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Antenatal prophylaxis of Rh isoimmunization: 28-weeks'-gestation service program

J.M. BOWMAN, MD; J.M. POLLOCK

Two (0.18%) of 1086 Rh-negative primigravidas or multigravidas treated similarly in all previous pregnancies, who were given a single injection of Rh immune globulin (300 µg) at 28 weeks' gestation and subsequently were delivered of Rh-positive babies, had demonstrable Rh isoimmunization at the time of that injection and must be considered "logistic" failures of antenatal prophylaxis. The remaining 1084 (who were treated again after delivery) had no evidence of Rh isoimmunization at delivery and none of the 512 screened at 6 months after delivery appeared to be immunized. If the 28th-week injection had not been protective, one would have expected 14 of the 1084 to have been demonstrably Rh isoimmunized and evidence of Rh isoimmunization to have persisted in 6 of the 512 observed 6 months after delivery.

Six of 719 Rh-negative multigravidas who had not received Rh immune globulin after previous pregnancies or had been treated only after delivery showed evidence of Rh isoimmunization despite a single injection of Rh immune globulin at 28 weeks in a subsequent pregnancy. In three of the six the cause was most likely "sensibilization" due to previous exposure to Rh-positive blood or an untreated Rh-positive pregnancy. In 3 of the remaining 716 (0.42%) there may have been true failure of antenatal Rh prophylaxis administered at the 28th week. One would have expected this figure to be 12 of 716 if antenatal Rh prophylaxis at 28 weeks' gestation were totally unsuccessful.

It is concluded that a single intramuscular injection of Rh immune globulin, 300 µg, is 88% effective in preventing Rh isoimmunization during pregnancy in Rh-negative primigravidas and in multigravidas treated antenatally in all previous pregnancies, and is 75% effective in preventing Rh isoimmunization in Rh-negative multigravidas untreated during previous pregnancies. The majority of failures are due to Rh isoimmunization during pregnancy prior to antenatal prophylaxis at 28 weeks.

Sur 1086 primigravides et multigravides Rh négatif ayant été traitées de la même façon aux grossesses précédentes, qui ont reçu une seule injection d'immunoglobuline Rh (300 µg) à la 28^e semaine de la grossesse et qui subséquemment ont donné naissance à un bébé Rh positif, 2 (0.18%) ont démontré une isoimmunisation Rh au moment de cette injection et doivent être considérées comme des échecs de "logistique" en ce qui a trait à la prévention prénatale. Les 1084 autres femmes (qui ont été traitées encore après l'accouchement) n'ont montré aucun signe d'isoimmunisation Rh lors de l'accouchement et aucune des 512 testées systématiquement 6 mois après l'accouchement n'a semblé être immunisée. Si l'injection à la 28^e semaine n'avait pas protégé, on se serait attendu à ce que 14 de ces 1084 patientes montrent une isoimmunisation Rh et à ce qu'il y eut persistance des signes d'isoimmunisation Rh chez 6 des 512 patientes observées 6 mois après l'accouchement.

Sur 719 multigravides Rh négatif qui n'ont pas reçu d'immunoglobuline Rh lors de leurs grossesses précédentes ou qui avaient été traitées seulement après la grossesse, 6 ont montré des

signes d'isoimmunisation Rh en dépit de l'injection d'immunoglobuline Rh à la 28^e semaine d'une grossesse subséquente. Chez trois des six patients la cause la plus probable est une sensibilisation due à une exposition antérieure à du sang Rh positif ou à une grossesse Rh positif traitée. Chez 3 des 716 autres femmes (0.42%) il peut y avoir eu échec réel du traitement préventif prénatal Rh administré à la 28^e semaine. On aurait pu s'attendre à un chiffre de 12 sur 716 si la prévention prénatale à la 28^e semaine de la gestation était complètement sans succès.

On conclut qu'une seule injection intramusculaire de 300 µg d'immunoglobuline Rh est efficace à 88% dans la prévention de l'isoimmunisation Rh durant la grossesse chez les primigravides Rh négatif et chez les multigravides Rh négatif qui ont été traitées avant la naissance durant chacune de leurs grossesses précédentes; elle est efficace à 75% chez les multigravides Rh négatif qui n'ont pas été traitées durant leurs grossesses précédentes. La majorité des échecs est due à une isoimmunisation Rh durant la grossesse survenant avant de recevoir le traitement préventif prénatal à la 28^e semaine.

