empiricist and a rationalist of sorts" but he cannot ascribe either to empiricism or rationalism its classical role as a source of knowledge. There are, in his view, no ultimate sources of knowledge; knowledge comes from critical examination apolied to assertions derived from any source whatever, including of course observation and experience. What makes science in some sense both rational and empirical is the way it grows, through the overthrow and replacement of theories, so that it progresses deeper and deeper into the problems.

So long as rationalism is relentlessly critical, and not a cartesian intellectualism, Professor Popper gives it his blessing: and he says, not inconsistently, that empiricism in some form or other, although perhaps in a modest and modified form, is the only interpretation of scientific method which can be taken seriously in our day. These views certainly fit the present state of knowledge and study in psychiatry. If, in the words I quoted from Henry VIII's charter to the Royal College of Physicians, the subject is to be furthered by men who are "profound, discreet, groundedly learned, and deeply studied in physic", it is by way of enlightened empiricism and critical rationalism that they will achieve that aim. Psychiatry is working in that direction, not without success.

I would like to have been able to finish by recalling that Thomas Linacre approached the problems of medicine—and particularly of psychiatry—in this spirit of critical rationalism. But it would not be true, nor in keeping with the spirit of his time. Authority prevailed then over inquiry, and refutation of accepted doctrine was no virtue. Nevertheless Linacre was steeped in the Greek learning, and he was, as his friend Erasmus said, a man of most acute and refined judgment. I hope it is not too far-fetched to suppose that if he had not been deflected into translating Galen, he would have encountered and pondered that aspect of Greek thought on which Prof. E. R. Dodds has enlightened us, and would have appreciated the necessity for studying the irrational factors in behaviour if we are to reach a realistic understanding of human nature and the means to mental health.

TRACHEOSTOMY AND ARTIFICIAL VENTILATION IN CHRONIC LUNG DISEASE

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Summary In the period 1955–65, 111 patients with chronic diffuse lung disease were treated with tracheostomy and intermittent positive-pressure (I.P.P.) ventilation for a total of a hundred and thirty-six episodes of life-threatening respiratory failure. The patients were followed up for one to ten years. Mortality has been correlated to various clinical data. The immediate and late prognosis depends mainly on the physical ability of the patients before the deterioration. Survival-rates on discharge after one tracheostomy were: (A) for patients previously able to work to some extent, 85%; (B) for patients unable to work, but able to leave home and manage personal requirements, 70%; and (C) for disabled patients unable to leave home, 50%. 3 years after discharge the corresponding figures were 58, 31, and 0%. If no chronic progressing malignant disease or severe cerebral affection is present artificial ventilation is considered indicated in episodes of severe respiratory failure in patients of groups A and B. In these cases treatment will usually be needed for a short period only. Patients of group C will be expected to require lifelong intermittent or constant artificial ventilation.

Introduction

BY means of artificial ventilation it is usually possible to reverse severe respiratory failure even when chronic diffuse lung disease is present. It seems that a number of such patients may regain fairly good health for some time (Munck, Sund Kristensen, and Lassen 1961, Bradley et al. 1964, Bates et al. 1965, Grendahl and Refsum 1965, Sadoul et al. 1965); but information is sparse regarding long-term prognosis and the relation between prognosis and clinical data. The uncertainty as to the results to be expected makes it difficult to decide when to institute intermittent positive-pressure (I.P.P.) ventilation (Barnett et al. 1960, Bradley et al. 1964).

We have reviewed our results over the period 1955–65, and reconsidered the indications for treatment with I.P.P. ventilation.

Patients and Methods

Patients

Included in the study were all patients (93 men and 18 women) with chronic diffuse lung disease, treated with tracheostomy and I.P.P. ventilation in a total of a hundred and thirty-six episodes of severe respiratory failure.

All patients had a record of chronic bronchitis, usually for more than ten years (table IV). Most patients had pulmonary emphysema, and electrocardiography indicated right-side axis and/or hypertrophy of the heart in 58 of the cases.

