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ERYTHROBLASTOSIS FETALIS;
PATHOGENESIS AND PROGNOSIS
A STUDY OF CLINICAL
OBSTETICAL DATA

JOHN HOLCOMBE MC CULLOCH AUSTIN


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ERYTHROBLASTOSIS FETALIS: PATHOGENESIS
AND PROGNOSIS - A STUDY OF
CLINICAL OBSTETRICAL DATA

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Harvard College, B.A., 1961

Presented in Partial Fulfillment
of the Requirements for the
Degree of Doctor of Medicine

Department of Obstetrics and Gynecology
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I am much indebted to Professor C.D. Davis, whose knowledge, enthusiasm, and concern have been continually helpful and encouraging.

I should also like to express gratitude for the statistical advice of Dr. Katherine Detre and for the secretarial assistance of Mrs. Jane Nerreau and Mrs. Florene Powers.

So wretched and miserable is the condition of mankind that not only are men tormented by innumerable ills throughout their lives, but foetuses also are not free from evils and sicknesses whilst they are still shut up within the prison of the womb, and before they breathe with joy the vital air and look upon the light...(and) from this it becomes abundantly clear that there is great sympathy and affinity between the mother and the foetus.

Phillipus Jacobus Düttel
Doctoral Thesis
University of Halle, 1702

TABLE OF CONTENTS

I.	Introduction	1
II.	Materials and Methods	3
	A. Criteria of Patient Selection	3
	B. Limitations and Values of Patient Selection	4
	C. Material Under Study	5
	D. Methods of Study	7
III.	Results	9
IV.	Discussion	65
V.	Summary	71
VI.	References	72

I. INTRODUCTION

Erythroblastosis fetalis has about a 5 percent chance of occurring in Rh negative mothers with Rh positive fathers, that is, once in every 150 to 200 births.¹ Among these cases, mortality in the first affected pregnancy is 7-10 percent, serious illness requiring transfusions accounts for 60 percent, and mild illness 30 percent.²

Studies of the pathogenesis of this disease, since Levine's original report in 1941,³ have centered on possible causes of isoimmunization in terms of sensitization following the entrance of fetal erythrocytes into the maternal circulation.⁴ This event has been shown to occur during all trimesters of pregnancy as well as postpartum.^{5,6} One striking finding has been that maternal-fetal ABO incompatibility is associated with a decreased probability of the Rh disease occurring,⁷ and, according to some investigators, decreased severity.⁸ These phenomena are explained by the hypothesis that when ABO incompatible fetal cells enter the maternal circulation they are likely to be destroyed by the appropriate anti-A or anti-B antibodies, thereby diminishing the potential source of sensitization.^{8,9} Factors promoting maternal uterine trauma at delivery, such as manual removal of the placenta and Cesarean section, have been suggested as promoting the transfer of fetal erythrocytes into the maternal circulation, but evidence linking such events to subsequent erythroblastosis fetalis is meager. Potter mentions an increased incidence of complications of labor as associated with later hemolytic disease of the newborn,

but provides no data.¹⁰ In a series of 46 patients, Gainey et al. noted 3 cases of traumatic deliveries, 4 of Cesarean section, and 3 of manual removal of the placenta compared to one Cesarean section in a control series of 38 patients, and suggest "induced pathology" may lead to maternal isoimmunization.¹¹

The prognosis of the disease once sensitization has occurred is that later pregnancies with Rh positive children tend to have the disease to the same or greater extent than the first affected child.¹² Factors relating to the prognosis of the first affected child have involved evaluation of the maternal anti-Rh antibody titer and the optical absorption spectrum of the amniotic fluid, both events which occur after sensitization. ^{To} ~~The~~ this writer's knowledge no reports relating prognosis to the events of presumed sensitization have appeared beyond the recognition of the "protective" effects of maternal-fetal ABO incompatibility.

This study, then, undertakes to evaluate the clinical events surrounding sensitization in terms of the subsequent development and prognosis of erythroblastosis fetalis in the first affected child. For instance, the hypothesis that prolonged or difficult labor is associated with an increased likelihood of maternal sensitization may be tested, as may also the hypothesis that prolonged or difficult labor is of prognostic importance. Thus subjected to analysis are the obstetrical data involving the presumed sensitizing pregnancy and delivery and the equally readily available pediatric data involving the presence and severity of erythroblastosis fetalis.

II. MATERIALS AND METHODS

A. Criteria of Patient Selection.

Twenty-five cases of first affected children with erythroblastosis fetalis were selected from the records of the Grace-New Haven Hospital for the period 1960-1962 according to the following criteria:

1. ABO blood types of mother, erythroblastotic child, and preceding sibling(s) are known, and the Rh types appropriate, i.e., mother Rh negative, erythroblastotic child Rh positive, a preceding sibling Rh positive, and the father (when known) Rh positive.
2. The mother had before delivery of the erythroblastotic child received no blood transfusions or injections.
3. The erythroblastotic child had a positive Coombs test.¹³
4. Patients were excluded which involved,
 - a. non-white racial background,
 - b. a multiple pregnancy, or
 - c. Cesarean section for an Rh positive child prior to delivery of a sensitized one.
5. Appropriate controls were available.

Controls were selected so that each case of erythroblastosis fetalis had an individual control meeting the following criteria:

1. No erythroblastosis fetalis was present (Coombs test negative in all children).
2. Maternal and paternal (when known) ABO and Rh blood types were the same as those of the corresponding mother and father (when known).
3. The ABO and Rh blood types of each living newborn were identical with those of the corresponding child, including the first affected. For example, if an O negative mother and an A positive father have a normal A positive first offspring, normal O negative second, and erythroblastotic A positive third, then these same blood types must be present in the control, i.e., O negative mother, A

positive father, A positive first offspring, O negative second, and A positive third.

4. Patients were excluded which had,
 - a. a non-white racial background,
 - b. a plural pregnancy, or
 - c. Cesarean section for an Rh positive child prior to delivery corresponding to the sensitized one.

These latter two restrictions were deemed necessary because twinning and Cesarean sections occur too infrequently to permit of controlling.

Using the above criteria, a series of twenty-five plus controls was obtained.

B. Limitations and Values of Patient Selection.

It will be noted that these criteria for case selection provide a sample of erythroblastosis fetalis which excludes the 15 to 20 percent of cases which die in utero, for on these children ABO, Rh, and Coombs testing are not done. Also tending to be eliminated from consideration are those cases involving unusual combinations of blood types, for controls with these same combinations are difficult to obtain.

The selection is skewed away from the most grave occurrence of the disease, and away from unusual combinations of blood types.

Also the series is rather small due to many incomplete records by the above criteria. However, because these limitations apply equally

to the control series, so comparison provides internally valid results.

C. Material Under Study

Three categories of data are considered: Personal maternal data, such as height and weight; data relating to the presumed sensitizing pregnancy and delivery, that is, of the preceding Rh positive child; and data relating to the erythroblastotic.

Personal maternal data analyzed are:

1. Height (in inches).
2. Weight (in pounds), before the first pregnancy.
3. Somatic index, which is height divided by the cube root of the weight - this is a useful measure of body type, since, for instance, a tall but light woman will have a higher somatic index than a shorter, heavier woman.
4. Age, at the delivery of the presumed sensitizing pregnancy, **and**
5. History of abortions, cervical dilatations and curettage.

Presumed sensitizing pregnancy data analyzed are those routinely recorded on the Grace-New Haven Obstetrical Service. These data are:

1. Duration of pregnancy, in days.
2. Duration of labor, in minutes,
 - a. total time elapsed,
 - b. first stage,
 - c. second stage,
 - d. third stage.
3. Manual **vs.** spontaneous placental delivery.
4. Oxytocics and the third stage of labor, in terms of use before and after delivery of the placenta.

5. Rupture of the membranes,
 - a. spontaneous vs. artificial,
 - b. time of rupture, in minutes, before fetal delivery.

6. Rectal and vaginal examinations performed during the first two stages of labor,
 - a. number of rectals,
 - b. number of vaginals,
 - c. number of rectals plus vaginals.

7. Duration of general anesthesia at delivery,
 - a. nitrous oxide, in minutes,
 - b. cyclopropane,
 - c. total.

8. Delivery spontaneous vs. operative.

To provide quantitation of the extent of the operative process, the following arbitrary "Operative Index" is used:

Elective low forceps	1 point
Breech, assisted	1 point
Low forceps	2 points
Low mid-forceps	3 points
Low mid-forceps with rotation	4 points
Spontaneous delivery	0 points

9. Birth canal lacerations at delivery.
10. Estimated blood loss at delivery.
11. Sex.
12. Birth weight, in grams.

Data analyzed concerning the erythroblastotic child are the following:

1. Sex.
2. Birth weight, in grams.

3. Physical examination normal, i.e., no signs of erythroblastosis fetalis were present; thus the diagnosis was made on the basis of laboratory and not clinical data.

4. Transfusion required.

It will be noted that the cases of erythroblastosis fetalis in this series may be divided by increasing severity into three groups - those with normal physical examinations, those with abnormal physical examinations but not requiring transfusion, and those severe enough to merit transfusion.

D. Methods of Study

Two methods are used - one relating to pathogenesis and one to prognosis.

The study of pathogenesis compares the erythroblastic series with the control, by determining in each group mean values, e.g., maternal height, and calculating statistical significance by the t-test.