As a result of the evidence of the occurrence of Rh isoimmunization during pregnancy and its successful prevention by antepartum intramuscular administration of approximately 300 µg of Rh immune globulin (Rho[D] immune globulin, Connaught Laboratories, Toronto) at 28 and 34 weeks' gestation, a service program of antenatal Rh prophylaxis was begun in Manitoba July 1, 1975. Because of calculations, based on a half-life of IgG of about 28 days, that 20 to 30

From the Rh laboratory and the department of pediatrics, University of Manitoba and Health Sciences Centre, Winnipeg

Reprint requests to: Dr. J.M. Bowman, Rh laboratory, 735 Notre Dame Ave., Winnipeg, Man. R3E 0L8

µg of Rh immune globulin would remain in the recipient 12 weeks after the injection was given, the program consisted of a single intramuscular injection of one vial (approximately 300 µg) of Rh immune globulin at 28 weeks' gestation.

Initially the service program was offered to urban Rh-negative pregnant women at risk. When approval was obtained in December 1975 from the Manitoba Health Services Commission for funding of antenatal prophylaxis on a province-wide basis, the services of a nurse on a half-time basis were obtained to organize and administer the program, and antenatal prophylaxis was extended to rural Rh-negative pregnant women at risk. The province-wide program began Feb. 1, 1976 and was fully operational by Mar. 1, 1976. The protocol and the results up to Aug. 31, 1977 are described in this paper.

Protocol

1. All pregnant Rh-negative women with Rh-positive husbands and without

evidence of Rh isoimmunization in their current pregnancy were offered Rh antenatal prophylaxis as close to 28 weeks' gestation as possible.

2. Urban women were contacted by the Rh prevention nurse, were interviewed in the Rh laboratory, and were given one prophylactic dose of Rh immune globulin intramuscularly.

3. A vial of Rh immune globulin was sent to the rural physician with instructions to administer the contents intramuscularly to his Rh-negative pregnant patient as close to 28 weeks' gestation as possible.

4. Blood samples were taken prior to the injection and were requested to be taken at 2-week intervals throughout the remainder of the pregnancy. Cord and maternal blood samples obtained immediately after delivery and maternal blood samples obtained 3 days, 6 weeks, 3 to 4 months and 6 months after delivery were screened as described in the accompanying paper in this issue of the Journal (page 623).

5. On occasion, because of the low

compliance of patients and physicians, particularly in rural areas, or inaccuracies in the recording of the duration of pregnancy, antenatal prophylaxis was not always given at 28 weeks' gestation. The intervals between injection and delivery are set out in Table I.

6. Since the program was intended to protect every Rh-negative woman at risk, some were treated who had not been treated antenatally or even postnatally in previous pregnancies. For this reason Rh-negative women taking part in the service program were divided into two groups:

- Group 1: Rh-negative primigravidas and multigravidas who had received Rh immune globulin antenatally and postnatally in all previous Rh-positive pregnancies and after all previous abortions. Women in this group are comparable to those treated in the previous clinical trial (described in the accompanying article).

- Group 2: Rh-negative multigravidas who had received Rh immune globulin only after delivery or not at all after previous Rh-positive pregnancies and abortions. Rh isoimmunization developing in women in this group may be due not to a failure of antenatal prophylaxis but to "sensibilization" as a result of inadequate treatment after previous pregnancies.

Effectiveness of antenatal coverage

In the 8-month period ending Oct. 31, 1976, 1211 women (84% of those at risk) and in the 8-month period ending June 30, 1977, 1346 women (93% of those at risk) were treated in our antenatal Rh prophylaxis service program.

Results

The results are set forth in Tables II and III for groups 1 and 2 respectively.

Group 1

The results in group 1 were similar to those of the previous clinical trial. (The women in the two series were comparable.) Two women (patients 1 and 2, Table II) of the 1086 in this group who were delivered of Rh-positive babies had evidence of Rh isoimmunization at the time of injection of Rh immune globulin at 28½ and 28 weeks' gestation respectively. Two other women (patients 3 and 4) in group 1 (not included in Table II) had evidence of Rh isoimmunization at the time of first examination of serum at 12½ and 6½ weeks' gestation respectively in what they stated was their first pregnancy. Neither had received blood transfusions. Both were undoubtedly sensitized prior to, not as a result of, their first pregnancy. They were

Table I—Interval between antenatal prophylaxis and delivery, Manitoba, July 1, 1975 to Aug. 31, 1977

Interval (wk)	Group 1*	Group 2†	Total (and %)
≤ 5	77	52	129 (4.8)
> 5 - < 8	156	107	263 (9.7)
> 8 - < 10	262	166	428 (15.8)
> 10 - < 13	752	442	1194 (44.1)
≥ 13	440	254	694 (25.6)
Total	1687	1021	2708 (100.0)

*Rh-negative primigravidas and multigravidas who had received Rh immune globulin antenatally and postnatally in all previous Rh-positive pregnancies and after all previous abortions.