The ages of the patients at the time of tracheostomy varied from 28 to 78 (average 60), the large majority being aged 50–70.

Most of the patients were referred to us from other hospitals in Copenhagen and the surrounding area. As a rule tracheostomy was resorted to as an ultimate measure after adequate conservative treatment; but in some cases no time was left for such attempts. The condition of all patients was considered life-threatening; it may be assessed from the frequency of coma or sopor (table IV) and from the arterial blood-gas values (table I).

We grouped the patients according to their physical ability before the acute episode that led to tracheostomy by the system proposed by Munck, Sund Kristensen, and Lassen (1961).

Group A.—Patients able to work, at least to some extent.

Group B.—Patients unable to work but able to manage personal requirements and to leave home for shopping, and so on.

Group C.—Severely disabled patients, unable to leave their rooms or homes, some of them bedridden.

At the first tracheostomy these groups numbered 53, 46, and 12 patients, respectively, and at later tracheostomies the numbers were 3, 13, and 9 patients.

Methods

The patients were treated and nursed in a respiratory-care unit (Sund Kristensen, Jessen, and Rasmussen 1967). Tracheostomy was performed under general anæsthesia with the patient intubated orally. The stoma was made at the level of the second and third tracheal rings and a curved, cuffed large-size rubber tube introduced. Ventilation was performed by means of a volume-cycled respirator (Lundia) with a preset frequency. After gradual weaning of the patient from the respirator the tube was replaced by a silver cannula, which was eventually removed.

TABLE I—ARTERIAL OXYGEN SATURATION, P_aCO_2, AND HYDROGEN-ION CONCENTRATION BEFORE, DURING, AND AFTER ARTIFICIAL VENTILATION

Time*	Group	Mean (± S.E.M.) of arterial: Oxygen saturation (%)	P_aCO_2 (mm. Hg)	Hydrogen-ion concentration (nEq./l.)	No. examined
Before tracheostomy	A	65·7 (± 3·0)	82·5 (± 3·9)	57·1 (± 2·5)	36
	B	68·2 (± 2·8)	87·1 (± 3·7)	58·8 (± 3·2)	42
	C	66·0 (± 4·6)	77·2 (± 4·7)	52·0 (± 3·5)	17
During treatment	A	92·1 (± 0·7)	51·3 (± 1·4)	37·1 (± 0·9)	53
	B	92·9 (± 1·0)	48·6 (± 1·1)	37·5 (± 1·0)	57
	C	93·9 (± 0·8)	47·6 (± 3·4)	36·4 (± 1·4)	18
After decannulation	A	85·3 (± 1·1)	47·9 (± 1·2)	39·7 (± 0·8)	43
	B	85·4 (± 1·1)	50·2 (± 1·6)	39·3 (± 0·7)	35
	C	84·0 (± 3·0)	47·0 (± 2·7)	38·1 (± 1·6)	10

* The analyses were made before tracheostomy during spontaneous respiration with oxygen-enriched air, during the most favourable period of artificial ventilation, and during spontaneous respiration without oxygen enrichment, after decannulation.

Arterial standard bicarbonate and P_{CO_2} values were calculated from pH determinations (glass electrode) before and after microequilibration (Siggaard-Andersen 1963). Oxygen saturation was determined photometrically (Siggaard-Andersen et al. 1962) with a special photometer (Radiometer ' OSM 1 ').

Results

Immediate Results of Respiratory Failure

All patients survived the operative procedure of tracheostomy. The degree of respiratory disturbances before tracheostomy is shown by the arterial blood-gas values (table I). Artificial ventilation usually normalised P_aCO_2 and oxygen saturation in all three groups of patients. There were no significant differences among these groups as to the degree of hypoxæmia and hypercapnia, neither in the acute stage before tracheostomy, nor in the post-tracheostomy period.