An interesting and important aspect of such correlations is the necessity for consideration of like subgroups within the total series, for significant differences between subgroups may be present in the absence of such differences for the larger group. "Unless patients with a particular disease are divided into comparable groups that are suitably homogenous in clinical properties, as well as in personal and in laboratory data, the precision of science is lost." ¹⁴ To obtain such precision in the present study, a number of subgroups are analyzed. These include a breakdown by blood types, e.g., type O in mother, child of the presumed sensitizing pregnancy, and the erythroblastotic.

Because ABO incompatibility is said to protect against the disease, the subgroup is considered in which the blood type of either the presumed sensitizing pregnancy or the erythroblastotic offspring is different from the blood type of the mother.

Also analyzed as subgroups, because of suggestive findings within the data, are those with somatic index greater than 13 (12 of the 25) and those in which cyclopropane anesthesia was used (10 of the 25).

Evaluation of prognosis, on the other hand, does not involve the "control group" at all, but rather considers like cases within the series with the disease, noting correlations between severity, e.g., whether transfusions were necessary, and the variables under consideration, e.g., operative intervention at the presumed sensitizing pregnancy. For this analysis, the control population is taken to be the remaining cases of the disease. The control for subgroup is non-subgroup. Thus, for example (see Table 5-B, page 18) in the group of ten patients in which transfusions were done, mean maternal age at delivery of the presumed sensitizing pregnancy is 22 years of age. The remaining fifteen, where no transfusions occurred, are taken as control--these have a mean maternal age at delivery of the presumed sensitizing pregnancy of 25 years. These data are then subjected to the t-test for statistical significance.

III. RESULTS

The data are presented in the following manner: Table 1 shows the overall distributions of ABO blood types. Thereafter, the raw data are presented on one page (e.g., Table 2-A) and on the next page (e.g., Table 2-B) is the evaluation of these data.

In order carefully to separate study of the subgroups relating to pathogenesis from the subgroups relating to prognosis, in the following tables a dotted line separates data referring to each of these areas.

Two abbreviations are employed:

EF - Erythroblastosis fetalis

PSP - Presumed sensitizing pregnancy, or the corresponding pregnancy in the control series.

TABLE 1
ABO BLOOD TYPES

<u>Case Number</u>	<u>Mother</u>	<u>Father</u>	<u>PSP Child</u>	<u>EF Child</u>
1.	A	A	A	A
2.	O	O*	O	O
3.	O		O	O
4.	O		O	O
5.	O	O	O	O
6.	A	A	A	A
7.	O	O	O	O
8.	A		A	A
9.	B	O	B	B
10.	O	B	B	B
11.	O		A	A
12.	O		O	O
13.	O		O	O
14.	A		A	O
15.	A		A	A
16.	O	A	O	A
17.	A		A	O
18.	O	A	A	A
19.	O	O	O	O
20.	A	O	A	A
21.	O	O	O	O
22.	O	O	O	O
23.	A		A	A
24.	A	O	A	O
25.	O		O	A

* A blank space indicates paternal ABO type unknown.

TABLE 2-A
MATERNAL HEIGHT
(in inches)

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
1.	65	65
2.	62	67
3.	66	64
4.	59	64
5.	65	67
6.	66	64
7.	65	64
8.	65	62
9.	65	63
10.	61	66
11.	68	64
12.	62	61
13.	*	*
14.	64	62
15.	60	65
16.	71	60
17.	68	61
18.	66	65
19.	65	63
20.	66	67
21.	61	65
22.	63	62
23.	64	66
24.	69	61
25.	68	61

* Height not known.

TABLE 2-B

MATERNAL HEIGHT
(in inches)

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	Number of Cases	Mean Value	Number of Cases	Mean Value	n	t	Pz
I. All Cases	24	65	24	64	46	1.025	0.35
II. Maternal O	14	64	14	64	26	insignificant	
a. PSP O, EF O	9	63	9	64	16	0.975	0.35
b. PSP O, EF A	2	70	2	61	2	5.692	0.04
c. PSP A, EF A	2	67	2	65	2	2.236	0.20
d. PSP O or A, EF A	4	68	4	63	6	3.652	0.015
III. Maternal A	9	65	9	64	16	1.365	0.20
a. PSP A, EF A	6	64	6	65	10	insignificant	
b. PSP A, EF O	3	67	3	61	4	3.624	0.03
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	67	8	63	14	3.228	0.01
V. Somatic Index ≥ 13	12	66	12	64	22	10.029	0.001
VI. Cyclopropane Anesthesia	10	64	10	64	18	insignificant	

VII. Physical Examination Normal for EF Infant	11	65	15	65	23	insignificant	
VIII. Transfusion(s) Given To EF Infant	9	65	15	65	23	insignificant	

TABLE 3-A

MATERNAL WEIGHT
(in pounds, before the first pregnancy)

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
1.	104	117
2.	115	140
3.	117	134
4.	110	170
5.	127	132
6.	115	130
7.	125	106
8.	131	120
9.	109	196
10.	109	142
11.	169	138
12.	120	140
13.	140	128
14.	113	138
15.	109	115
16.	117	117
17.	120	115
18.	130	121
19.	132	120
20.	118	140
21.	115	124
22.	115	96
23.	110	156
24.	140	130
25.	168	90

TABLE 3-B

MATERNAL WEIGHT
(in pounds)

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	Number of Cases	Mean Value	Number of Cases	Mean Value	n	t	P <
I. All Cases	25	123	25	130	48	1.280	0.25
II. Maternal O	15	127	15	127	28	insignificant	
a. PSP O, EF O	10	122	10	129	18	1.051	0.35
b. PSP O, EF A	2	143	2	104	2	1.352	0.35
c. PSP A, EF A	2	150	2	130	2	0.940	0.45
d. PSP O or A, EF A	4	146	4	117	6	5.630	0.005
III. Maternal A	9	118	9	129	16	1.874	0.09
a. PSP A, EF A	6	115	6	130	10	2.006	0.08
b. PSP A, EF O	3	124	3	128	4	insignificant	
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	133	8	124	14	0.904	0.40
V. Somatic Index ≥ 13	12	118	12	133	22	2.032	0.06
VI. Cyclopropane Anesthesia	11	127	11	136	20	1.280	0.25

VII. Physical Examination Normal for EF Infant	11	122	14	124	23	insignificant	
VIII. Transfusion(s) Given to EF Infant	10	122	15	124	23	insignificant	

TABLE 4-A

MATERNAL SOMATIC INDEX
(height divided by cube root of weight)

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
1.	13.82	13.29
2.	12.75	12.90
3.	13.49	12.51
4.	12.32	11.55
5.	12.93	13.16
6.	13.57	12.63
7.	13.00	13.52
8.	12.80	12.57
9.	13.60	10.85
10.	12.77	12.65
11.	12.30	12.38
12.	12.57	11.75
13.	*	*
14.	13.24	12.00
15.	12.56	13.36
16.	14.52	12.27
17.	13.79	12.54
18.	13.03	13.11
19.	12.77	12.77
20.	13.46	12.90
21.	12.54	13.04
22.	12.95	13.54
23.	13.36	12.26
24.	13.29	12.04
25.	12.32	13.61

* Unable to calculate somatic index, because height not known.

TABLE 4-B

MATERNAL SOMATIC INDEX

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	Number of Cases	Mean Value	Number of Cases	Mean Value	n	t	P _z
I. All Cases	24	13.07	24	12.63	46	1.983	0.06
II. Maternal O	14	12.88	14	12.77	26	insignificant	
a. PSP O, EF O	9	12.81	9	12.75	16	insignificant	
b. PSP O, EF A	2	13.42	2	12.94	2	0.373	0.75
c. PSP A, EF A	2	12.66	2	12.75	2	insignificant	
d. PSP O or A, EF A	4	13.04	4	12.84	6	insignificant	
III. Maternal A	9	13.32	9	12.62	16	3.156	0.01
a. PSP A, EF A	6	13.26	6	12.84	10	1.600	0.15
b. PSP A, EF O	3	13.44	3	12.19	4	5.699	0.01
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	13.16	8	12.58	14	1.777	0.10
(V. Somatic Index ≥ 13)							
VI. Cyclopropane Anesthesia	10	13.06	10	12.57	18	1.525	0.20

VII. Physical Examination Normal for EF Infant	11	13.06	13	13.09	22	insignificant	
VIII. Transfusion(s) Given to EF Infant	9	13.12	15	13.04	22	insignificant	

TABLE 5-A

MATERNAL AGE
(in years, at delivery of pre-
sumed sensitizing pregnancy)

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
1.	22	20
2.	21	18
3.	25	18
4.	25	33
5.	31	31
6.	21	33
7.	26	24
8.	33	19
9.	21	23
10.	23	29
11.	22	26
12.	19	21
13.	22	20
14.	30	24
15.	19	22
16.	25	25
17.	22	31
18.	26	20
19.	23	30
20.	25	26
21.	25	27
22.	27	20
23.	17	22
24.	25	33
25.	19	19

TABLE 5-B

MATERNAL AGE, IN YEARS, AT DELIVERY
OF PRESUMED SENSITIZING PREGNANCY

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	Number of Cases	Mean Value	Number of Cases	Mean Value	n	t	P ₂
I. All Cases	25	24	25	25	46	0.629	0.55
II. Maternal O	15	24	15	24	28	insignificant	
a. PSP O, EF O	10	24	10	24	18	insignificant	
b. PSP O, EF A	2	22	2	22	2	insignificant	
c. PSP A, EF A	2	24	2	23	2	insignificant	
d. PSP O or A, EF A	4	23	4	23	6	insignificant	
III. Maternal A	9	24	9	26	16	0.710	0.50
a. PSP A, EF A	6	23	6	24	10	insignificant	
b. PSP A, EF O	3	26	3	29	4	1.021	0.40
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	24	8	26	14	0.889	0.40
V. Somatic Index ≥ 13	12	26	12	25	22	insignificant	
VI. Cyclopropane Anesthesia	11	24	11	25	20	0.020	1.00
<hr style="border-top: 1px dashed black;"/>							
VII. Physical Examination Normal for EF Infant	11	24	14	24	23	insignificant	
VIII. Transfusion(s) Given to EF Infant	10	22	15	25	23	0.400	0.70

TABLE 6

MATERNAL ABORTION, CERVICAL DILATATION,
AND CURETTAGE (D AND C) HISTORY

Only cases with abortions or D and C's are listed.

