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ELECTROENCEPHALOGRAPHIC STUDIES
IN RESPIRATORY FAILURE

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In recent years acute or subacute respiratory failure has been added to the long list of diseases in which there is disorder of mental and nervous function from a primarily extraneural cause. The major changes in this state are known to be hypoxia, hypercarbia, and acidosis of respiratory origin.

Imperfect oxygenation of pulmonary venous blood, with a fall in arterial oxygen tension and saturation, is easily produced by alterations in the relative distribution of inspired gas or pulmonary blood flow. Later, when total effective alveolar ventilation is reduced, carbon dioxide elimination progressively fails, with consequent respiratory acidosis, and below critical levels the clinical syndrome of carbon dioxide retention appears. The manifestations of this syndrome are now well recorded (Donald, 1949; Westlake, Simpson and Kaye, 1955; Sieker and Hickam, 1956). The salient features are headache, confusion, drowsiness, flapping tremor, like that of liver disease, muscular twitching, and coma. It is accompanied by an increase of cerebral blood flow caused by the high arterial carbon dioxide levels (Kety and Schmidt, 1948; Patterson, Heyman, and Duke, 1952), which also cause a rise in C.S.F. pressure (Davies and Mackinnon, 1949). If papilloedema then develops, as it may, cerebral tumour may be mimicked (Cameron, 1933; Leggat, 1958; Conn, Dunn, Newman, and Belkin, 1957).

The effects of giving oxygen when carbon dioxide retention is established are well known (Davies and Mackinnon, 1949; Donald, 1949). Its administration removes the anoxic stimulus to respiration and so results in further decline in alveolar ventilation, which is already defective. There is a further rise in alveolar and arterial carbon dioxide tension with clinical deterioration and coma in some cases.

Although these aspects of respiratory failure have been closely studied, little attention has been devoted to the E.E.G., which might be expected to reflect alterations in cerebral physiology. In an attempt to define the E.E.G. changes, and the conditions under which they occur, we have studied 16 patients on 19 occasions during 18 hospital admissions for acute or subacute pulmonary insufficiency with carbon dioxide retention, and with or without congestive heart failure. Clinical data are presented in Table I. Blood gas studies were made at varying stages in the first two weeks after admission, with one exception when they were made late in convalescence. It was possible to repeat the studies in only one patient during the same hospital admission, but in two patients they were repeated on a second admission. In every case arterial blood gas studies and the E.E.G. were made on the same day and in most cases simultaneously.