The period from tracheostomy until the patient was completely independent of artificial ventilation, or until death, was usually one to six weeks (table II).

17 patients died during this period of treatment. At least 8 of the fatalities were due to infection of the lung or to septicæmia, caused as a rule by *Staphylococcus aureus* and/or *Pseudomonas aeruginosa*. Probably the infecting strains were most often acquired in hospital, which is in accord with the experience of other workers (Gotsman and Whitby 1964). The remaining deaths during treatment were chiefly due to cardiac complications. No deaths could be attributed to failure of the technical equipment.

When spontaneous respiration was regained the patients were usually transferred to other wards or other hospitals.

TABLE II—DURATION OF RESPIRATOR TREATMENT

Duration (wk.)	No. of episodes	Deaths during treatment
<1	44	4
1–4	60	9
>4	32	4

TABLE III—PHYSICAL ABILITY BEFORE AND AFTER TREATMENT

Status before episode of respiratory failure	Total no. of episodes	Deaths during treatment	Deaths later during admission	Discharged	Group on discharge* A	B	C
Group A	56	2	6	48 (*86%*)	26	17	2
Group B	59	11	6	42 (*71%*)	0	25	15
Group C	21	4	5	12 (*57%*)	0	1	11

* Status on discharge was not recorded in 5 cases.

During this continued hospitalisation a further 17 patients died, practically all of them in cardiorespiratory failure for which retracheostomy was not considered indicated.

3 patients did not become independent of the respirator and seem to require lifelong artificial ventilation.

In the remaining ninety-nine episodes spontaneous respiration was regained, and the patients could be discharged.

Changes in Physical Ability

The grouping of the patients according to their general physical ability reflects their respiratory reserve. Changes in this respect during the period of exacerbation and treatment are shown in table III.

Fully a half of those who survived the episode that led to tracheostomy were, on discharge, placed in the same functional group as before admission. In all other cases but 1, disability increased; but only in exceptional cases were patients of group A discharged as true respiratory " cripples " (group C).

TABLE IV—CLINICAL DATA CORRELATED TO IMMEDIATE PROGNOSIS

Clinical findings	No. of patients	Deaths during treatment	Deaths later during admission	Deaths during admission
Total	136	17	17	34 (*25%*)
Age:				
<50 yr.	19	2	3	5 (*26%*)
51–60 yr.	49	3	5	8 (*16%*)
61–70 yr.	51	8	7	15 (*29%*)
71–79 yr.	17	4	2	6 (*35%*)
*Duration of lung symptoms:**				
≤10 yr.	37	5	5	10 (*27%*)
11–20 yr.	40	4	6	10 (*25%*)
>20 yr.	51	6	3	9 (*18%*)
Cor pulmonale	58	6	8	14 (*24%*)
Peripheral œdema:				
<1 yr.	23	5	4	9 (*39%*)
>1 yr.	38	3	4	7 (*18%*)
Absent	75	9	9	18 (*24%*)
Obesity	19	3	2	5 (*26%*)
Precipitating factors:†				
Pneumonia or acute bronchitis	81	12	8	20 (*25%*)
Asthma, bronchitis	4	1	0	1 (*25%*)
Opiates	11	0	0	0 ..
Oxygen	19	2	1	3 (*16%*)
Mental state before tracheostomy:‡				
Conscious	10	0	3	3 (*30%*)
Agitated	11	2	0	2 (*18%*)
Somnolent	59	9	9	18 (*31%*)
Comatose	44	5	5	10 (*23%*)

* Not recorded in 8 cases.
† A group of miscellaneous and unknown precipitating factors has been omitted.
‡ Not recorded in 12 cases.

Immediate Results Correlated to Pretracheostomy Data

The correlation between the immediate prognosis and the physical ability of the patients before the deterioration of their condition is clear from table III.

Other data considered in the survey were: age, duration of lung symptoms, electrocardiographic patterns of chronic cor pulmonale, right-sided cardiac failure, obesity, cause of deterioration, and state of consciousness before tracheostomy (table IV).