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
5.		Abortion, D+C - Before PSP
13.		Abortion, D+C - after PSP
14.	Abortion - before PSP	
19.	Abortion - before PSP	
20		2 Abortions, 1 D+C - all before PSP
21.		Abortion, D+C - after PSP
22.	Abortion, D+C - after PSP	
24.		Abortion, D+C - after PSP

By inspection there is no difference between the EF and control series.

TABLE 7-A

PRESUMED SENSITIZING PREGNANCY: DURATION
(in days)

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
1.	270	*
2.	285	288
3.	276	260
4.	273	268
5.	276	285
6.	280	283
7.	283	281
8.	273	300
9.	268	295
10.	292	275
11.	262	291
12.	266	282
13.	265	272
14.	282	273
15.	281	282
16.	279	274
17.	280	259
18.	294	291
19.	288	258
20.	284	275
21.	264	267
22.	306	265
23.	285	274
24.	275	262
25.	284	249

* Duration of pregnancy not known.

TABLE 7-B

PRESUMED SENSITIZING PREGNANCY: DURATION
(in days)

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	Number of Cases	Mean Value	Number of Cases	Mean Value	n	t	P <
I. All Cases	25	279	24	275	47	1.038	0.35
II. Maternal O	15	280	15	275	29	insignificant	
a. PSP O, EF O	10	278	10	273	18	1.056	0.35
b. PSP O, EF A	2	282	2	268	2	2.077	0.20
c. PSP A, EF A	2	278	2	291	2	0.081	0.95
d. PSP O or A, EF A	4	280	4	280	6	insignificant	
III. Maternal A	9	279	8	276	15	0.622	0.55
a. PSP A, EF A	6	279	5	283	9	0.791	0.50
b. PSP A, EF O	3	279	3	265	4	3.025	0.05
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	281	8	272	14	1.464	0.20
V. Somatic Index ≥ 13	12	280	11	275	21	1.116	0.30
VI. Cyclopropane Anesthesia	11	277	10	277	19	insignificant	

VII. Physical Examination Normal for EF Infant	11	278	14	280	23	insignificant	
VIII. Transfusion(s) Given to EF Infant	10	277	15	280	23	insignificant	

TABLE 8-A

PRESUMED SENSITIZING PREGNANCY: DURATION
OF LABOR - TOTAL TIME ELAPSED
(in minutes)

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
1.	306	506
2.	369	280
3.	857	412
4.	398	332
5.	300	294
6.	531	427
7.	85	175
8.	424	727
9.	209	444
10.	387	130
11.	1013	671
12.	472	606
13.	259	691
14.	535	952
15.	1246	524
16.	504	870
17.	771	525
18.	766	625
19.	534	505
20.	118	329
21.	303	664
22.	404	175
23.	834	630
24.	282	240
25.	915	1095

TABLE 8-B

PRESUMED SENSITIZING PREGNANCY: DURATION
OF LABOR - TOTAL TIME ELAPSED (in minutes)

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	Number of Cases	Mean Value	Number of Cases	Mean Value	n	t	P ₂
I. All Cases	25	513	25	513	48	0.004	1.00
II. Maternal O	15	504	15	502	28	insignificant	
a. PSP O, EF O	10	398	10	413	18	0.172	0.90
b. PSP O, EF A	2	710	2	983	2	1.165	0.40
c. PSP A, EF A	2	890	2	648	2	1.922	0.20
d. PSP O or A, EF A	4	800	4	815	6	insignificant	
III. Maternal A	9	561	9	540	16	insignificant	
a. PSP A, EF A	6	577	6	524	10	0.212	0.85
b. PSP A, EF O	3	529	3	572	4	insignificant	
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	647	8	639	14	insignificant	
V. Somatic Index ≥ 13	12	483	12	511	22	0.324	0.75
VI. Cyclopropane Anesthesia	11	506	11	505	20	insignificant	

VII. Physical Examination Normal for EF Infant	11	494	14	527	23	insignificant	
VIII. Transfusion(s) Given to EF Infant	10	554	15	485	23	0.568	0.60

TABLE 9-A

PRESUMED SENSITIZING PREGNANCY:
DURATION OF FIRST STAGE OF LABOR
(in minutes)

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
1.	270	425
2.	285	180
3.	805	390
4.	375	315
5.	270	282
6.	450	405
7.	70	160
8.	395	690
9.	180	390
10.	360	120
11.	960	630
12.	435	540
13.	230	615
14.	480	945
15.	1215	495
16.	420	790
17.	660	480
18.	735	555
19.	520	450
20.	96	315
21.	230	630
22.	360	150
23.	800	570
24.	260	180
25.	840	1050

TABLE 9-B

PRESUMED SENSITIZING PREGNANCY: DURATION
OF FIRST STAGE OF LABOR (in minutes)

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	Number of Cases	Mean Value	Number of Cases	Mean Value	n	t	P ₂
I. All Cases	25	468	25	470	48	0.027	1.00
II. Maternal O	15	460	15	457	28	insignificant	
a. PSP O, EF O	10	358	10	371	18	0.157	0.90
b. PSP O, EF A	2	630	2	920	2	1.174	0.40
c. PSP A, EF A	2	848	2	593	2	2.150	0.20
d. PSP O or A, EF A	4	749	4	756	6	insignificant	
III. Maternal A	9	514	9	501	16	insignificant	
a. PSP A, EF A	6	538	6	483	10	insignificant	
b. PSP A, EF O	3	467	3	535	4	0.272	0.80
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	589	8	594	14	insignificant	
V. Somatic Index ≥ 13	12	436	12	467	22	0.279	0.80
VI. Cyclopropane Anesthesia	11	461	11	458	20	insignificant	

VII. Physical Examination Normal for EF Infant	11	449	14	483	23	insignificant	
VIII. Transfusion(s) Given to EF Infant	10	502	15	446	23	insignificant	

TABLE 10-A

PRESUMED SENSITIZING PREGNANCY:
DURATION OF SECOND STAGE
(in minutes)

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
1.	34	79
2.	83	98
3.	40	17
4.	14	14
5.	28	10
6.	76	21
7.	11	22
8.	26	21
9.	28	52
10.	16	7
11.	52	38
12.	34	62
13.	27	62
14.	46	6
15.	30	24
16.	83	77
17.	105	44
18.	27	23
19.	12	52
20.	26	6
21.	57	32
22.	31	15
23.	30	55
24.	20	57
25.	70	43

TABLE-10- B

PRESUMED SENSITIZING PREGNANCY: DURATION
OF SECOND STAGE (in minutes)

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	<u>Number of Cases</u>	<u>Mean Value</u>	<u>Number of Cases</u>	<u>Mean Value</u>	<u>n</u>	<u>t</u>	<u>Pz</u>
I. All Cases	25	40	25	38	48	0.385	0.75
II. Maternal O	15	39	15	38	28	insignificant	
a. PSP O, EF O	10	34	10	38	18	0.406	0.70
b. PSP O, EF A	2	77	2	60	2	0.907	0.50
c. PSP A, EF A	2	40	2	31	2	0.617	0.60
d. PSP O, or A, EF A	4	58	4	45	6	0.766	0.50
III. Maternal A	9	44	9	35	16	0.702	0.50
a. PSP A, EF A	6	37	6	34	10	insignificant	
b. PSP A, EF O	3	57	3	36	4	0.686	0.55
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	52	8	37	14	1.095	0.30
V. Somatic Index ≥ 13	12	44	12	38	22	0.500	0.65
VI. Cyclopropane Anesthesia	11	39	11	39	20	insignificant	

VII. Physical Examination Normal for EF Infant	11	39	14	42	23	insignificant	
VIII. Transfusion(s) Given to EF Infant	10	49	15	34	23	1.452	0.20

TABLE 11-A

PRESUMED SENSITIZING PREGNANCY: DURATION
OF THIRD STAGE (in minutes),
AND SPONTANEOUS VS. MANUAL DELIVERY OF PLACENTA

Delivery is spontaneous unless noted otherwise.

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
1.	2	2
2.	1	2
3.	12	5
4.	9	3
5.	2	2
6.	5	1
7.	4	3
8.	3	16
9.	1	2
10.	11	3
11.	1	3
12.	3	4
13.	2	14
14.	9	1
15.	1	5
16.	1	3
17.	6	1
18.	4	47, manual
19.	2	3, manual
20.	2	8, manual
21.	16	2
22.	13	10
23.	4	5
24.	2	3
25.	5	2

By inspection no significant difference exists between the EF control and control series for spontaneous vs. manual delivery of placenta.

