Table showing Comparison between Newborn Infants Treated with Exchange Transfusion and Cases of Icterus Gravis not so Treated

No. of Families	No. of Pregnancies	Normal Children	Mild Cases of E.F. (Haemol. Anaemia and Mild Jaundice)	Icterus Gravis		Stillbirth (5th to 9th Month)	Abortion
				Alive	Died		
88	465	192 (41%)	25 (5.3%)	41	115	57 (12.2%)	38 (8.1%)
				156 (33.5%)			

Mortality rate of icterus gravis, 73.7%.

Mortality rate of icterus gravis, mild cases included, 63.5%.

Mortality rate of 160 cases of icterus gravis treated with exchange transfusion 22.5%.

that of cases treated by exchange transfusion, for we have not sufficient personal experience of the latter.

It is beyond doubt that the prognosis in icterus gravis of the newborn has improved considerably owing to the treatment with exchange transfusion, whether preceded or not by partus arte praematurus.

Summary

After a short introduction the method of exchange transfusion applied to 160 newborn infants suffering from haemolytic disease is described.

The indications for the application of exchange transfusion are discussed.

The mortality rate of 160 babies treated by this method was 22.5%.

In order to determine whether the mortality of icterus gravis was reduced by this therapy, the results of treatment with exchange transfusion were compared with those in icterus gravis of children not so treated. Although we have no data on the results of treatment with simple transfusion of Rh-negative blood, the difference (63.5 to 22.5%) seems to indicate that the prognosis of the newborn suffering from icterus gravis has improved considerably by the application of exchange transfusion.

We wish to express our gratitude to Dr. R. R. Race for all his kind help and much useful advice.

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The Minister of Health intends to dispose of all hospital land and premises other than those which are being used or are likely to be needed for the hospital service. Hospital management committees have been asked to consider what property is suitable for disposal. The Minister will agree to the retention of endowed property only where there is a clear need for it—for example, when in the hospital board's opinion it should be reserved for future development. If the development and disposal of hospital property near a hospital is likely to injure the amenities of the hospital, the Ministry's attention should be drawn to the risk, so that it can consider including restrictive covenants in the conveyance of the property. In some cases boards may wish to make a case for the retention of such property.

A CASE OF ANAMNESTIC REACTION WITH Rh AGGLUTININS

BY

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Since the recognition of the importance of Rh agglutinins in relation to pregnancy and haemolytic disease of the newborn the interpretation of the serological findings has become a rather complex problem. The discovery of Rh agglutinins during the antenatal period does not necessarily foreshadow damage to the foetus, as it may represent a "carry-over" from the previous pregnancy. Of much greater significance is the demonstration of a rising titre, which is generally accepted as evidence of specific antigenic stimulation by the Rhesus-incompatible cells from the foetus. The importance of this assumption hardly needs to be emphasized, since on it may depend the decision to induce premature labour.

The following case is recorded because of its rarity and to draw attention to a possible alternative interpretation of the serological findings in pregnancy.

Case Report

The patient, a woman aged 34, had been married twice. By the first marriage she had a normal male child. Eight years later, in December, 1945, she was delivered of a normal male infant (by the second marriage). In December, 1947, she gave birth to a male child which was normal at birth but became jaundiced on the second day and died on the sixth day, deeply jaundiced and exhibiting kernicterus.

At this time the mother was found to be Rh-negative and her husband was thought to be homozygous positive. The infant was found to be R_{2r} (cDE/cde). The mother's serum contained albumin agglutinins to a serum dilution of 1:16.

In 1948 she became pregnant again and attended the antenatal clinic of this hospital. At the 17th week of pregnancy her serum was found to contain albumin agglutinins (anti-D) to a titre of 1:8. Examination of the patient's cells showed her to be group A_1N,rr . At the 32nd week the titre was estimated to be 1:16, and two weeks later it had risen to 1:64. Taking into account the past history and the rising titre of antibodies, it was decided to induce labour in the 35th week. A normal female infant was subsequently delivered and has since made good and uneventful progress.

Examination of the cord blood yielded the following information: Group A_1MN,rr . Direct Coombs's test, negative. Serum contained albumin agglutinins (anti-D) to a titre of 1:32. The serum bilirubin was 1.75 mg. per 100 ml. A blood film showed marked anisocytosis and polychromasia and a number of nucleated red cells (late forms)—approximately 9 per 100 white cells. A haemoglobin estimation performed on capillary blood was 18.9 g. per 100 ml. The picture was consistent with the degree of prematurity.

Examination of the mother's serum four and 17 days after delivery gave titres of 1:32 and 1:64 respectively—in albumin (see Chart). No saline agglutinins were detected, and the indirect Coombs's test gave fairly comparable results as shown. No anti-M could be detected in the mother's serum. Examination of the father's blood showed him to be group A_1, R_{2r} .

Discussion

The delivery of a D-negative infant came as a surprise in the face of the alleged genotype of the father, but, this

having been satisfactorily explained, interest was focused on the rising anti-D titre. After repetition of the tests it was concluded that the rise was more than could be accounted for by technical error.

