prescribed—3 drops of cells in 12 drops of saline. On account of this result with A₃, the directions were accordingly revised, so that only two drops of cells are required if the blood sample has been centrifuged.

Clinically, the two errors with A₃ blood are insignificant; no complications have been reported—so far as I am aware—through A₃ recipients getting O blood; nor have any complications been caused even by O patients receiving A₃ blood. The incidence of A₃ in Denmark is reported to be approximately 1 per 1,000 (Andresen, 1952).

There were four rhesus errors, Rh-positive patients being grouped as Rh-negative by technique 1. In none of the tests in question was the recommended procedure applied.

One investigator had spent such a long time in stirring the mixtures that they had dried so much as to remain immovable in the panels when tilted. Hence the blood cells could not contact each other and agglutinate.

In the other three cases too much water had been added in order to dissolve the reagents. One investigator had slanted the pipette so much as to produce a water drop twice as big as that formed when the pipette is held exactly vertical. Another investigator had held the pipette so close to the card that the drop did not fall freely, and consequently was uncontrollable and too big. The third investigator had deliberately added too much water. Moreover, in one of these tests far too little blood had been used, giving the panels a faint pink colour only. These errors were disclosed at the laboratories.

Doubtful Cases

Uncertain ABO reactions, occasioning no actual errors, occurred in one case in the anti-A panel and in three cases in the anti-B panel.

A doctor, making her first independent blood grouping on cards by technique 2, obtained only a faint agglutination in the anti-A panel from an emergency determination on an A₂B patient carried out at night. The reason was that she had dissolved only a small part of the anti-A reagent. She did not test the patient's serum against known A and B cells—which would have been futile unless the A cells were A₂—since the patient's serum contained strong anti-A₁. However, she repeated the typing with the same technique and result, gave the patient B blood, and postponed the final blood grouping until the next morning.

In three cases, at one hospital, technique 1 brought out small-grained agglutination, of unreliable appearance, of A blood in the anti-B panel. There was reason to believe that this might be ascribable to excessive heat during the drying of the cards. The technique of the drying process was accordingly altered.

Uncertain Rh reactions occurred in six patients when technique 1 was incorrectly applied.

All the patients were of the normal Rh-positive type and not Du. When the results were read, no or only faint agglutination showed in the anti-D panel; but, since the anti-D-panel agglutination was of normal appearance two to thirty minutes later, the investigations were repeated. In all these tests too much water had been added on the panels, as was also the case with the Rh errors previously mentioned.

ABO as well as Rh results of three simultaneous tests, by technique 2, were uncertain, the blood cells giving the appearance of being haemolysed in the panels.

This phenomenon proved to be traceable to the complete haemolysis of the blood cells before the grouping, the samples having been frozen during storage in a refrigerator after sedimentation.

Seven cards could not be read owing to agglutination in all panels, including the control panel. It was demonstrated that in all these cases the blood agglutinated in all panels by technique 1. In two cases of diseases in the biliary tract the grouping was performable by technique 2. In three cases with autoagglutinins the cells could first be grouped by technique 2 after washing the cells at a raised temperature. In two cases of infectious haemolytic anaemia the cells could not be grouped on cards even after washing them at 56° C. Application of the classic saline technique involved no difficulties except in one of the two latter cases,* in which the O Rh-positive cells agglutinated in some anti-A and anti-B sera, but not in others.

*The other case was investigated by Dr. P. Ejby Poulsen and will be reported by him elsewhere.

Summary

In Denmark, during a period of one year, approximately 60,000 ABO and rhesus groupings were made on cards. The following errors have been reported: two technical ABO errors, four technical Rh errors, and two errors of recording. The ABO errors consisted in the rare and weak A₃ factor escaping notice as regards two A₃ patients grouped by technique 2, by which the reagents are dissolved in a blood-cell suspension; the errors were caused by the suspensions being too dense. The Rh errors consisted in four Rh-positive patients being grouped as Rh-negative by technique 1, by which the reagents are dissolved in plain tap-water before addition of capillary blood; the errors were caused by incorrect quantities of liquid. In 20 cases—that is, about 0.3 per 1,000—the results were doubtful or could not be read; in 13 of these cases this was attributable to misapplied technique, and in the remaining seven cases to the blood cells being abnormally agglutinable.

The results give the impression that to be of use the method must be closely adhered to, and the directions followed carefully.