TABLE 11-B

PRESUMED SENSITIZING PREGNANCY: DURATION
OF THIRD STAGE (in minutes)

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	<u>Number of Cases</u>	<u>Mean Value</u>	<u>Number of Cases</u>	<u>Mean Value</u>	<u>n</u>	<u>t</u>	<u>P₂</u>
I. All Cases	25	5	25	6	48	0.562	0.60
II. Maternal O	15	6	15	7	28	insignificant	
a. PSP O, EF O	10	6	10	5	18	0.737	0.50
b. PSP O, EF A	2	3	2	3	2	insignificant	
c. PSP A, EF A	2	3	2	25	2	1.020	0.45
d. PSP O or A, EF A	4	3	4	14	6	0.988	0.40
III. Maternal A	9	4	9	5	16	0.485	0.65
a. PSP A, EF A	6	3	6	6	10	1.454	0.20
b. PSP A, EF O	3	6	3	2	4	1.874	0.15
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	5	8	8	14	0.522	0.65
V. Somatic Index ≥ 13	12	4	12	7	22	0.629	0.55
VI. Cyclopropane Anesthesia	11	6	11	8	20	0.649	0.55

VII. Physical Examination Normal for EF Infant	11	7	14	3	23	1.949	0.07
VIII. Transfusion(s) Given to EF Infant	10	4	15	6	23	1.082	0.30

TABLE 12-A

PRESUMED SENSITIZING PREGNANCY:
OXYTOCICS AND THE THIRD STAGE

Expressed as time in minutes oxytocic given before or after delivery of placenta. "0" means given at time of delivery. "?" means given, time not known. A blank space indicates no oxytocic was used. Except as noted otherwise, i.e., intravenously (IV), oxytocics were administered intramuscularly.

<u>Case Number</u>	<u>PSP: Oxytocics Given Before Delivery of Placenta</u>		<u>PSP: Oxytocics Given After Delivery of Placenta</u>	
	<u>EF Series</u>	<u>Control Series</u>	<u>EF Series</u>	<u>Control Series</u>
1.	4	?	0	?
2.			1	1
3.			?	2
4.	7		0	1
5.	2,IV		?	0
6.			?	0
7.			0	1
8.	?			1
9.	1,IV	1	?	1
10.		3,IV	1	2
11.			?	0
12.	?	4	?	1
13.			0	0
14.		1	1	1
15.	Continuous,IV		?	1
16.			0	2
17.			?	?
18.		48,IV	1	1,IV
19.	?	?		?
20.		?	?	
21.			?	2
22.		7	0	0
23.			0	1
24.			?	0
25.			0	0
Total Number of Cases	8	9	23	24

By inspection no significant difference exists between the EF and control groups concerning the use of oxytocics after delivery of the placenta.

TABLE 12-B

PRESUMED SENSITIZING PREGNANCY: OXYTOCICS
USED PRECEDING PLACENTAL DELIVERY

Subgroup	EF Series		Control Series		Statistical Significance		
	Total Number of Cases	Number of Cases with Oxytocics Used Before Placental Delivery	Total Number of Cases	Number of Cases with Oxytocics Used Before Placental Delivery	n	t	P ₂
I. All Cases	25	8	25	9	48		insignificant
II. Maternal O	15	4	15	5	28		insignificant
a. PSP O, EF O	10	4	10	3	18		insignificant
b. PSP O, EF A	2	0	2	0	2		insignificant
c. PSP A, EF A	2	0	2	1	2		insignificant
d. PSP O or A, EF A	4	0	4	1	6		insignificant
III. Maternal A	9	3	9	3	16		insignificant
a. PSP A, EF A	6	3	6	2	10		insignificant
b. PSP A, EF O	3	0	3	1	4		insignificant
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	0	8	3	14	1.094	0.30
V. Somatic Index ≥ 13	12	2	12	5	22	1.342	0.20
VI. Cyclopropane Anesthesia	11	4	11	4	20		insignificant

VII. Physical Examination Normal for EF Infant	11	3	14	5	23		insignificant
VIII. Transfusion(s) Given to EF Infant	10	3	15	5	23		insignificant

TABLE 13-A

PRESUMED SENSITIZING PREGNANCY: RUPTURE
OF MEMBRANES - SPONTANEOUS VS. ARTIFICIAL

<u>Case Number</u>	<u>EF Series</u>		<u>Control Series</u>	
	Spontaneous	Artificial	Spontaneous	Artificial
1.	x			x
2.		x		x
3.	x		x	
4.		x	x	
5.		x		x
6.	x		x	
7.		x	x	
8.	x			x
9.	x			x
10.	x			x
11.		x	x	
12.		x	x	
13.	x		x	
14.		x		x
15.		x	x	
16.		x		x
17.	x		x	
18.		x		x
19.	*	*	x	
20.		x		x
21.	x		*	*
22.		x	x	
23.		x	x	
24.		x	x	
25.		x		x
Total Number of Cases	9	15	13	11

* Not known.

TABLE 13-B

PRESUMED SENSITIZING PREGNANCY: RUPTURE
OF MEMBRANES - SPONTANEOUS VS. ARTIFICIAL

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	Total Number of Cases	Number of Cases with Spontaneous Rupture of Membranes	Total Number of Cases	Number of Cases with Spontaneous Rupture of Membranes	n	t	P ₂
I. All Cases	24	9	24	13	46	1.151	0.30
II. Maternal O	14	4	14	8	26	1.537	0.15
a. PSP O, EF O	9	3	9	7	16	2.108	0.06
b. PSP O, EF A	2	0	2	0	2	insignificant	
c. PSP A, EF A	2	0	2	1	2	insignificant	
d. PSP O or A, EF A	4	0	4	1	6	insignificant	
III. Maternal A	9	4	9	5	16	insignificant	
a. PSP A, EF A	6	3	6	3	10	insignificant	
b. PSP A, EF O	3	1	3	2	4	insignificant	
IV. PSP or EF ABO Type Different from Maternal ABO Type	8	2	8	3	14	insignificant	
V. Somatic Index ≥ 13	12	5	12	6	22	insignificant	
VI. Cyclopropane Anesthesia	11	5	10	6	19	0.628	0.55

VII. Physical Examination Normal for EF Infant	11	5	14	9	23	0.480	0.65
VIII. Transfusion(s) Given to EF Infant	10	3	15	6	23	insignificant	

TABLE 14-A

PRESUMED SENSITIZING PREGNANCY: TIME
ELAPSED (in minutes) FROM RUPTURE
OF MEMBRANES UNTIL DELIVERY OF INFANT

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
1.	64	128
2.	23	248
3.	745	452
4.	26	509
5.	13	67
6.	121	201
7.	81	12
8.	406	6
9.	208	7
10.	46	3
11.	232	323
12.	49	572
13.	47	12
14.	216	1
15.	435	25
16.	*	102
17.	255	1784
18.	992	308
19.	23	1282
20.	32	6
21.	407	*
22.	221	40
23.	223	65
24.	20	27
25.	295	28

* Not known

TABLE 14-B

PRESUMED SENSITIZING PREGNANCY: TIME
ELAPSED (in minutes) FROM RUPTURE
OF MEMBRANES UNTIL DELIVERY OF INFANT

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	<u>Number of Cases</u>	<u>Mean Time Elapsed</u>	<u>Number of Cases</u>	<u>Mean Time Elapsed</u>	<u>n</u>	<u>t</u>	<u>P₂</u>
I. All Cases	24	216	24	259	46	0.419	0.70
II. Maternal O	14	229	14	283	26	insignificant	
a. PSP O, EF O	10	164	9	355	17	1.350	0.20
b. PSP O, EF A	1	295	2	65	1	3.594	0.20
c. PSP A, EF A	2	612	2	316	2	0.769	0.55
d. PSP O or A, EF A	3	506	4	190	5	1.425	0.25
III. Maternal A	9	197	9	249	16	0.278	0.80
a. PSP A, EF A	6	214	6	72	10	1.825	0.01
b. PSP A, EF O	3	164	3	604	4	0.741	0.50
IV. PSP or EF ABO Type Different from Maternal ABO Type	7	294	8	322	13	0.110	0.95
V. Somatic Index ≥ 13	11	269	12	265	21	insignificant	
VI. Cyclopropane Anesthesia	11	244	10	324	19	0.434	0.70

VII. Physical Examination Normal EF Infant	11	198	13	231	22	insignificant	
VIII. Transfusion(s) Given to EF Infant	9	172	15	242	23	0.704	0.50

TABLE 15-A

PRESUMED SENSITIZING PREGNANCY: NUMBER
OF RECTAL EXAMINATIONS PERFORMED
DURING THE FIRST TWO STAGES

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
1.	3	6
2.	1	5
3.	4	5
4.	1	4
5.	3	3
6.	5	4
7.	0	2
8.	4	6
9.	3	4
10.	5	3
11.	7	2
12.	1	2
13.	2	4
14.	2	2
15.	6	4
16.	5	4
17.	11	3
18.	4	3
19.	6	4
20.	0	3
21.	3	3
22.	5	1
23.	5	2
24.	3	3
25.	4	1

