any action on the vasomotor centre, for the following reasons: signs of vasomotor failure as shown in experimental acapnia are uncommon in lobar

pneumonia at this stage. Also, a similar rise may be demonstrated in a normal person whose arterial CO_2 is not diminished.

Cyanosis

There is usually little or no change in the cyanosis. What there is cannot be due to increased arterial oxygenation (see table), but might be explained by an increase in the minute-volume of the heart or by a local vasomotor change. Otherwise it is difficult by the bedside to point to any immediate change in a patient as a result of small quantities of CO_2 at all comparable to the effect of O_2 in lobar pneumonia.

CONCLUSION

The practical conclusion of this paper is that in the absence of respiratory failure, as evinced by shallow

breathing, the clinical benefits of CO_2 administration in air are not sufficiently demonstrated by these observations to warrant its routine use in lobar pneumonia.

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RENAL TUBERCULOSIS

WITH A SURVEY OF SEVENTY CASES

BY

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Renal tuberculosis is an insidious disease, for the focus in the kidney is usually well established before its presence gives rise to symptoms. In the majority of cases the outstanding symptoms are referred to the bladder, and consist of increased frequency in urination, with pain before and after the act. The frequency may be variable, but tends to increase, and, as the disease progresses, the patient may require to urinate as often as every twenty minutes, night and day. The urine is acid or neutral, contains albumin and pus, and, frequently, blood. Pain in the renal area is often absent altogether, or is insignificant in degree. Usually a diagnosis of "cystitis" is at first made, but the symptoms fail to respond to the medical treatment commonly prescribed for this complaint. All such cases of persistent frequency, particularly when occurring in adults between 20 and 40, should be suspect.

It is the present consensus of opinion that a normal kidney cannot filter tubercle bacilli from the blood stream into the urine. If, therefore, tubercle bacilli are found in the urine, and a genital tuberculosis can be ruled out, a renal focus must be present, because there is no such thing as a primary tuberculosis of the bladder. Recognition of a genital tuberculosis in the male is usually easy, but it should not be forgotten that this condition is frequently accompanied by a coincident renal infection. In the female the diagnosis of a genital tuberculous lesion may not be so obvious. In the following case a tuberculous cystitis was found to be secondary to infection of a Fallopian tube.

A woman, aged 24, a school teacher, was referred for consultation because of a persistent frequency and dysuria of one year's duration; she required to urinate several times in an hour. She had had a period of sanatorium treatment in Switzerland four years previously for pulmonary tuberculosis, but it was considered that this lesion had healed. The urine contained a heavy deposit of pus. Examination of numerous smears failed to reveal the tubercle bacilli, but a guinea-pig inoculation was positive. Cystoscopy showed a generalized cystitis, and, in places, superficial ulceration. There was considerable adherent purulent lymph on the right side. The base of the bladder to the right of the left ureteric orifice was markedly elevated. The ureteral orifices looked normal, and both ureters were catheterized to the renal pelves. An abundant flow of clear urine came from either side, and both specimens were found to be free from pus, and sterile. Bilateral ascending pyelograms were normal. The x-ray films, however, showed a large, rounded, calcareous shadow in the left side of

the pelvis, above the level of the ischial spine. It was obvious that the tuberculous cystitis was not of renal origin. The diagnosis was settled by a vaginal examination, which revealed an extensive pelvic mass, due to a tuberculous pyosalpinx.

The discovery of the tubercle bacillus is not essential in order to establish a diagnosis. The presence of pus in the urine, but no organisms, is strongly suggestive of a tuberculous infection, and a guinea-pig inoculation should be made. I cannot, however, agree with Wade, who states that "if, on examining the cellular deposit, no organisms are found in it, it is safe to assume that the infection is tuberculous and that you have failed to detect the causal virus."¹ This infers that every case of aseptic pyuria is tuberculous; contrary to this, I have had under observation several such cases, in which an investigation of the complete urinary tract, including guinea-pig inoculation, failed to reveal evidence of a tuberculous lesion.

Since January, 1928, I have seen in hospital and private practice seventy cases of tuberculosis of the kidney. Forty of the patients were males and thirty females; forty-eight were between 20 and 40 years of age, ten were under 20 (the youngest being 7), nine were in the fifth decade, and three in the sixth. Renal pain was a symptom in twenty-two, and in four of these bladder symptoms were absent. The tubercle bacillus was found by examination of direct smears of the centrifugized urine in forty-five, and by guinea-pig inoculation in another ten. The only specimen submitted to the bacteriologist in many instances was the urine taken from the bladder at cystoscopy. The proportion of positives would undoubtedly have been higher if further specimens, taken from twenty-four-hour collections of urine, had been examined. Thirteen patients out of forty-six who were subjected to nephrectomy had the operation performed in the absence of positive urine findings. In two of these a pre-operative diagnosis of hydronephrosis had been made, and the tuberculous nature of the lesion recognized only at operation. In the other eleven a correct pre-operative diagnosis was made in the absence of the positive urine smears, and without waiting for confirmation by animal inoculation.

INVESTIGATION OF A CASE OF RENAL TUBERCULOSIS

(A) *Cystoscopy*.—The appearances of the bladder in cases of renal tuberculosis often make a diagnosis possible in the absence of the causal organism. The evidence thus obtained is frequently characteristic and of immediate diagnostic significance. The first point usually noticed is the reduced capacity of the bladder, which normally is eight to twelve ounces. In addition, the viscus is easily irritated, so that, if too quickly filled with the distending lotion, spasm is induced and completion of the cystoscopy may be prevented. Generally speaking, if the capacity is