TABLE I.—*Clinical Data*

Case No.	Age and Sex	Diagnosis	History of Chest Disease (Years)	History of "Acute" Illness (Days)	Cardiac Failure	B.P.	X-ray Findings	E.C.G. Findings	Duration of Admission (Days)	Result	Time of Study*	Mental Symptoms	E.E.G. Abnormality	Notes
1	46 M	Chronic bronchitis	3½	9	No	120/90	Ht. + R.V. + Congestion +	S.R. R.B.B.B.	24	Died	1	Confusion. Tremor. Headache	Moderate	Same patient as Case 12; 2nd admission
2	57 F	Asthma. Chronic bronchitis. Emphysema	20	7	Yes	120/80	Ht. + R.V. + Congestion +	S.R. R.A.D. P. pulmonale	53	Discharged ambulant	1	Tremor	Mild	Same patient as Case 8; 1st admission
3	73 F	Kyphoscoliosis. Bronchitis. Old myocard. infarct	3	90	..	185/90	Ht. ++ R.V. ++ Emphysema + Kyphoscoliosis	A.F. Old infarct	55	Died	2	Confusion. Drowsy. Headache	Moderate	Previous myocardial infarct 3 years
4	61 M	Bronchitis. Emphysema. Pulmonary fibrosis	20	10	..	160/80	Ht. ++ R.V. ++ Fibrosis +	S.R.	20	Discharged ambulant	2	Coma in O ₂ . Confused. Tremor. Headache	Severe	
5	72 F	Bronchitis. Emphysema. Fibrosis	12	7	..	170/90	Ht. ++ R.V. + Basal reticulation	S.R. V.E.S.	49	..	3	Confused	Moderate	1 previous admission
6	58 M	Chronic bronchitis. Emphysema	10	56	..	170/120	Emphysema	S.R. L.A.D.	23	..	3	Confused. Tremor	Mild	
7	57 M	Chronic bronchitis. Emphysema. Fibrosis	10	14	No	130/90	Ht. + R.V. + Congestion + Reticulation rt. base	S.R. A.E.S. R.A.D.	75	..	4	Coma in O ₂ . Confused. Tremor. Headache	Severe	
8	57 F	Asthma. Chronic bronchitis. Emphysema	20	14	..	120/70	Ht. + R.V. + Congestion + Emphysema	S.R. R.A.D. P. pulmonale	50	..	4	Drowsy	Moderate	Same patient as Case 2; 2nd admission
9	59 M	Bronchitis	2	42	..	190/115	Ht. + L.V. + Emphysema	S.R. Ischaemic changes L.V.	14	..	4	Confused. Headache	..	Hypertensive. Small cerebral thrombosis 1 year prev. No residual paralysis
10	49 M	Chronic bronchitis. Emphysema	5	42	Yes	140/90	Ht. + R.V. + Congestion + Emphysema Reticulation	S.R. R.V. +	16	..	5	Headache. Drowsy	..	
11	53 M	" "	9	29	No	150/115	Ht. ++ R.V. + Congestion + Emphysema	S.R. R.V. +	25	Discharged bedridden	6	Headache	..	Hypertensive. 3 previous admissions
12	46 M	" "	3	19	..	120/60	Ht. + R.V. + Emphysema +	S.R. R.B.B.B.	19	Discharged ambulant	7	Coma in O ₂ . Drowsy. Headache. Tremor	..	Same patient as Case 1; 1st admission
13	54 M	" "	7	84	..	140/90	Emphysema	Not done	12	..	9	None	Mild	Admitted for investn. of headache, but this had gone by time of exam.
14	56 M	Bronchitis. Emphysema	5	28	Yes	170/120	Ht. + Congestion + Emphysema	S.R. R.V. + P. pulmonale	40	..	9	Drowsy. Confused. Tremor. Paranoid	Moderate	Hypertensive. Same patient as Case 19
15	48 F	Bronchiectasis. Emphysema. P. fibrosis	44	30	..	110/70	Ht. + R.V. + Congestion + Fibrosis +	S.R. R.V. +	28	Died	10	Tremor. Headache	..	2 previous admissions
16	66 M	Chronic bronchitis. Emphysema	3	12	..	170/110	Ht. + R.V. + Congestion + Emphysema	S.R. R.V. +	18	..	11	Confused. Tremor	..	Hypertensive
17	52 M	" "	16	40	..	170/110	Ht. + R.V. + Patchy consolidation Effusion Right	S.R. R.A.D.	56	Discharged ambulant	12	Headache. Drowsy. Confused. Tremor	Severe	2 previous admissions. Hypertensive
18	46 F	Bronchiectasis. Emphysema	44	14	..	130/70	Ht. + R.V. + Cystic bronchiectasis + Emphysema	S.R. R.A.D.	33	..	32	None	Normal	4 previous admissions
19	56 M	Bronchitis. Emphysema	5	28	No	160/115	Emphysema	S.R. R.V. + P. pulmonale	40	..	39	..	Mild	Same patient as Case 14. Day before discharge

X-ray findings: Ht.=Heart. R.V.=Right ventricle. L.V.=Left ventricle. E.C.G. findings: S.R.=Sinus rhythm. A.F.=Auricular fibrillation. A.E.S.=Auricular extrasystoles. V.E.S.=Ventricular extrasystoles. R.A.D.=Right axis deviation. L.A.D.=Left axis deviation. R.B.B.B.=Right bundle branch block. +, slight abnormality; ++, moderate abnormality; +++, gross abnormality. * Days after admission.

FIG. 1.—High-amplitude delta bursts appear in both cerebral hemispheres at intervals of 10 to 15 seconds. Moderate-amplitude theta activity is also present in all channels and unsustained alpha rhythm can be seen.