TABLE 15-B

PRESUMED SENSITIZING PREGNANCY: NUMBER
OF RECTAL EXAMINATIONS PERFORMED
DURING THE FIRST TWO STAGES

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	<u>Number of Cases</u>	<u>Mean Number of Rectal Examinations</u>	<u>Number of Cases</u>	<u>Mean Number of Rectal Examinations</u>	<u>n</u>	<u>t</u>	<u>P<</u>
I. All Cases	25	3.7	25	3.3	48	0.721	0.50
II. Maternal O	15	3.4	15	3.1	28	insignificant	
a. PSP O, EF O	10	2.6	10	3.3	18	0.270	0.80
b. PSP O, EF A	2	4.5	2	2.5	2	1.265	0.35
c. PSP A, EF A	2	5.5	2	2.5	2	1.898	0.20
d. PSP O or A, EF A	4	5.0	4	2.5	6	8.257	0.001
III. Maternal A	9	4.3	9	3.7	16	insignificant	
a. PSP A, EF A	6	3.8	6	4.2	10	insignificant	
b. PSP A, EF O	3	5.3	3	2.7	4	0.930	0.45
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	5.1	8	2.6	14	2.400	0.04
V. Somatic Index ≥ 13	12	3.8	12	3.4	22	insignificant	
VI. Cyclopropane Anesthesia	11	4.3	11	3.2	20	1.181	0.30

VII. Physical Examination Normal for EF Infant	11	3.8	14	3.6	23	insignificant	
VIII. Transfusion(s) Given to EF Infant	10	3.7	15	3.7	23	insignificant	

TABLE 16-A

PRESUMED SENSITIZING PREGNANCY: NUMBER
OF VAGINAL EXAMINATIONS PERFORMED
DURING THE FIRST TWO STAGES

Only cases with vaginal examinations are listed.

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
2.	1	1
3.	1	
4.	1	
7.	1	
10.	1	1
14.	2	
15.	1	
16.		1
18.		2
22.	1	
23.	1	
25.	1	

TABLE 16-B

PRESUMED SENSITIZING PREGNANCY: NUMBER
OF VAGINAL EXAMINATIONS PERFORMED
DURING THE FIRST TWO STAGES

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	Number of Cases	Mean Number of Vaginal Examinations	Number of Cases	Mean Number of Vaginal Examinations	n	t	P ₂
I. All Cases	25	0.4	25	0.2	48	1.562	0.14
II. Maternal O	15	0.5	15	0.3	28	0.650	0.55
a. PSP O, EF O	10	0.5	10	0.1	18	2.058	0.06
b. PSP O, EF A	2	4.5	2	2.5	2	1.265	0.35
c. PSP A, EF A	2	5.5	2	2.5	2	1.898	0.20
d. PSP O or A, EF A	4	0.3	4	0.8	6	insignificant	
III. Maternal A	9	0.4	9	0	16	1.835	0.09
a. PSP A, EF A	6	0.3	6	0	10	insignificant	
b. PSP A, EF O	3	0.7	3	0	4	3.162	0.04
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	0.5	8	0.5	14	insignificant	
V. Somatic Index ≥ 13	12	0.4	12	0.3	22	insignificant	
VI. Cyclopropane Anesthesia	11	0.3	11	0.2	20	0.392	0.70

VII. Physical Examination Normal for EF Infant	11	0.5	14	0.4	23	insignificant	
VIII. Transfusion(s) Given To EF Infant	10	0.5	15	0.4	23	insignificant	

TABLE 17-A

PRESUMED SENSITIZING PREGNANCY: NUMBER
OF RECTAL PLUS VAGINAL EXAMINATIONS
PERFORMED DURING THE FIRST TWO STAGES

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
1.	3	6
2.	2	6
3.	5	5
4.	2	4
5.	3	3
6.	5	4
7.	1	2
8.	4	6
9.	3	4
10.	6	4
11.	7	2
12.	1	2
13.	2	4
14.	4	2
15.	7	4
16.	5	5
17.	11	3
18.	4	5
19.	6	4
20.	0	3
21.	3	3
22.	6	1
23.	6	2
24.	3	3
25.	5	1

TABLE 17-B

PRESUMED SENSITIZING PREGNANCY: NUMBER
OF RECTAL PLUS VAGINAL EXAMINATIONS
PERFORMED DURING THE FIRST TWO STAGES

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	Number of Cases	Mean Number of Examinations	Number of Cases	Mean Number of Examinations	n	t	P ₂
I. All Cases	25	4.2	25	3.5	48	1.139	0.30
II. Maternal O	15	3.9	15	3.4	28	insignificant	
a. PSP O, EF O	10	3.1	10	3.4	18	0.090	0.95
b. PSP O, EF A	2	5.0	2	3.0	2	1.000	0.45
c. PSP A, EF A	2	5.5	2	3.5	2	1.333	0.35
d. PSP O or A, EF A	4	5.3	4	3.3	6	1.656	0.20
III. Maternal A	9	4.8	9	3.7	16	0.975	0.35
a. PSP A, EF A	6	4.2	6	4.2	10	insignificant	
b. PSP A, EF O	3	6.0	3	2.7	4	1.313	0.30
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	5.6	8	3.1	14	2.441	0.04
V. Somatic Index ≥ 13	12	4.2	12	3.7	22	0.562	0.60
VI. Cyclopropane Anesthesia	11	4.5	11	3.4	20	1.270	0.25

VII. Physical Examination Normal for EF Infant	11	4.4	14	4.0	23	insignificant	
VIII. Transfusion(s) Given To EF Infant	10	4.2	15	4.1	23	insignificant	

TABLE 18-A

PRESUMED SENSITIZING PREGNANCY: NITROUS OXIDE
ANESTHESIA-DURATION (in minutes)

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
1.	15	65
2.	15	25
3.	10	15*
4.	5	
5.	2	10
6.		20
7.	30	15
8.		5
9.	10	10
10.	55	
11.	5	25
12.	20	20
13.	14	20
14.	30	15
15.	10	10
16.		45
17.		15
18.	15	15
19.	25	25
20.	15	10
21.	20	
22.	10	15
23.	25	12
24.	15	
25.	25	25

* Blank space indicates nitrous oxide anesthesia was not used, or was but duration of use is not known.

TABLE 18-B

PRESUMED SENSITIZING PREGNANCY: NITROUS OXIDE
ANESTHESIA - DURATION (in minutes)

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	<u>Number of Cases</u>	<u>Duration of Nitrous Oxide Anesthesia</u>	<u>Number of Cases</u>	<u>Duration of Nitrous Oxide Anesthesia</u>	<u>n</u>	<u>t</u>	<u>P₂</u>
I. All Cases	21	18	21	20	40	0.666	0.55
II. Maternal O	14	18	12	21	24	insignificant	
a. PSP O, EF O	10	15	8	18	16	0.909	0.40
b. PSP O, EF A	1	25	2	35	1	0.577	0.70
c. PSP A, EF A	2	10	2	20	2	1.414	0.30
d. PSP O or A, EF A	3	15	4	28	5	1.409	0.25
III. Maternal A	6	18	8	20	12	insignificant	
a. PSP A, EF A	4	16	6	20	8	0.349	0.75
b. PSP A, EF O	2	23	2	15	2	1.000	0.45
IV. PSP or EF ABO Type Different From Maternal ABO Type	6	24	6	23	10	insignificant	
V. Somatic Index ≥ 13	9	18	10	22	17	0.510	0.65
VI. Cyclopropane Anesthesia	10	12	15	18	23	1.521	0.15
<hr style="border-top: 1px dashed black;"/>							
VII. Physical Examination Normal For EF Infant	10	20	11	15	19	insignificant	
VIII. Transfusion(s) Given to EF Infant	8	14	13	20	21	1.287	0.25

TABLE 19-A

PRESUMED SENSITIZING PREGNANCY: CYCLOPROPANE
ANESTHESIA-DURATION (in minutes)

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
1.	20	*
2.		15
3.		25
4.	15	
5.	3	20
6.		
7.		
8.		15
9.	10	10
10.		
11.	10	10
12.		20
13.	6	
14.		15
15.		10
16.		15
17.		
18.	22	20
19.		10
20.		
21.	5	
22.	10	
23.	10	13
24.		15
25.		20

* Blank space indicates cyclopropane anesthesia was not used, or was but duration of use is not known.

TABLE 19-B

PRESUMED SENSITIZING PREGNANCY: CYCLOPROPANE
ANESTHESIA - DURATION (in minutes)

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	Number of Cases	Cyclopropane Anesthesia Duration	Number of Cases	Cyclopropane Anesthesia Duration	n	t	P ₂
I. All Cases	10	11	16	16	24	2.130	0.05
II. Maternal O	7	10	9	18	14	3.007	0.01
a. PSP O, EF O	5	8	5	20	8	4.598	0.005
b. PSP O, EF A	0	-	2	18	0	-	-
c. PSP A, EF A	2	16	2	15	2	insignificant	
d. PSP O, or A, EF A	2	16	4	16	4	insignificant	
III. Maternal A	2	15	6	13	6	0.671	0.55
a. PSP A, EF A	2	15	4	12	4	0.840	0.50
b. PSP A, EF O	0	-	2	15	0	-	-
IV. PSP or EF ABO Type Different From Maternal ABO Type	2	16	6	16	6	insignificant	
V. Somatic Index ≥ 13	4	16	8	15	10	insignificant	
(VI. Cyclopropane Anesthesia)							

VII. Physical Examination Normal for EF Infant	5	11	5	12	8	insignificant	
VIII. Transfusion(s) Given To EF Infant	4	9	6	13	8	insignificant	

TABLE 20-A

PRESUMED SENSITIZING PREGNANCY:
ANESTHESIA-TOTAL DURATION (in minutes)

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
1.	35	65
2.	15	40
3.	10	40*
4.	20	
5.	5	30
6.		20
7.	30	15
8.		20
9.	20	20
10.	55	35
11.	15	35
12.	20	40
13.	20	20
14.	30	30
15.	10	20
16.		60
17.	75	15
18.	37	50
19.	25	25
20.	15	20
21.	25	75
22.	20	15
23.	35	25
24.	15	15
25.	25	45

* Blank space indicates general anesthesia was not used, or was but duration of use is not known.