Apart from the favourable prognosis in cases where opiates had been given, the data included were not correlated to prognosis. Neither did the results of arterial blood-gas analyses before tracheostomy give any information of prognostic significance in the individual case (table V).

A previous tracheostomy had been made in 21 cases. The immediate prognosis was the same at the first and the later episodes (table VI).

BLE V—ARTERIAL OXYGEN SATURATION, P_aCO_2, AND HYDROGEN-ION CONCENTRATION BEFORE TRACHEOSTOMY, CORRELATED TO IMMEDIATE PROGNOSIS

—	No. of patients	Mean (± S.E.M.) of arterial: Oxygen saturation (%)	P_aCO_2 (mm. Hg)	Hydrogen-ion concentration (nEq./l.)
Death during admission	26	63·0 (± 3·3)	77·9 (± 3·2)	54·3 (± 2·3)
Survival	69	68·4 (± 2·2)	85·9 (± 3·1)	57·9 (± 2·3)

Analyses were made shortly before tracheostomy during spontaneous respiration with oxygen-enriched air (usually $^1/_2$–1 litre per minute by nasopharyngeal tube).

TABLE VI—IMMEDIATE PROGNOSIS AT FIRST AND AT LATER TRACHEOSTOMIES

Tracheostomy	No. of patients	Deaths during treatment	Deaths later during admission	Total deaths during admission
First	111	13	15	25%
Second ..	21	4	2	29%
Third	3	0	0	..
Fourth	1	0	0	..

Period of Survival after First Tracheostomy

The results of follow-up of the 111 patients after their first tracheostomy are shown in fig. 1. Survival curves are given for each of the groups A, B, and C, for the total series of patients, and for the general population of the same composition as to sex and age (*Statistisk Årbog* 1965).

Of the 111 patients 83 (75%) could be discharged and 51 (46%) were still alive after 1 year, which was the minimum observation period for the total series.

The prognostic significance of physical ability (table III) is evident also when later prognosis is considered (fig. 1, table VII). Only 1 of the 12 patients of group C was alive one year after discharge, whereas the one-year-survival rates in groups B and A were 37% and 62%, respectively.

Survival after Repeat Tracheostomies

Of the 83 patients discharged after treatment 21 had a later tracheostomy and renewed period of I.P.P. ventilation after an interval of two to sixty-seven (average sixteen) months. The classification of these 21 patients on discharge after the first tracheostomy was: group A, 4; group B, 9; and group C, 8. At subsequent tracheostomy the figures were 3, 10, and 8, respectively.

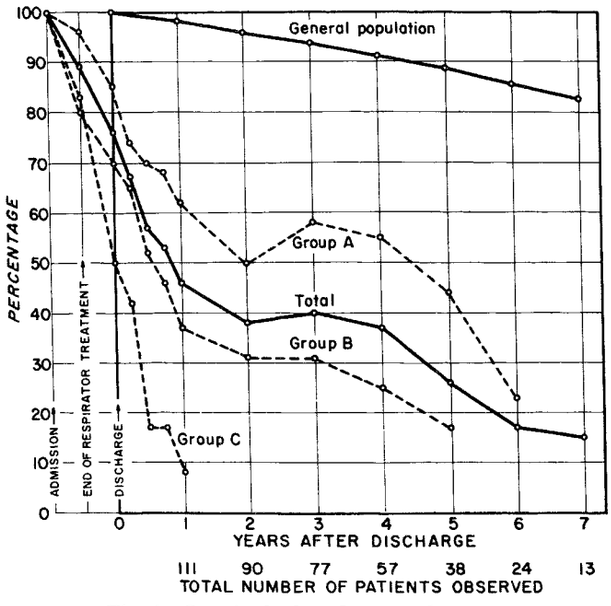

Fig. 1—Survival after first tracheostomy.