Methods

Arterial blood was obtained from an indwelling brachial artery needle and was analysed for carbon dioxide ($p\text{CO}_2$) and oxygen ($p\text{O}_2$) tensions by the bubble method of Riley, Proemmel, and Franke (1945) as modified by Riley, Campbell, and Shepard (1957), using personally established correction factors. Arterial whole blood CO_2 content was determined by the method of Van Slyke and Neill, and plasma CO_2 was estimated from this value, using the nomogram of Van Slyke and Sendroy (1928). The oxygen capacity was measured spectrophotometrically; arterial $p\text{H}$ was calculated from the $p\text{CO}_2$ and plasma CO_2 content, using the Henderson-Hasselbach equation with a pK of 6.11. Serum electrolytes were determined by flame photometry, and serum urea and haemoglobin by standard methods in current use at this hospital.

The E.E.G.s were recorded on a Marconi eight-channel instrument using either standard 10/20 electrode placements or a simpler arrangement often used in this hospital for restless and uncooperative patients. The electrodes were silver/silver-chloride with gauze pads soaked in 5% sodium chloride. All recordings were bipolar, and a standard gain of 0.5 cm. to 50 μV was employed.

Results

The E.E.G. tracings have been classified into four groups: normal, mildly abnormal, moderately

abnormal, and severely abnormal. They have been regarded as mildly abnormal if low-amplitude theta activity is intermittently seen temporo-centrally; as moderately abnormal if theta frequencies are more prominent—that is, of higher amplitude, greater persistence, and wider diffusion; and severely abnormal if, in addition to theta activity, delta activity is present. In severely abnormal tracings the delta waves tend to be paroxysmal and of high amplitude, and may occur in bursts which are repeated at fairly regular intervals (Fig. 1). In all the abnormal records the dysrhythmias have appeared in exactly symmetrical positions, and signs of focus or clear unilateral preponderance have been absent. In a number, random sharp waves without fixed location have also been a feature. Oxygen (100% O_2 at 5 l./min.) was given for 15 minutes to seven patients during recording, but no change in the appearance of the E.E.G. resulted, though in each case the arterial $p\text{O}_2$ rose to above normal levels (Table II), and in the five cases in which it changed the $p\text{CO}_2$ rose by a mean of 11 mm. Hg. Only one of our records was normal; four were mildly abnormal, 11 moderately abnormal, and three severely abnormal.

With the use of the degree of E.E.G. dysrhythmia to subdivide the patients, our data show that increasing E.E.G. abnormality is accompanied by a rise in the mean arterial $p\text{CO}_2$ and plasma CO_2 levels and by a fall in the mean arterial $p\text{O}_2$. No distinct trend in arterial

TABLE II.—Blood Studies

Case No.	E.E.G. Grade	Hb g./100 ml.	At Rest off O_2 30 min.			On O_2 15 min.			mEq/l.			Urea mg./100 ml.
			$p\text{O}_2$ mm. Hg	$p\text{CO}_2$ mm. Hg	CO_2 mEq/l.	$p\text{H}$	$p\text{O}_2^*$ mm. Hg	$p\text{CO}_2$ mm. Hg	Na	K	Cl	
1	Moderate	16.7	39	72	40.02	7.352	—	—	134	4.4	105	112
2	Mild	15.5	37	76	38.09	7.301	—	—	130	5.2	101	67
3	Moderate	13.6	34	75	42.74	7.364	129+	—	127	4.5	79	54
4	Severe	13.0	26	85	46.28	7.343	119+	93	127	5.6	93	34
5	Moderate	15.7	61	50	31.30	7.407	—	—	109	3.8	73	36
6	Mild	11.8	68	49	28.36	7.371	144+	59	126	4.7	101	35
7	Severe	17.2	36	92	47.31	7.317	—	—	130	4.6	89	52
8	Moderate	16.0	30	62	28.18	7.259	—	—	136	4.6	101	33
9	"	13.3	56	47	30.76	7.430	—	—	—	—	—	38
10	"	14.8	45	62	32.89	7.330	144+	61	134	4.1	93	95
11	"	14.5	37	74	33.48	7.257	—	—	134	4.9	97	52
12	"	12.6	47	83	30.06	7.212	135+	91	140	5.1	102	23
13	Mild	14.8	51	63	30.12	7.280	—	—	—	—	—	—
14	Moderate	18.2	30	82	44.35	7.340	148+	102	—	—	—	42
15	"	11.1	46	76	28.38	7.167	—	—	134	3.7	85	19
16	"	14.8	31	81	—	—	—	—	135	4.6	92	56
17	Severe	17.2	38	75	40.04	7.324	—	—	136	6.2	96	39
18	Normal	13.2	54	65	30.10	7.258	123+	65	134	3.9	97	37
19	Mild	18.2	65	57	35.66	7.406	—	—	—	—	—	—