TABLE 20-B

PRESUMED SENSITIZING PREGNANCY: ANESTHESIA -
TOTAL DURATION (in minutes)

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	<u>Number of Cases</u>	<u>Duration of Anesthesia</u>	<u>Number of Cases</u>	<u>Duration of Anesthesia</u>	<u>n</u>	<u>t</u>	<u>P₂</u>
I. All Cases	22	26	24	33	44	1.460	0.20
II. Maternal O	14	23	14	39	26	3.466	0.005
a. PSP O, EF O	10	19	9	36	17	3.328	0.01
b. PSP O, EF A	1	25	2	53	1	2.086	0.30
c. PSP A, EF A	2	26	2	43	2	1.239	0.35
d. PSP O or A, EF A	3	26	4	48	5	2.683	0.05
III. Maternal A	7	31	9	26	14	0.550	0.60
a. PSP A, EF A	4	24	6	28	8	0.433	0.70
b. PSP A, EF O	3	40	3	20	4	1.069	0.35
IV. PSP or EF ABO Type Different From Maternal ABO Type	7	36	8	36	13	insignificant	
V. Somatic Index ≥ 13	10	30	11	32	19	insignificant	
(VI. Cyclopropane Anesthesia)							

VII. Physical Examination Normal For EF Infant	11	30	11	21	20	1.435	0.20
VIII. Transfusion(s) Given to EF Infant	8	19	14	29	20	1.532	0.15

TABLE 21-A

PRESUMED SENSITIZING PREGNANCY: DELIVERY
SPONTANEOUS VS. OPERATIVE. "OPERATIVE INDEX".

"Operative index" arbitrarily defined as follows: Elective low forceps 1 point; Breech, assisted, 1 point; low forceps, 2 points; low mid forceps, 3 points; low mid forceps with rotation, 4 points; spontaneous delivery, no points.

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
1.	1	4
2.	1	2
3.	0	1
4.	0	0
5.	0	0
6.	0	0
7.	0	1
8.	0	1
9.	1	2
10.	1	1
11.	1	0
12.	4	4
13.	1	0
14.	3	2
15.	3	1
16.	1	4
17.	1	0
18.	2	1
19.	0	4
20.	0	0
21.	2	2
22.	3	0
23.	1	0
24.	0	1
25.	1	1

TABLE 21-B

PRESUMED SENSITIZING PREGNANCY:
DELIVERY SPONTANEOUS VS. OPERATIVE

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	<u>Number of Cases</u>	<u>Mean "Operative Index"</u>	<u>Number of Cases</u>	<u>Mean "Operative Index"</u>	<u>n</u>	<u>t</u>	<u>P <</u>
I. All Cases	25	1.1	25	1.3	48	0.445	0.70
II. Maternal O	15	1.1	15	1.4	28	0.539	0.60
a. PSP O, EF O	10	1.1	10	1.4	18	0.443	0.70
b. PSP O, EF A	2	1.0	2	2.5	2	1.000	0.20
c. PSP A, EF A	2	1.5	4	0.5	2	2.000	0.20
d. PSP O, or A, EF A	4	1.3	4	1.5	6	insignificant	
III. Maternal A	9	1.0	9	1.0	16	insignificant	
a. PSP A, EF A	6	0.8	6	1.0	10	insignificant	
b. PSP A, EF O	3	1.3	3	1.0	4	insignificant	
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	1.3	8	1.3	14	insignificant	
V. Somatic Index ≥ 13	12	0.8	12	1.3	22	1.445	0.20
VI. Cyclopropane Anesthesia	11	1.2	11	0.8	20	0.759	0.50

VII. Physical Examination Normal For EF Infant	11	0.5	14 10*	1.4 1.8*	23 19*	1.870 2.565*	0.08 0.02*
VIII. Transfusion(s) Given To EF Infant	10	1.8	15	0.6	23	1.359	0.20

* Control taken as the 10 cases in which the EF infant received transfusion(s).

TABLE 22

PRESUMED SENSITIZING PREGNANCY:
BIRTH CANAL LACERATIONS AT DELIVERY

Only cases with lacerations are listed.

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
9.		3° extension of episiotomy.
12.		2 cm. left sulcus laceration.
16.	shallow right sulcus laceration.	left sulcus laceration.
17.	2 inch cervical laceration.	
23.		deep vaginal tear, 2° laceration.
25.	episiotomy extension to right fornix.	4° laceration.

By inspection there is no difference between the EF and control series.

TABLE 23-A

PRESUMED SENSITIZING PREGNANCY: ESTIMATED
BLOOD LOSS (in cubic centimeters) AT DELIVERY

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
1.	400	100
2.	300	300
3.	200	300
4.	200	200
5.	200	200
6.	300	275
7.	300	100
8.	150	200
9.	200	200
10.	100	150
11.	250	300
12.	200	200
13.	150	200
14.	300	200
15.	250	200
16.	150	400
17.	375	75
18.	350	400
19.	50	250
20.	175	100
21.	100	250
22.	100	200
23.	250	300
24.	200	150
25.	400	300

TABLE 23-B

PRESUMED SENSITIZING PREGNANCY: ESTIMATED BLOOD
LOSS (in cubic centimeters) AT DELIVERY

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	Number of Cases	Estimated Blood Loss	Number of Cases	Estimated Blood Loss	n	t	P <
I. All Cases	25	226	25	222	48	0.154	0.90
II. Maternal O	15	203	15	250	28	1.374	0.20
a. PSP O, EF O	10	180	10	220	18	1.251	0.25
b. PSP O, EF A	2	225	2	350	2	0.928	0.50
c. PSP A, EF A	2	300	2	350	2	0.707	0.60
d. PSP O or A, EF A	4	288	4	350	6	1.000	0.40
III. Maternal A	9	267	9	178	16	2.294	0.04
a. PSP A, EF A	6	254	6	196	10	1.159	0.30
b. PSP A, EF O	3	292	3	142	4	2.405	0.08
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	266	8	247	14	insignificant	
V. Somatic Index ≥ 13	12	267	12	217	22	1.209	0.25
VI. Cyclopropane Anesthesia	11	234	11	220	20	insignificant	

VII. Physical Examina- tion Normal For EF Infant	11	248	14	209	23	insignificant	
VIII. Transfusion(s) Given to EF Infant	10	220	15	230	23	insignificant	

TABLE 24-A

PRESUMED SENSITIZING PREGNANCY:
SEX OF CHILD

<u>Case Number</u>	<u>EF Series</u>		<u>Control Series</u>	
	Male	Female	Male	Female
1.	x		x	
2.	x			x
3.		x		x
4.		x	x	
5.		x		x
6.	x			x
7.	x			x
8.	x		x	
9.	x			x
10.		x	x	
11.		x		x
12.	x		x	
13.		x	x	
14.	x			x
15.	x		x	
16.	x		x	
17.	x		x	
18.	x			x
19.	x			x
20.	x		x	
21.	x		x	
22.		x		x
23.		x	x	
24.	x		x	
25.	x			x

TABLE 24-B

PRESUMED SENSITIZING PREGNANCY:
SEX OF CHILD

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	<u>Number of Cases</u>	<u>Percent with Male Children</u>	<u>Number of Cases</u>	<u>Percent with Male Children</u>	<u>n</u>	<u>t</u>	<u>P₂</u>
I. All Cases	25	68%	25	52%	48	1.147	0.30
II. Maternal O	15	47%	15	40%	28	insignificant	
a. PSP O, EF O	10	50%	10	40%	18	insignificant	
b. PSP O, EF A	2	100%	2	50%	2	insignificant	
c. PSP A, EF A	2	0%	2	0%	2	insignificant	
d. PSP O or A, EF A	4	50%	4	25%	6	insignificant	
III. Maternal A	9	89%	9	78%*	16	insignificant	
a. PSP A, EF A	6	83%	6	83%	10	insignificant	
b. PSP A, EF O	3	100%	3	67%	4	insignificant	
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	75%	8	50%	14	insignificant	
V. Somatic Index ≥ 13	12	83%	12	50%	22	2.000	0.06
VI. Cyclopropane Anesthesia	11	45%	11	55%	20	insignificant	

VII. Physical Examination Normal For EF Infant	11	54%	14	79%	23	insignificant	
VIII. Transfusion(s) Given to EF Infant	15	67%	10	70%	23	insignificant	

* Were the control value the expected 50%, P would be < 0.09 , i.e., not significant.