Survival curves for the total series and for the groups A, B, and C individually, calculated from the time of discharge. Included is the survival curve for the general population of the same composition as to sex and age.

TABLE VII—IMMEDIATE AND LATE PROGNOSIS AFTER FIRST TRACHEOSTOMY

Group	No. of patients	No. discharged	No. surviving for: 1 yr.	3 yr.	5 yr.
A	53	45 (*88%*)	33/53 (*62%*)	21/36 (*58%*)	8/18 (*44%*)
B	46	32 (*70%*)	17/46 (*37%*)	10/32 (*31%*)	2/12 (*17%*)
C	12	6 (*50%*)	1/12 (*8%*)	0/9 (*0%*)	0/8 (*0%*)

The minimum observation period was one year.

TABLE VIII—IMMEDIATE AND LATE PROGNOSIS AFTER SECOND TRACHEOSTOMY

Group	No. of patients	No. discharged	No. alive after: $^1/_2$ yr.	1 yr.	2 yr.	3 yr.	4 yr.	5 yr.	6 yr.
A	3	3	2/3	2/2	0/1	0/0	..	..	..
B	10	7	7/10	3/8	2/6	2/5	0/3	0/1	0/1
C	8	5	2/8	2/8	0/4	0/3	0/2	0/2	0/1
Total	21	15 (*71%*)	11/21 (*52%*)	7/18 (*39%*)	2/11 (*18%*)	2/8	0/5	0/3	0/2

The minimum observation period for the series was 8 months.

When regard is paid to the functional ability of the patients (A, B, or C), survival-rates after the second period of treatment are comparable with those after the first episode (table VIII).

In 3 patients a third tracheostomy has been performed after eleven to forty-three months. In 1 of these patients a fourth tracheostomy was made after a further interval of about six months. Survival after these later tracheostomies was about six months.

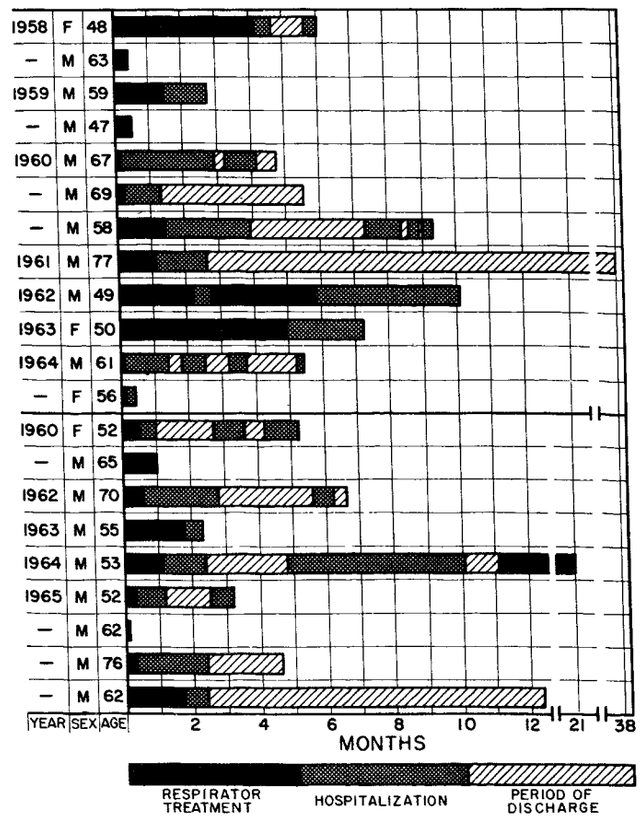

Fig. 2—Duration of treatment and admission, and survival in group-C patients.

A complete follow-up until death of the 21 patients referred to group C before tracheostomy. Year of tracheostomy, sex, and age are given. First tracheostomy for patients 1–12; subsequent tracheostomy for patients 13–21.