* Uncorrected.

pH is evident (Table III and Fig. 2). Age does not seem to be a material factor, nor do variations of serum electrolytes, urea, or haemoglobin show any reciprocity with the E.E.G. pattern.

Attempts to find a relation between E.E.G. change and the duration of the acute illness or the length of time after admission of the date of study have been unsuccessful. The three patients with severe abnormality were discharged ambulant. Four patients died.

Comparison of E.E.G. tracings with mental and physical neurological signs reveals a definite interconnexion (Fig. 3). The more severe the E.E.G. disorder the more likely is the presence of florid clinical manifestations.

Discussion

The E.E.G. changes we have observed in this group of patients correspond with those reported previously by Austen, Carmichael, and Adams (1957) and by Wilson and Sieker (1958). The mild and moderate grades of dysrhythmia do not show any pathognomonic signs, and whilst the occurrence of bursts of high-voltage bilateral synchronous delta discharge can be striking in severe grades, this, too, is a non-specific sign. A similar E.E.G. pattern is a common feature of confusional states of metabolic origin, most notably in hepatic coma but sometimes in uraemia and insulin overdosage, and we have also seen it occasionally with hypercalcaemia and in hypertensive encephalopathy. It should be mentioned, however, that the high-amplitude triphasic complexes described by Bickford and Butt (1955) as a special characteristic of hepatic encephalopathy were not seen.

Though our data demonstrate a link between the degree of E.E.G. abnormality and the severity of hypercarbia and hypoxia, there is no clear connexion between them in individual cases. Indeed, our solitary patient with a normal record had a grossly abnormal arterial $p\text{CO}_2$ and considerable acidosis and hypoxia (Case 18, Tables I and II). This phenomenon compares with our previous experience and that of others (Westlake *et al.*, 1955; Sieker and Hickam, 1956) that the presence of mental and other

neurological symptoms does not tie closely with the individual arterial blood gas figures.

The absence of correlation in our patients between arterial pH and E.E.G. appearance is interesting, since other writers have stressed that neurological symptoms in pulmonary insufficiency may be related to pH fall as

FIG. 2.—Blood gas E.E.G. relationships (arterial blood).

FIG. 3.—The proportion of patients with mental symptoms within the four groups of E.E.G. changes.

TABLE III.—Mean Blood Values According to E.E.G. Group

Group (No. of Patients)	Mean Age Years	Hb g./ 100 ml.	$p\text{O}_2$ mm. Hg	$p\text{CO}_2$ mm. Hg	Plasma CO_2 mEq/l.	pH	Serum Values mEq/l.			Urea mg./ 100 ml.	Individual Day of Study After Admission
							Na	K	Cl		
Normal E.E.G. (1)	46	13.2	54	65	30.1	7.26	134	3.9	97	37	32
Mildly abnormal E.E.G. (4)	56	15.1	55	61	33.06	7.338	128	5.0	101	51	1, 4, 9, 39
Moderately abnormal E.E.G. (11)	57	14.8	41.5	69.5	34.22	7.312	131	4.4	92	51	1, 2, 3, 4, 4, 5,
Severely abnormal E.E.G. (3)	57	15.8	33	84	44.54	7.328	128	5.5	93	42	6, 7, 9, 10, 11
Mean values all cases	56	14.9	44	70	38.33	7.318	131	4.7	94	49	2, 4, 12

distinct from arterial $p\text{CO}_2$ rise (Westlake *et al.*, 1955). The work of Swanson, Stavney, and Plum (1958) bears on this point in support of our findings, as they have shown experimentally that acute changes in arterial pH affect the cats' E.E.G. only when there is an accompanying rise or fall in blood CO_2 tension.