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RECENT STATISTICS OF CARBON MONOXIDE POISONING

REPORT TO THE MEDICAL RESEARCH COUNCIL

BY

A. BRADFORD HILL, C.B.E., F.R.S.

*Professor of Medical Statistics, London School of Hygiene
and Tropical Medicine; Honorary Director of the
Statistical Research Unit of the Medical
Research Council*

In a letter to the *British Medical Journal* of February 11, 1956 (p. 347), Dr. H. L. Marriott wrote that at about the end of 1952 and during 1953 "CO₂/O₂ mixtures were withdrawn from the first-aid services of the country, and only pure oxygen allowed, on advice by the Medical Research Council's Committee for Research on Breathing Apparatus for Protection against Dangerous Fumes and Gases." In criticizing the wisdom of this advice, and the change in first-aid treatment that had followed it, he pointed out that the Registrar-General's Statistical Review of England and Wales for the year 1954 had shown a "sharp rise in deaths from carbon monoxide poisoning", in the two years 1953 and 1954. He suggested that this rise "may possibly have been due to the withdrawal of CO₂/O₂ mixtures, and many preventable deaths may possibly be continuing to occur. The alternative explanation, that there has been a rise in total cases of carbon monoxide poisoning, with proportionate increase in deaths, needs statistics of the annual totals of such cases dealt with by first-aid services in England and Wales during the last seven years."

In view of the obvious importance of this problem I was asked by the Medical Research Council to make a special statistical inquiry.

Time Trend of Mortality in England and Wales

At the request of the Ministry of Health the appropriate local authorities in England and Wales made a special return of the resuscitation gases carried in their ambulances. They were asked: (a) whether their ambulances carried pure oxygen for resuscitation and, if so, between what dates; and (b) whether they carried oxygen and carbon dioxide (with the proportion of CO₂) and, if so, between what dates. An analysis of the replies to this request shows that very few changes from CO₂/O₂ mixture to O₂ took place before 1951, and that they were mainly concentrated within the three years 1951, 1952, and 1953. Table I sets out the data.

TABLE I

Year	Deaths in England and Wales from Carbon Monoxide Poisoning	No. of Administrative Areas (C.B.s or A.C.s) Changing During the Year from CO ₂ /O ₂ to O ₂ (in Parenthesis, Total Populations of these Areas in Thousands)
1948	2,384	4 (954)
1949	2,377	2 (611)
1950	2,234	2 (319)
1951	2,501	27 (9,848)
1952	2,409	34 (15,716)
1953	2,848	35 (6,963)
1954	3,129	18 (4,458)
1955	3,166	3 (417)

Apart from the rise in 1953 and 1954 referred to by Dr. Marriott (which extended into 1955), the figures reveal one point which does not support his first hypothesis. By the end of 1951 some 35 areas, with a population of about 12 millions, had already changed to pure oxygen; during 1952 many other areas were also changing over. It follows that in 1952 some quite large population must have been "at risk" to pure oxygen—at least a third of the population of England and Wales would seem probable. Yet the deaths in 1952 (2,409) were not significantly above the number in 1948 (2,384), when virtually no change at all to pure oxygen had been made.

Time correlations are, however, notorious for their difficulties, and firm conclusions can never be based upon them alone. In this particular case, it may be noted, the great majority of the deaths are attributable to suicide, and these are well recognized as liable to changes in space, time, and method for unknown reasons.

Experience of London Ambulance Service

A special scrutiny was made of the records of the London Ambulance Service of the London County Council over the five years 1950 to 1955. In view of the magnitude of the task it was initially limited to emergency calls classified as "suicide" or "attempted suicide." All those attributed to coal-gas poisoning were extracted. The results are shown

TABLE II.—*London. Emergency Calls Classified as Suicide or Attempted Suicide Due to Coal-gas Poisoning*

Year	Total No. of Cases	No. Treated in Ambulance		Of those Treated in Ambulance the Number Certified Dead on Arrival at Hospital	
		No.	%	No.	%
1951	119	69	58	20	29
1952	104	66	63	27	41
1953	243	155	64	44	28
1954	249	170	68	61	36
1955	230	155	67	43	28

in Table II. The change from CO₂/O₂ mixture to pure oxygen took place in the latter half of 1952. It will be seen that since that time the number of cases carried has, in fact, increased very substantially—from, roughly, a little over 100 in 1951 to 1952, to well over 200 in 1953 to 1955. On the other hand, the proportion of cases treated in ambulance has not appreciably changed year by year, and the proportion found to be dead on arrival at hospital reveals no increase. It was 35% in 1951–2 and 31% in 1953–5.