Survival of Group-C Patients

The results of treatment were unsatisfactory in group C. Since these results may be of importance for the indications and principles of future treatment the course of the disease in these patients has been tabulated in detail (fig. 2) on the basis of a complete follow-up until death.

Most patients died within six months of the day of tracheostomy, and the periods of discharge were short. 5 patients died during respirator treatment. In 10 patients who died during continued admission or at later admissions this treatment was not reinstituted.

Discussion

Acute severe respiratory failure in patients seen for the first time practically always indicates artificial ventilation, since it is seldom possible in the acute situation to evaluate the underlying condition or to predict the outcome of the episode. Extreme disturbances of blood-gas values and severe neurological symptoms including profound coma should not restrain the therapeutic efforts. Usually, the apparently desolate condition can be reversed without residual damage; only 2 of our patients had severe anoxic brain lesions. In those special cases where use of respiratory depressants or uncontrolled administration of oxygen are suspected, treatment is imperative.

In our series tracheostomy and a course of respirator treatment were the standard treatment in a group of patients with life-threatening respiratory failure superimposed on chronic diffuse lung disease.

The rationale for such temporary substitution of the ventilatory function is the assumption that the failure may partly be due to reversible factors, such as lung infections, heart-failure, drugs, oxygen, fever, asthma, anæmia, or mere exhaustion. The aim is to restore the state preceding the acute deterioration.

This aim was attained in about half of our patients in so far as they left hospital with their usual physical ability.

This habitual physical ability is the decisive prognostic factor. Due regard is too seldom paid to this seemingly simple fact, and therefore a comparison of results reported from different medical centres is impeded.

Our patients of group A (previously able to live a fairly active life) usually regained complete independence of the respirator within less than four weeks. Their prospects of several years' survival were fair, and about half of them could resume some work.

Patients with a more restricted physical ability (group B) had a higher mortality during and after admission; but more than half of those discharged were still able to manage personal requirements.

It seems that patients in these two groups are likely to benefit from a limited period of artificial ventilation; and with very few exceptions, such as rapidly progressing malignancies or severe cerebral affections not due to hypoventilation, we consider this treatment indicated.

The same treatment was used for the severely incapacitated patients of group C, and it was intended to be temporary. Certainly most of the patients could be weaned from the respirator; but the later results were poor. 9 of the 21 patients died during admission; 1 survived for nearly three years, 1 (in a respirator) survived for twenty months, and the remaining patients died within ten months of tracheostomy.

The prognosis of the group-C patients in this period is grave. If respirator treatment is instituted, one must realise that in most cases it must be continued permanently or as intermittent ventilation for part of the day or with somewhat longer intervals. A few patients of the initially less incapacitated groups, and some patients undergoing tracheostomy before anamnestic information is available, may prove to have similar requirements.

This small number of patients dependent on continuous care require supervision and surroundings that are not provided by ordinary hospital departments (Bertoye et al. 1965, Engberg 1961). For some of them organised home care may be feasible; others will need institutions analogous with those existing for persons disabled by respiratory insufficiency of another ætiology—e.g., poliomyelitis.

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EFFECTS OF ATROPINE ON HEART-RATE IN HEALTHY MAN

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Summary Increasing doses of intravenous atropine were given to ten healthy volunteers in whom the sympathetic innervation of the heart had been blocked by propranolol, and the effect on heart-rate was measured both at rest and during exercise. The dose required to produce maximum inhibition of vagal control of the sinoatrial node ranged from 0·025 to 0·04 mg. per kg. body-weight. The degree of vagal tone was an important determinant of dose requirement.

Introduction

ATROPINE is used to block parasympathetic activity on the heart, both for research and therapeutically in the treatment and prevention of bradycardia and arrhythmias. An intravenous dose of 2 mg. has been considered adequate to produce complete blockade of vagal action on the sinoatrial node in man (Jones et al. 1961, Kahler et al. 1962), but Jose and Collison (1965) have used 0·04 mg. per kg. body-weight for this purpose, implying that 3 mg.