TABLE 25-A

PRESUMED SENSITIZING PREGNANCY:
BIRTH WEIGHT OF CHILD (in grams)

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
1.	2990	3748
2.	3590	3995
3.	2885	3985
4.	3755	4350
5.	2960	3355
6.	3725	3150
7.	4000	2410
8.	3695	3820
9.	2240	2480
10.	3390	3405
11.	3030	3510
12.	3405	3480
13.	3180	2830
14.	4015	3280
15.	4090	3355
16.	3810	3275
17.	3090	2795
18.	3345	3165
19.	3275	3415
20.	3750	2410
21.	2705	2730
22.	3505	3420
23.	2745	3055
24.	3985	3220
25.	4080	1945

TABLE 25-B

PRESUMED SENSITIZING PREGNANCY:
BIRTH WEIGHT OF CHILD (in grams)

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	Number of Cases	Mean Weight of Child	Number of Cases	Mean Weight of Child	n	t	P ₂
I. All Cases	25	3410	25	3223	48	0.040	1.00
II. Maternal O	15	3394	15	3285	28	insignificant	
a. PSP O, EF O	10	3326	10	3397	18	insignificant	
b. PSP O, EF A	2	3945	2	2610	2	1.699	0.25
c. PSP A, EF A	2	3188	2	3338	2	0.091	0.95
d. PSP O or A, EF A	4	3566	4	2974	6	1.405	0.25
III. Maternal A	9	3565	9	3204	16	1.642	0.15
a. PSP A, EF A	6	3499	6	3256	10	0.814	0.45
b. PSP A, EF O	3	3697	3	3098	4	1.761	0.20
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	3593	8	3074	14	2.207	0.05
V. Somatic Index ≥ 13	12	3382	12	3080	22	1.352	0.20
VI. Cyclopropane Anesthesia	11	3050	11	3222	20	0.847	0.45

VII. Physical Examination Normal For EF Infant	11	3326	14	3475	23	insignificant	
VIII. Transfusion(s) Given to EF Infant	10	3459	15	3377	23	insignificant	

TABLE 26-A

ERYTHROBLASTOSIS FETALIS:
SEX OF CHILD

Control is sex of corresponding non-erythroblastotic child.

<u>Case Number</u>	<u>EF Series</u>		<u>Control Series</u>	
	Male	Female	Male	Female
1.		x	x	
2.	x			x
3.		x		x
4.	x			x
5.		x	x	
6.	x			x
7.	x			x
8.		x	x	
9.	x		x	
10.		x	x	
11.		x		x
12.	x			x
13.		x	x	
14.		x		x
15.	x			x
16.		x	x	
17.	x		x	
18.		x		x
19.	x		x	
20.	x			x
21.	x			x
22.	x		x	
23.		x		x
24.		x		x
25.		x	x	

TABLE 26-B

ERYTHROBLASTOSIS FETALIS:
SEX OF CHILD

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	Number of Cases	Percent with Male Children	Number of Cases	Percent with Male Children	n	t	P<
I. All Cases	25	48%	25	44%	48		insignificant
II. Maternal O	15	47%	15	47%	28		insignificant
a. PSP O, EF O	10	70%	10	40%	18	1.342	0.20
b. PSP O, EF A	2	0%	2	100%	1*		0.15*
c. PSP A, EF A	2	0%	2	0%	2		insignificant
d. PSP O or A, EF A	4	0%	4	50%	6	1.732	0.15
III. Maternal A	9	44%	9	33%	16		insignificant
a. PSP A, EF A	6	50%	6	33%	10		insignificant
b. PSP A, EF O	3	33%	3	33%	4		insignificant
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	13%	8	50%	14	1.655	0.15
V. Somatic Index ≥ 13	12	50%	12	25%	22	1.254	0.25
VI. Cyclopropane Anesthesia	11	45%	11	55%	20		insignificant

VII. Physical Examination Normal For EF Infant	11	36%	14	57%	23	1.307	0.25
VIII. Transfusion(s) Given To EF Infant	10	60%	15	40%	23	0.974	0.35

* t-test not applicable ($s^2 = 0$). By chi square testing, $n=1$, chi square= 2, $P < 0.15$.

TABLE 27-A

ERYTHROBLASTOSIS FETALIS:
BIRTH WEIGHT OF CHILD
(in grams)

Control is weight of corresponding non-erythroblastotic child.

<u>Case Number</u>	<u>EF Series</u>	<u>Control Series</u>
1.	3285	2900
2.	4080	3475
3.	2665	4120
4.	3775	4415
5.	3020	3945
6.	3950	3600
7.	3350	2835
8.	2065	3425
9.	1800	2335
10.	3155	3155
11.	2300	3265
12.	3140	3400
13.	3230	4085
14.	2940	3405
15.	3125	3575
16.	3375	3180
17.	2300	3360
18.	3860	2890
19.	3810	3355
20.	3210	2680
21.	2520	3360
22.	3000	3575
23.	3015	3075
24.	4180	3615
25.	4360	2865

TABLE 27-B

ERYTHROBLASTOSIS FETALIS:
BIRTH WEIGHT OF CHILD (in grams)

<u>Subgroup</u>	<u>EF Series</u>		<u>Control Series</u>		<u>Statistical Significance</u>		
	Number of Cases	Mean Weight of Child	Number of Cases	Mean Weight of Child	n	t	P ₂
I. All Cases	25	3180	25	3353	48	1.053	0.30
II. Maternal O	15	3309	15	3401	28	0.776	0.50
a. PSP O, EF O	10	3259	10	3657	18	1.817	0.09
b. PSP O, EF A	2	3868	2	3023	2	1.175	0.40
c. PSP A, EF A	2	3080	2	3078	2	insignificant	
d. PSP O or A, EF A	4	3474	4	3050	6	0.937	0.40
III. Maternal A	9	3119	9	3293	16	0.690	0.50
a. PSP A, EF A	6	3108	6	3209	10	insignificant	
b. PSP A, EF O	3	3140	3	3460	4	0.574	0.60
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	3309	8	3161	14	0.515	0.65
V. Somatic Index ≥ 13	12	3161	12	3166	22	insignificant	
VI. Cyclopropane Anesthesia	11	2919	11	3382	20	1.758	0.10
<hr style="border-top: 1px dashed black;"/>							
VII. Physical Examination Normal For EF Infant	11	3239	14	3135	23	insignificant	
VIII. Transfusion(s) Given to EF Infant	10	3094	15	3238	23	0.522	0.65

TABLE 28-A

ERYTHROBLASTOSIS FETALIS: CASES WITH
NORMAL NEONATAL PHYSICAL EXAMINATIONS

"Normal" here defined as "no signs of erythroblastosis fetalis were present."

Only cases with normal physicals are listed.

<u>Case Number</u>	<u>Normal Physical Examination</u>
1.	x
3.	x
4.	x
5.	x
7.	x
10.	x
17.	x
21.	x
23.	x
24.	x
25.	x

Note that in Tables 28-B and 29-B each control series consists of the remaining cases; for instance, the 15 "Maternal 0" cases are controlled by the 10 cases for which the maternal ABO type is not 0.

TABLE 28-B

ERYTHROBLASTOSIS FETALIS: CASES WITH
NORMAL NEONATAL PHYSICAL EXAMINATIONS

<u>Subgroup</u>	<u>Cases Within The Subgroup</u>		<u>Control: Remaining Cases</u>		<u>Statistical Significance</u>		
	Number of Cases	Percent with Normal Physical Examinations	Number of Cases	Percent with Normal Physical Examinations	n	t	P ₂
I. All Cases	25	44%	-	-	-	-	-
II. Maternal O	15	47%	10	40%	23	insignificant	
a. PSP O, EF O	10	50%	15	40%	23	0.476	0.65
b. PSP O, EF A	2	50%	23	43%	23	0.017	1.00
c. PSP A, EF A	2	0%	23	48%	23	1.299	0.25
d. PSP O or A, EF A	4	25%	21	48%	23	0.812	0.45
III. Maternal A	9	44%	16	44%	23	insignificant	
a. PSP A, EF A	6	33%	19	47%	23	insignificant	
b. PSP A, EF O	3	67%	22	41%	23	0.848	0.45
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	50%	17	41%	23	insignificant	
V. Somatic Index ≥ 13	12	50%	13	38%	23	0.548	0.60
VI. Cyclopropane Anesthesia	11	55%	14	36%	23	0.895	0.40

TABLE 29-A

ERYTHROBLASTOSIS FETALIS:
TRANSFUSION GIVEN

Only cases in which transfusion was administered are listed.

<u>Case Number</u>	<u>Number of Transfusions Given</u>
2.	1
6.	1
9.	2
11.	1
12.	2
13.	2
14.	1
15.	1
16.	2
22.	2

TABLE 29-B.

ERYTHROBLASTOSIS FETALIS:
TRANSFUSION GIVEN

<u>Subgroup</u>	<u>Cases Within The Subgroup</u>		<u>Control: Remaining Cases</u>		<u>Statistical Significance</u>		
	<u>Number of Cases</u>	<u>Percent of Cases Receiving Transfusions</u>	<u>Number of Cases</u>	<u>Percent of Cases Receiving Transfusions</u>	<u>n</u>	<u>t</u>	<u>P₂</u>
I. All Cases	25	40%	-	-	-	-	-
II. Maternal O	15	53%	10	20%	23	1.696	0.15
a. PSP O, EF O	10	40%	15	40%	23	insignificant	
b. PSP O, EF A	2	50%	23	39%	23	insignificant	
c. PSP A, EF A	2	50%	23	39%	23	insignificant	
d. PSP O or A, EF A	4	50%	21	38%	23	0.434	0.70
III. Maternal A	9	33%	16	44%	23	insignificant	
a. PSP A, EF A	6	33%	19	42%	23	insignificant	
b. PSP A, EF O	3	33%	22	41%	23	insignificant	
IV. PSP or EF ABO Type Different From Maternal ABO Type	8	38%	17	41%	23	insignificant	
V. Somatic Index ≥ 13	12	25%	13	54%	23	1.460	0.20
VI. Cyclopropane Anesthesia	11	36%	14	43%	23	insignificant	

IV. DISCUSSION

The most striking finding of the preceding data is the preponderance of negative correlations. These are summarized in Table 30.