There is one possible flaw in these comparisons, in that a somewhat different method of recording was instituted in London in 1952. Up till that year a call was entered as "accident" unless it was definitely known to be a "suicide"; after 1952 it was entered as a "suicide" unless it was definitely known to be an accident. To overcome the possibility of any error due to this change, all the thousands of accident records were specially scrutinized for the years 1951 and 1953 and those attributed to coal-gas poisoning were extracted. It was thus found that the total emergency calls for coal-gas poisoning—suicide and accident—were 262 in 1951 and 357 in 1953. Thus between these two years—the former while CO₂/O₂ mixture was in use, the latter while pure oxygen was in use—there was a rise in the relevant emergency calls of 36%. At the same time the accidental deaths and suicides from carbon monoxide poisoning recorded in London A.C. increased from 231 in 1951 to 298 in 1953—that is, by 29% (figures provided by the Registrar-General). In short, the deaths for these two crucial years, before and after the change in resuscitation method, appear merely to have kept in step with the number of emergency calls for all carbon-monoxide poisoning cases.

Experience of some Provincial Towns

Statistics of the number of cases of carbon monoxide poisoning occurring in the last few years were also sought from local authorities outside London. Very few maintained such records, but, of the 30 approached, nine were able to provide some relevant data. Particulars for eight of them are given in Table III.

TABLE III

Local Authority (County Boroughs)	Average No. of Cases per Annum of CO Poisoning Removed by Ambulance		1953–5 as % of 1951–2
	1951–2	1953–5	
Birkenhead	6*	11	183
Croydon	23	31†	135
Doncaster	4*	9	225
Grimsby	2	4	200
Kingston-upon-Hull ..	56*	49	88
Nottingham	41	51	124
Salford	12	21†	175
Stoke-on-Trent	21	37	176
Total	165	213	130
Deaths recorded in England and Wales	2,455	3,047	124

* 1952 figures only.

† 1953 figure only.

‡ Excluding 18 cases in 1954 from an accident at the gas-works. If they are included the Croydon percentage becomes 161.

It will be seen that in seven of these eight large towns the numbers of cases have increased appreciably between 1951–2 and 1953–5. In total their increase in cases has been 30%, whereas the deaths for all England and Wales showed an increase of 24%.

The ninth town, Norwich C.B., could provide figures for 1953 to 1955 only. The number of cases carried in 1953 was 8, in 1954 it rose to 16, in 1955 it was 13. Again a rise in incidence is revealed.

For seven of these towns it is possible to give annual figures from 1952 to 1955. In Table IV they are compared with the deaths recorded for all England and Wales, and show, it will be seen, a close parallelism. As in London, cases appear to have moved concurrently with deaths.

TABLE IV

Year	Total No. of Cases of CO Poisoning Removed by Ambulance in Seven County Boroughs		Total No. of Deaths from CO Poisoning in all England and Wales	
	No.	As % of Cases in 1952	No.	As % of Deaths in 1952
1952	160	100	2,409	100
1953	189	118	2,848	118
1954	205	128	3,129	129
1955	198	124	3,166	131

Conclusion

The figures presented here, both from London and from some provincial towns, do not support the belief that the large rise in the deaths from carbon monoxide poisoning that occurred in England and Wales in 1953 and 1954 (and 1955) has been due to the change in resuscitation procedures adopted in local authority ambulances. That rise in mortality appears to have been associated with a concurrent, and no less, rise in the actual number of cases occurring, as measured by ambulance emergency calls.

The data are clearly not precise enough to prove accurately the relative advantages (or disadvantages) of the CO₂/O₂ mixture compared with pure oxygen and they were not collected for that purpose. They are, however, sufficient to make it extremely difficult to believe that the pronounced increase in mortality of recent years is primarily due to any such difference.

I am indebted to the many medical officers of health who assisted me, to the Registrar-General of England and Wales for mortality data, and to Dr. J. T. Boyd for help in the tabulation and analysis.

Medical Memorandum

Glandular Fever at the Age of 6 Weeks

In his Lumleian lecture for 1934 Tidy states that probably no age is immune from glandular fever, and until that year cases had been described occurring at ages ranging from infancy to 70 years (Moir, 1930). The youngest patient was aged 7 months, and three cases at this age have been reported (West, 1896; Davis, 1929; Price, 1930). Like Bernstein (1940), we have found no account of the case in a baby of 4 months cited by Tidy and Morley (1921) from the 21 cases reported by Schäffer (1908), nor of that in a 6-month infant in Robertson's report (1909). The two youngest cases to which we have found reference since 1934 were recently reported from the United States: one in a negro child of 9 weeks (Walker, 1951) and the other in a Filipino aged "1 month" (Woodward *et al.*, 1954). Each case was associated with a positive Paul-Bunnell reaction and a generalized lymphadenopathy; but, whereas one baby was not very ill and had only a mild diarrhoea, the other had a severe illness accompanied by marked enlargement of liver and spleen, an "icteric tint," and diarrhoea. Because of this diversity of features in such young patients details of a case of glandular fever in a male infant of 6 weeks may be of interest.