†Rh-negative multigravidas who had received Rh immune globulin only after delivery or not at all after previous Rh-positive pregnancies and abortions.

Table II—Prophylaxis of Rh isoimmunization by a single antepartum injection of Rh immune globulin: group 1

Interval between injection and delivery (wk)	No. (and %) of women			
	Received injection	Delivered of Rh-positive baby	Followed up for 6 months	Rh isoimmunized
≤ 8	233	163	86	0
> 8 - < 16	1454	923	426	2* (0.22)
Total	1687	1086	512	2* (0.18)

*Methods used to determine Rh antibody titre: †one-stage papainized erythrocyte panel, ‡two-stage papainized erythrocyte panel, §AutoAnalyzer low-ionic screen and ¶saline screen.

†Patient 1: No Rh antibody at 25 weeks' gestation. ‡§ Rh antibody present at 28½ weeks' gestation before injection of Rh immune globulin. †§¶ No Rh antibody 6 months after delivery. ‡§ Rh of woman's mother unknown.

‡Patient 2: Rh immune globulin given postabortion in previous pregnancy. No Rh antibody at 20 weeks' gestation. ‡§ Rh antibody strongly positive by indirect Coombs' test, with albumin titre 1:2 and saline titre 1:2 at 28 weeks' gestation prior to injection of Rh immune globulin. Woman's mother Rh-negative.

‡Patient 3 (not included in table): Primigravida by history; no abortions, no transfusions. Rh antibody strongly positive at 12½ weeks' gestation. ‡§ Rh immune globulin given at 23, 29 and 35 weeks' gestation with no increase in titre of Rh antibodies. Baby group O, Rh-positive, direct-Coombs'-positive at 8 minutes (passive) 17 days after third injection. Rh status of woman's mother unknown.

‡Patient 4 (not included in table): Primigravida by history; no abortions, no transfusions. First test for Rh antibody at 6½ weeks' gestation strongly positive. †‡§ Moved to Saskatchewan. Antibody became fully developed, necessitating amniocentesis, induced delivery and exchange transfusion. Woman's mother Rh-negative.

Table III—Prophylaxis of Rh isoimmunization by a single antepartum injection of Rh immune globulin: group 2

Interval between injection and delivery (wk)	No. (and %) of women			
	Received injection	Delivered of Rh-positive baby	Followed up for 6 months	Rh isoimmunized
≤ 8	159	110	44	0
> 8 — < 16	862	609	251	6* (0.99)
Total	1021	719	295	6* (0.83)

*Symbols as in Table II.

Patient 1 (not included in table): Three Rh-positive pregnancies in preprevention era. Present pregnancy: at 26½ weeks Rh antibody demonstrable, albumin titre 1:1, indirect Coombs' test positive at 2 minutes. Not given Rh immune globulin antenatally. At 36 weeks' gestation albumin titre 1:2, indirect Coombs' test strongly positive at 1 minute. Baby Rh-positive, direct-Coombs'-positive. "Sensibilization" by preprevention pregnancies?

Patient 2: Nonspecific antibody present in 1966 preprevention pregnancy. In 1976, at 26½ weeks' gestation, prior to administration of Rh immune globulin, Rh antibody weakly positive. At 40 weeks' gestation 8-mL fetal transplacental hemorrhage, indirect Coombs' screen positive at 11 minutes, Rh antibody present. Three days post partum, before injection of Rh immune globulin, Rh antibody detected. Six weeks after delivery indirect Coombs' test strongly positive at 1 minute, albumin titre 1:2. "Sensibilization" by preprevention pregnancy?