TABLE 30

NEGATIVE CORRELATIONS, BETWEEN MATERNAL BLOOD
TYPES, SOMATIC INDEX, AND CYCLOPROPANE
ANESTHESIA, OCCURRED WITH THE FOLLOWING:

Maternal:	Age, Abortion, cervical dilatation and curettage history.
PSP:	Duration of pregnancy, Duration of labor, including each of the three stages, Spontaneous vs. manual delivery of the placenta, Use of oxytocics before and after placental delivery, Spontaneous vs. artificial rupture of membranes, Duration of nitrous oxide anesthesia, Birth canal lacerations at delivery, Estimated blood loss at delivery, Sex of child.
EF:	Sex and weight of child, Normal physical examination, Transfusions.

Noteworthy among these findings is the lack of confirmation of the hypothesized association between the development of erythroblastosis fetalis and manual removal of the placenta.¹⁵ In this series of 25 cases with controls, there were three manual removals of the placenta, all three occurring in the control population (see Table 11-A, page 28.). For the hypothesis to be true and consistent with these data, one would have to further speculate that manual removal of the placenta in the presumed sensitizing pregnancy be associated with stillborn erythroblastotic

infants, that subgroup having been eliminated from this series.

Another negative finding is that among the subgroup in which the maternal type is different from either that of the PSP or EF child the prognosis is not significantly different from the ABO maternal - PSP-EF compatible group (see Tables 28-B and 29-B, pages 62 and 64.) This agrees with the findings of Kelly and Jacobs¹⁶, but differs from the findings of Reepmaker et al⁸ and Donohue¹⁷.

Positive data regarding the presence or absence of disease, suggesting an association of possible pathogenetic importance, involve data in four areas: 1. Maternal height, weight, and somatic index from the presumed sensitizing pregnancy and delivery; 2. Rectal and vaginal examinations; 3. Anesthesia, and; 4. Birth weight.

I. Positive data concerning maternal height, weight and somatic index:

a. PSP or EF, ABO type different from maternal ABO type (8 cases) - the mother is taller in the EF subgroup than in the control (n=14, $P < 0.001$).

b. Maternal type A (9 cases) - the somatic index is greater in the EF subgroup than in the control (n=16, $P < 0.01$).

c. Maternal type O, PSP O or A, EF A (4 cases) - the mother is taller (n=6, $P < 0.015$) and heavier (n=6, $P < 0.005$) in the EF subgroup than in the control.

d. Maternal type A, PSP A, EF O (3 cases) - the mother is taller (n=4, $P < 0.03$) and the somatic index greater (n=4, $P < 0.01$) in the EF subgroup than in the control.

e. Maternal type O, PSP O, EF A (2 cases) - the mother is taller in the EF subgroup than in the control (n=2, $P < 0.04$).

In evaluating these positive findings, it should be remembered in caution that not only are the subgroups small (from 2 to 9 cases) but

also that in such a large series of correlations a certain number of positive results are to be expected by chance. Some 400 correlations have been made, so that at $P < 0.05$, 5 percent of 400 yields 20 positive correlations, or at $P < 0.01$, 4 positive correlations, which might be expected by chance alone. (In this study 9 positive correlations occurred at $P < 0.01$ or less).

I know of no correlations in the literature between the occurrence of erythroblastosis fetalis and maternal height, weight, and body type data. While the data here presented are significant statistically, the smallness of the series (and perhaps random chance) leads this observer to infer that the results may be suggestive medically, but that additional similarly closely controlled series would be necessary before further conclusions should be attempted.

2. Positive data concerning rectal and vaginal examinations during the first two stages:

a. Maternal type O, PSP O or A, EF A (4 cases) - the number of rectal examinations is higher in the EF subgroup than in the control ($n=6$, $P < 0.001$).

The importance of "splitting", i.e., analyzing a group in terms of its subgroups is here well illustrated, for these highly statistically significant subgroup data lead to the following results for larger groups of which they are a part: PSP or EF, ABO type different from maternal ABO type (8 cases) - the number of rectal examinations is higher in the EF group than in the control ($n=14$, $P < 0.04$); the number of rectal plus vaginal examinations is higher in the EF group than in the control ($n=14$, $P < 0.04$). These latter two results at $P < 0.04$

are significant statistically only by virtue of the contribution of the 4 cases at $P < 0.001$, a value which is diluted forty-fold in this instance by the 4 other cases in the 8 of the larger group.* This is a good example of medically insignificant, statistically significant data. It is necessary to "split" one's data before one can justifiably "lump" them.

b. Maternal type A, PSP A, EF 0 (3 cases) - the number of vaginal examinations is greater in the EF subgroup than in the control ($n=4$, $P < 0.04$).

As with the data of maternal height and weight, I know of no reference in the literature to the potential contribution of rectal and vaginal examinations during the first two stages to later maternal isoimmunization. While the data presented imply a correlation within certain subgroups of blood type combinations, the smallness of the series limits one to inferring that the data are suggestive, but by no means conclusive. The obstetric implications of this possible correlation are obvious.

3. Positive data concerning anesthesia during delivery:

a. Maternal type 0 - general anesthesia (14 cases): anesthesia was of shorter duration in the EF subgroup than in the control ($n=26$, $P < 0.005$). Cyclopropane anesthesia (7 cases): anesthesia was of shorter duration in the EF subgroup than in the control ($n=14$, $P < 0.01$).

* The reader is referred to the data on pages 36 through 41 to check the validity of this observation.

b. Cyclopropane anesthesia, all cases (10 cases) - anesthesia was of shorter duration in the EF group than in the control (n=24, $P < 0.05$).

c. Maternal type 0, PSP 0, and EF 0 - general anesthesia (10 cases): anesthesia was of shorter duration in the EF subgroup than in the control (n=17, $P < 0.01$). Cyclopropane anesthesia (5 cases): anesthesia was of shorter duration in the EF subgroup than in the control (n=8, $P < 0.005$).

d. Maternal type 0, PSP 0 or A, EF A - general anesthesia (3 cases): anesthesia was of shorter duration in the EF subgroup than in the control (n=5, $P < 0.05$).

The author undertook this aspect of the study expecting to find, if anything, a correlation between later isoimmunization and prolonged duration of anesthesia in the presumed sensitizing pregnancy delivery. Instead, the data indicate a "protective" effect of prolonged anesthesia, especially in association with maternal type 0. Inquiry into possible explanation is being made at the time of this writing.¹⁸

4. Positive data concerning birth weight of the presumed sensitizing pregnancy child:

PSP or EF, ABO type different from maternal ABO type (8 cases) - birth weight of the presumed sensitizing pregnancy child is greater in the EF subgroup than in the control (n=14, $P < 0.05$).

Finally, in the group of data relating prognosis to the properties and events analyzed, results were negative with one exception. Among the children with erythroblastosis fetalis the severity of the disease correlates with the "Operative Index", that is, with the extent of obstetric operative intervention at delivery of the presumed sensitizing pregnancy, (see Table 21-B, page 49; n=19, $P < 0.02$). To follow this finding to its logical extension, one would be advised to include Cesarean section among the obstetric operative interventions and stillborn fetuses within the range of clinical erythroblastosis fetalis, each of these groups having

been excluded from the present series. If the data of this small series are confirmed, one might expect to find the spectrum of operative intervention at delivery of the presumed sensitizing pregnancy to correlate with the spectrum of prognosis for the first affected child. One would expect the least operative interference, i.e., spontaneous delivery, to be associated statistically with the best prognosis, i.e., a clinically normal neonate; moderate operative interference, e.g., low forceps, to be associated statistically with poorer prognosis, e.g., need for neonatal transfusions; and the greatest operative interference, Cesarean section, to be associated statistically with the worst prognosis, intrauterine death.

At present the small series of data present are certainly suggestive; the potential obstetric implications evident.

V. SUMMARY

1. A series of twenty-five cases of first affected erythroblastosis fetalis children, with appropriately matched non-diseased controls, is presented in terms of clinical obstetrical data relating to (a) maternal personal properties, (b) clinical events and properties of the presumed sensitizing pregnancy, delivery, and child, and, (c) the presence and severity of erythroblastosis fetalis.

2. Positive correlations are found relating increased frequency of erythroblastosis fetalis according to various combinations of maternal, presumed sensitizing pregnancy child, and erythroblastotic child blood types, occurring in relations to (a) maternal height, weight, and somatic index, (b) number of rectal and vaginal examinations at delivery of the presumed sensitizing pregnancy, (c) duration of anesthesia at delivery of the presumed sensitizing pregnancy and, (d) birth weight of the presumed sensitizing child.

3. Data are presented relating increased severity of prognosis to the extent of operative obstetric intervention at delivery of the presumed sensitizing pregnancy.

4. Suggestions for further study are discussed.

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