CASE REPORT

The patient's early progress had been poor; feeds were frequently regurgitated, and the birth weight (6 lb. 5 oz. = 2.863 kg.) had not been recovered until the fifth week. On the 42nd day of life he became listless and vomited forcibly; no alteration in the stools had been observed. On admission to hospital on this day he weighed 6½ lb. (2.949 kg.) and was thin and apathetic, but afebrile and not dehydrated. No enlargement of lymph nodes or spleen was noted at this stage and there was no apparent respiratory infection. His condition then improved, and 72 hours later he was alert and feeding well. Regurgitation of feeds persisted intermittently, but without vomiting, and stools remained normal. In the next 36 hours his rectal temperature had risen to 101° F. (38.3° C.), and during the succeeding 14 days it ranged between 97.6° and 100° F. (36.4° and 37.8° C.); it then fell and remained around 99° F. (37.2° C.). After five days the spleen became palpable to ½ in. (20 mm.) below the costal margin. On the eighth day after admission inguinal lymphadenopathy was noted, the nodes being discrete and enlarged to ¼–½ in. (6.4–8.5 mm.) across; this subsided within eight days. No other lymph nodes were found to

TABLE I.—Blood Count

Age (Days)	Total W.B.C. per c.mm.	Neutrophils %	Eosinophils %	Basophils %	Monocytes %	Lymphocytes %	Abnormal Forms %	Platelets per c.mm.
44	26,000	18	4	0	4	74	14	—
54	24,000	28	1	0	12	59	50+	—
63	21,000	35	3	0	5	57	70	44,000
70	23,000	43	3	0	8	46	98	120,000
75	23,400	55	1	0	3	41	70	550,000
104	22,600	26	4	0	5	65	63	301,000

TABLE II.—Paul-Bunnell Reaction

Age (Days)	Non-absorbed Titre	Titre after Guinea-pig Absorption
49	1 : 1,024	—
54	1 : 1,536	1 : 192
63	1 : 2,048	1 : 768
104	1 : 0,512	1 : 192

be enlarged except, though to a lesser degree, those of the occipital group. Splenomegaly persisted for two months, after which the spleen receded to the costal margin. The liver was not enlarged.

In the first week a transient tracheobronchitis developed, with relapse in the third and sixth weeks; the second episode was treated with benzathine penicillin by mouth, no other drug being given. The Wassermann reaction was negative at 10 weeks, and the urine showed no microscopical abnormality or albuminuria. The baby remained in hospital for five weeks; on discharge he had gained 2½ lb. (1.134 kg.) and splenomegaly was the only clinical abnormality. Thereafter improvement was maintained.

The haematological findings are shown in Tables I and II. Note the lymphocytosis and high proportion of abnormal forms characteristic of glandular-fever cells; also the thrombocytopenia.

COMMENT

The haematological and serological findings in the above case are regarded as characteristic of glandular fever. Attention is drawn to the high titre attained in the Paul-Bunnell reaction, in well-recognized contrast to the minimal constitutional reaction and slight lymphadenopathy. That such trivial symptoms may occur in this condition suggests that it may not be so uncommon at an early age. Another feature of note is the transient depression of the platelet count, with recovery, in the absence of haemorrhagic manifestations. Blood-streaking of regurgitated milk was indeed observed, but this is attributed to an abnormal reflux with a lax oesophagus, and it occurred both before and after the thrombocytopenia. Depression of the platelet count with resulting purpura has been observed in glandular fever. That haemorrhage may not accompany thrombocytopenia in this condition has also been noted (Cottrell, 1927). The source of infection in the present case is not known, and the Paul-Bunnell reactions of the parents and the one sibling were negative. The patient had been closely admired by many neighbours, and so had ample opportunity for acquiring infection.

We wish to thank Dr. Doyne Bell for his interest and help in the preparation of this paper. Our thanks are also due to Dr. H. E. Thorn for kindly referring the child, and to Mr. M. Pollard for haematological investigations.

K. D. PHILLIPS, M.B., B.S.,
D. G. H. STONE, M.B., M.R.C.P., D.C.H.,
Charing Cross Hospital Group.

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