Patient 3: Preprevention pregnancy in 1965. In 1967 and 1969 pregnancies no Rh antibody present; Rh immune globulin given after each delivery. In 1973 pregnancy no Rh antibody demonstrable; baby Rh-negative. In 1977 pregnancy no Rh antibody at 20 weeks' gestation. Rh antibody present at 28½ weeks' gestation; albumin screening test positive; indirect Coombs' screening test positive at 4 minutes prior to administration of Rh immune globulin. At 35 weeks' gestation indirect Coombs' antibody screen strongly positive at 1 minute, albumin titre 1:2. Baby Rh-positive, direct-Coombs'-positive at 2 minutes. "Sensibilization" as result of 1965 pregnancy?

Patient 4: Received Rh-positive transfusion in childhood. No Rh antibody at 26 weeks' gestation prior to injection of Rh immune globulin. At delivery, at 40 weeks' gestation, indirect Coombs' test positive at 7 minutes, Rh antibody demonstrable. At 6 weeks after delivery maternal Rh antibody present by indirect Coombs' screen, strongly positive at 1 minute; albumin titre 1:1. "Sensibilized" by Rh-positive transfusion?

Patient 5: Abortion 1967, no Rh prophylaxis. Next pregnancy, no Rh antibody at 23 weeks' gestation; at 29 weeks' gestation, prior to administration of Rh immune globulin, Rh antibody (trace, weak, negative with three Rh-positive calls). Rh antibody strongly positive at 35 weeks' gestation and at 40 weeks' gestation, with indirect Coombs' screening test positive at 1 minute. "Sensibilized" after abortion? Possible failure of antepartum prophylaxis?

Patient 6: October 1971, Rh immune globulin given after delivery of Rh-positive baby; no Rh antibody throughout pregnancy. In 1972, following abortion, given Rh immune globulin. In 1973 Rh-negative baby; Rh antibody trace positive at 16 weeks' gestation. Present pregnancy, at 28 weeks' gestation, prior to Rh immune globulin administration, no Rh antibody. At 34 weeks' gestation Rh antibody strongly positive. At 40 weeks' gestation Rh antibody strongly positive and weakly positive; indirect Coombs' test negative. Four months after delivery indirect Coombs' test strongly positive at 1 minute (indirect Coombs' titre 1:16), albumin titre 0, saline titre 0. "Sensibilized" post partum before injection in 1971? Failure of antepartum prophylaxis?

Patient 7: In 1974 Rh-positive baby; no Rh antibody present; Rh immune globulin given after delivery. In 1975 no Rh antibody after delivery of Rh-positive baby; Rh immune globulin given after delivery. In 1977 pregnancy no Rh antibody at 11, 21 and 27 weeks' gestation; given Rh immune globulin at 27 weeks' gestation. At 30 weeks' gestation Rh antibody present (? passive); saline screen negative. At 39½ weeks' gestation one screen positive and one negative. Three days after delivery of Rh-positive baby, prior to injection of Rh immune globulin, Rh antibody demonstrable; albumin titre 1:1. Failure of antepartum prophylaxis? Interval of 14½ weeks from antenatal prophylaxis to delivery.

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excluded from our statistics since their cases could not be considered failures of antenatal Rh prophylaxis.

The first two cases must be considered as failures of the logistics of antenatal prophylaxis, since the women had become isoimmunized too early for prophylaxis at 28 weeks to be effective. This represents a failure rate of 0.18%, in comparison with a failure rate for the same reason of 0.07% in the previous clinical trial and of 0.14% for the same reason in 3533 women not treated antenatally. These differences are not significant.

The remaining 1084 women in group 1 showed no evidence of Rh isoimmunization at delivery, nor did any of the 512 re-examined 6 months after delivery show such evidence. On the basis of the 1.6% incidence of development of Rh antibodies in primigravidas between 28 weeks' gestation and 3 days after delivery (in 45 of 2768 women) determined from the previous clinical trial, if antenatal prophylaxis were unsuccessful one would have expected 17 of the 1084 women to have been Rh isoimmunized in the

interval between antenatal and postnatal injections; in 14 of the 17 this would not be masked by passive antibody. Similarly, if antenatal prophylaxis at 28 weeks' gestation were unsuccessful, 8 of the 512 women examined 6 months after delivery would have been Rh isoimmunized; 6 of the 8 would still show evidence of such immunization. The fact that none of the 1084 women delivered of Rh-positive babies or of the 512 examined 6 months after delivery showed evidence of Rh isoimmunization is sound evidence that a single injection of one prophylactic dose of Rh immune globulin at 28 weeks' gestation was as effective in preventing Rh isoimmunization during pregnancy in group 1 as two injections were in the group previously studied (there were no failures in either group). If one considers the two logistic failures due to isoimmunization prior to antenatal Rh prophylaxis, the protection rate in group 1 is 88%.