It has been claimed by Wilson and Sieker (1958) that age is important in determining E.E.G. dysrhythmia in respiratory insufficiency, but our results do not demonstrate this. Failure to observe any change in the E.E.G. from inhalation of oxygen during recording is in agreement with similar lack of effect mentioned by others (Brazier quoted by Austen *et al.*, 1957; Wilson and Sieker, 1958).

The immediate causal mechanism of E.E.G. disorder from impaired respiratory function presumably lies in hypercapnia and hypoxia, and our data do not allow choice of which is the more important factor. Though there may be more remote metabolic changes, such as alteration in intracellular electrolyte concentrations, which have an effect on cerebral neuronal activity, our observations, unlike those of Wilson and Sieker (1958), do not disclose any consistent abnormality of serum electrolytes in relation to E.E.G. appearances. This fact must, however, be treated with reserve, as it is generally appreciated that the electrolyte levels of the circulating blood, and in particular potassium, are not a reliable index of ionic levels within tissue cells.

Lastly, we would suggest that the variability of development of E.E.G. disorder in patients with respiratory insufficiency must predicate a great range in individual cerebral homeostasis in the face of alterations of blood gas levels. In some instances the tolerance of the central nervous system against disturbance by this means must be high and in others relatively low, and the unpredictable behaviour of neural and mental signs and symptoms, *vis à vis* $p\text{O}_2$ and $p\text{CO}_2$ values, can be interpreted in the same light. Our studies satisfy us that there is a close interrelation between neurological semeiology clinically and the presence of E.E.G. dysrhythmia—a closer nexus than exists between either of these phenomena and the arterial oxygen and carbon dioxide tensions.

Summary

Sixteen patients have been studied during 18 hospital admissions for acute or subacute respiratory failure. The E.E.G., clinical signs and symptoms in the nervous system, and blood gas findings have been compared.

The E.E.G. shows symmetrical changes from intermittent theta activity to paroxysmal delta discharge of high amplitude, and the changes resemble those found in other types of confusional state, particularly those of metabolic origin.

There is good correlation between the E.E.G. abnormality and the clinical neurological findings. There is also a correlation between increasing E.E.G. abnormality and a falling $p\text{O}_2$ and rising $p\text{CO}_2$ and plasma CO_2 content when the patients are considered as groups, but not in individual cases. No relationship with arterial pH was observed. No other relationships were noted.

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SYPHILIS AS A CAUSE OF MENTAL DEFICIENCY

BY

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Figures derived from the Ministry of Health (1958) report for 1957 illustrate the fact that syphilis is becoming increasingly rare in England and Wales (Tables I–III).

TABLE I.—Cases of Syphilis Dealt With at Centres in England and Wales

Year	No. of Cases, in all Stages, Dealt with for First Time	No. of Cases of Acquired Syphilis with Infections of Less than One Year
1931	—	8,924
1939	11,878	4,986
1946	23,878	17,675
1952	7,122	1,353
1957	4,977	747

1946 was the post-war peak year. The dramatic decline in the disease is indicated by the fall in attendances to a record low level 11 years later.

Let it be thought that modern methods of treatment obscure the true incidence of syphilis, the figures in Table II demonstrate that general paralysis of the insane, one of the main late clinical forms of the disease, is now much less important than it was.

TABLE II.—Deaths from General Paralysis of the Insane in England and Wales

Years	No. of Deaths
1911–20	2,080*
1936–9	852*
1945–9	359*
1953	117
1957	68

* Average annual deaths.

The decline in acquired syphilis has been paralleled by a similar change in the incidence of the congenital disease, as shown in Table III. In this case the peak of the relatively small wartime rise was reached in 1943, with a steady decline thereafter.

Routine serological tests for syphilis on pregnant women at various regional blood transfusion centres in England during 1957 showed a percentage incidence of