This would therefore appear to be an example of an anamnestic reaction. While others have apparently observed the phenomenon in connexion with Rh agglutinins, only one case has been recorded so far (Davidsohn, 1948). The latter described the case of a woman who had an affected child by a homozygous husband and three years later became pregnant by a D-negative artificial insemination donor. A normal D-negative child was subsequently born, but a marked rise in agglutinins was observed about the sixth month of pregnancy. In the bacteriological field, in which anamnestic reactions have previously been studied, attempts to reproduce the phenomenon experimentally have not given consistent results. However, it has been pointed out (Topley and Wilson, 1936) that where an appreciable rise did occur in response to the introduction of a second antigen, the latter bore some relation to the primary antigen.

Our knowledge of the chemistry of the blood-group antigens has been considerably increased in respect of the ABO system (Morgan, 1947), but is very much more scanty so far as the other antigens are concerned. However, one might reasonably look in this direction for a source of antigenic stimulation in anamnestic reactions, since they apparently occur amongst the ABO substances (Davidsohn, 1948).

In Davidsohn's case there was no ABO incompatibility between the mother and infant, and the MN grouping of the mother was not known. In the present case the only foreign antigen is the M derived from the MN cells of the infant. This is known to be a weak antigen in man, and anti-M has been detected in human serum (Paterson, Race, and Taylor, 1942). Whether M has anything in common with the Rh antigens is a matter for speculation, but the failure to detect anti-M in the mother's serum would seem to rule out any possibility of M being responsible for the rise in anti-D titre in this case.

The problem remains, therefore, in both its clinical and its more academic aspects. From a practical point of view a rising anti-D titre will result in one of three possibilities: (1) an affected D-positive infant, (2) an unaffected D-positive infant, or (3) an unaffected D-negative infant (anamnestic reaction). In coming to a decision the obstetrician will undoubtedly set against induction the second and third possibilities. There are grounds for hoping that in the not too distant future an explanation of why a positive infant may escape can be turned to practical advantage, and in order that the third possibility may be put into its proper perspective it is obviously relevant to know how often an anamnestic reaction may occur.

I am indebted to Dr. A. E. Mourant, of the Lister Institute, for his advice and help in genotyping and MN grouping; to Dr. J. Murray, of Queen Charlotte's Hospital, for kindly supplying details of previous investigations; to Mr. G. F. Gibberd and Dr. F. A. Knott for permission to publish this case; and to various members of the laboratory staff for their assistance.

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CARCINOMA OF THE BREAST IN CASTRATED WOMEN

BY

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Although it well known that carcinoma of the breast may occur after the natural menopause, and although it is also established that women of 60 and 70 may suffer from acute carcinomatous mastitis, carcinoma of the breast occurring after castration, performed either by irradiation or by surgery, is a less familiar condition. At a time when castration is being suggested by many workers as a sound adjuvant in the treatment of cancer it is useful to recall the following facts.

Anatomical and Clinical Data

1. *Frequency*.—In 2,000 cases of carcinoma of the breast I have found 32 (1.6%) occurring in castrated women (statistics from the Centre Anticancéreux, Lyons). This figure is higher than that of carcinoma occurring during pregnancy (21, or 1.05%) or in men (16, or 0.8%).

Summary of Results

Case No.	Castration			Age at Onset of Carcinoma	Age at Death	Remarks
	Reason	Means	Age			
1	Fibroids	X rays	28	43	49	
2	"	Surgery	32	35	36	
3	"	X rays	32	53	54	
4	Miscellaneous	Surgery	36	37	43	
5	Fibroids	"	37	41	42	
6	Miscellaneous	"	37	51	56	
7	Fibroids	X rays	38	45	57	
8	"	Surgery	39	46	47	
9	"	"	40	63		Alive aged 85. No recurrence
10	Miscellaneous	"	40	64		Alive aged 67. No recurrence
11	"	"	41	58	62	
12	Carcinoma of cervix	"	42	49	52	
13	Double pyosalpinx	"	42	50	51	
14	Fibroids	"	42	55	58	
15	"	"	42	62		Alive aged 80. No recurrence
16	"	"	43	44		Alive aged 65. No recurrence
17	"	Radium	43	53	57	
18	Ovarian tumour	Surgery	43	57		Alive aged 62. Recurrence
19	Fibroids	"	44	64	66	
20	Metropathia	X rays	45	47	57	
21	Fibroids	Surgery	45	51		Alive aged 55. Recurrence
22	"	"	46	60	63	
23	"	"	46	63	73	
24	Miscellaneous	"	48	66	69	
25	Metropathia	Radium	50	51		Not followed up
26	Miscellaneous	Surgery	52	59	60	
27	Fibroids	"	55	64	67	
28	Prolapse	"	60	61	65	
29	Fibroids	"	63	64		Alive aged 85. No recurrence
30	Miscellaneous	"	67	85	87	
31	"	"	70	75	77	
32	Carcinoma of cervix	Radium	71	74	75	

2. *Age of Onset*.—The Table shows the age at castration and the age at onset of carcinoma, the limits of which are 35 to 85 years. There are seven cases between 50 and 55 years and nine between 60 and 65. These are the same as the highest figures for carcinoma of the breast in non-castrated subjects, but with a particular predilection for the 55 to 65 age group.

3. *Interval Between Castration and the Onset of Carcinoma*.—This ranged from two months to 24 years. In nine cases only was it less than five years, and it must be admitted that the cancer might have already been established at the time of castration. In 23 cases the interval was over five years.