Group 2

Protection was not so complete in

multigravidas treated only after delivery or not at all after previous Rh-positive pregnancies and abortions. Analysis of the seven failures among the 720 women in this group (719 plus 1 woman not treated antenatally) (Table III) indicates that three of the seven (patients 1, 2 and 3 in Table III) had had pregnancies in the preprevention era and one other (patient 4) had received an Rh-positive transfusion in childhood. These "failures" of antenatal Rh prophylaxis probably represent "sensibilization". They are excluded as failures of antenatal prophylaxis.

One of the seven women (patient 5) did not receive Rh immune globulin after an abortion. Although this instance also may be one of "sensibilization" the exceedingly weak antibody demonstrated just prior to antenatal prophylaxis at 29 weeks may represent primary immunization in her current pregnancy — that is, a "logistic" failure of 28th-week antenatal Rh prophylaxis.

Although the other two instances (in patients 6 and 7) may also be examples of "sensibilization" prior to injection of Rh immune globulin on the 3rd day after delivery in previous pregnancies, we must consider them as failures of 28th-week antenatal Rh prophylaxis.

In group 2, therefore, there was a failure rate of 28th-week antenatal Rh prophylaxis of 0.42% (3 of 716 women). This should be compared with the expected rate of 2.2% (17 of 765) in multigravidas treated postnatally in our control series (described in the accompanying paper). We would have expected 16 of the 716 women to be isoimmunized. In 12 of the 16 the isoimmunization would not have been masked by passive Rh antibody at delivery. The protection rate of antenatal Rh prophylaxis in group 2 was 75% (prevention of 9 of 12 instances of demonstrable Rh isoimmunization prior to prophylaxis after delivery).

Conclusions

This study has indicated that a single intramuscular injection of approximately 300 µg of Rh immune globulin at 28 weeks' gestation is highly effective in preventing Rh isoimmunization during pregnancy in Rh-negative primigravidas and multigravidas treated antenatally and postnatally during and after previous pregnancies and abortions. It is also effective, but less so, in preventing Rh isoimmunization during pregnancy in Rh-negative multigravidas treated only postnatally or not at all after preceding Rh-positive pregnancies and abortions. Its lessened effectiveness in this group is probably due to the likelihood of Rh isoimmunization ("sensibilization") as a result of inadequate prophylaxis in previous pregnancies.

The final proof of the effectiveness of antenatal prophylaxis is its effect on the incidence of Rh isoimmunization in Manitoba (Table IV). The incidence has fallen from 3.5 per 1000 total births in the 2-year period ending Oct. 31, 1975 to 2.7 in the next 12 months and to 2.0 in the 6-month period ending Apr. 30, 1977. These figures compare with an incidence of Rh isoimmunization of 10.6 per 1000 total births in the 12-month period ending Oct. 31, 1964.

In the 2-year period ending Oct. 31, 1975, 48 of the 121 instances of Rh isoimmunization in pregnant women were due to immunization during pregnancy or within 3 days after delivery; 26 of the 48 were the result of immunization during the current pregnancy. We would have expected 47 instances of such immunization during the current pregnancy. Hence our clinical trial of antenatal prophylaxis during these 2 years had prevented 21 (45%) of expected instances of Rh isoimmunization during pregnancy. In the following year the institution of province-wide antenatal prophylaxis prevented 13 of 23 (57%) and in the 6-month period ending Apr. 30, 1977, 10 of 12 (83%)

instances of Rh isoimmunization that might have occurred during pregnancy. These figures afford further proof of the value of antenatal Rh prophylaxis in the province of Manitoba. ■

BOOKS

This list is an acknowledgement of books received. It does not preclude review at a later date.

ADVANCES IN CARDIOLOGY. Vol. 21. *Electrocardiology III.* 3rd International Congress on Electrocardiology (17th International Symposium on Vectorcardiography). Brussels, June 28-30, 1976. Edited by F. Kornreich. 348 pp. Illust. S. Karger AG, Basel, 1978. \$60. ISBN 3-8055-2650-4

ADVANCES IN CARDIOLOGY. Vol. 22. *Results and Evaluation of New Methodology in Cardiology.* 8th Conference of Cardiovascular Disease in Snowmass-at-Aspen, Aspen, Colo., January 10-14, 1977. Edited by John H.K. Vogel. 270 pp. Illust. S. Karger AG, Basel, 1978. \$60. ISBN 3-8055-2748-9

LES ARTERIOPATHIES AU STADE DE CLAUDICATION INTERMITTENTE. Rapport présenté au 79^e Congrès Français de Chirurgie, Paris, 19 au 22 septembre 1977. J.B. Lévy et A. Gédéon. 167 pp. Illust. Masson, Paris, 1977. Prix non mentionné, broché. ISBN 2-225-47707-8

BIBLIOTHECA ANATOMICA. No. 15. *Recent Advances in Clinical Microcirculatory Research.* 9th European Conference on Microcirculation, Antwerp, July 5-9, 1976 (Part I). Edited by D.H. Lewis. 752 pp. Illust. S. Karger AG, Basel, 1977. \$79.25. ISBN 3-8055-2757-8

BIBLIOTHECA ANATOMICA. No. 16. *Recent Advances in Clinical Microcirculatory Research.* 9th European Conference on Microcirculation, Antwerp, July 5-9, 1976 (Part II). Edited by D.H. Lewis. 553 pp. Illust. S. Karger AG, Basel, 1977. \$79.25. ISBN 3-8055-2758-6

BREAST CANCER RESEARCH. A Series of Workshops on the Biology of Human Cancer. Report No. 4. UICC Technical Report Series — Vol. 27. Edited by Michael J. Brennan. International Union Against Cancer, Geneva, 1977. Price not stated, paperbound

CHIRURGIE 77. Résumés de la Conférence, des Tables Rondes, des Forums et Communications du 79^e Congrès Français de Chirurgie, Paris, 19 au 22 septembre 1977. Textes publiés sous la direction de J.-Cl. Patel. 183 pp. Illust. Masson, Paris, 1977. Prix non mentionné, broché. ISBN 2-225-48004

CLINICAL HAEMATOLOGY. 5th ed. R.D. Eastham. 326 pp. John Wright & Sons Ltd., Bristol; Year Book Medical Publishers, Inc., Chicago, 1977. Price not stated, paperbound. ISBN 0-8151-3009-0

CLINICAL MEDICINE AND THERAPEUTICS. Edited by Peter Richards and Hugh Mather. 274 pp. Illust. Blackwell Scientific Publications, Oxford; J.B. Lippincott Company of Canada Ltd., Toronto, 1977. Price not stated, paperbound. ISBN 0-632-00026-8

COCCIDIOIDOMYCOSIS. Current Clinical and Diagnostic Status. Third International Coccidioidomycosis Symposium, Tucson, Arizona. Edited by Libero Ajello. 475 pp. Illust. Stratton International Medical Book Corporation, New York; Longman Canada Limited, Don Mills, 1977. \$43.25. ISBN 0-88372-095-7

COMPUTED TOMOGRAPHY OF THE HUMAN BODY. An Atlas of Normal Anatomy. Ralph J. Alfidi, John Haaga, Meredith Weinstein and others. 197 pp. Illust. The C.V. Mosby Company, Saint Louis, 1977. \$37.50. ISBN 0-8016-0116-9

CROSS-SECTIONAL ANATOMY — an Atlas for Computerized Tomography. Robert Steven Ledley, H.K. Huang and John C. Mazziotto. 330 pp. Illust. Williams & Wilkins Company, Baltimore; Burns & MacEachern Limited, Don Mills, 1977. \$80.40. ISBN 0-683-04920-8

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Table IV—Rh isoimmunization in Manitoba

Datum	No. (and %)			
	Year ending Oct. 31, 1974	Year ending Oct. 31, 1975	Year ending Oct. 31, 1976	6 months ending Apr. 30, 1977
Rh isoimmunized pregnancies	59	62	46	17
Rh isoimmunized during pregnancy or within 3 days after delivery	24 (41)	24 (38)	20 (44)	6 (35)
During previous pregnancy	22	10	10	4
During current pregnancy	26	10	10	2
Expected and demonstrable if no antenatal prophylaxis program	47	23	12	12
Protected by antenatal prophylaxis program	21 (45)	13 (57)	10 (83)	
Incidence of Rh isoimmunization per 1000 total births	3.5	2.7	2.0	