**Title:** Anti-D doesn’t grow on trees: stop unnecessary use for first trimester abortion

**Authors**: Katherine Whitehouse1\*, Patricia Lohr1, John Reynolds-Wright2,3, Jonathan Lord4,5, Stephen Robson6, Tracey Masters5,7, Yvonne Neubauer8, Lydia Kingsley9, Sharon Cameron2,3

1British Pregnancy Advisory Service (BPAS), Centre for Reproductive Research & Communication, 30-31 Furnival St, London, EC4A 1JQ

2Centre for Reproductive Health, University of Edinburgh, 4-5 Little France Drive, Edinburgh, EH16 4UU

3Chalmers Centre, NHS Lothian, 2a Chalmers Street, Edinburgh, EH3 9ES

4Department of Obstetrics & Gynaecology, Royal Cornwall Hospitals NHS Trust, Treliske, Truro, TR1 3LJ

5British Society of Abortion Care Providers, c/o RCOG, 10-18 Union St, London, SE1 1SZ

6Department of Obstetrics & Gynaecology, Newcastle-upon-Tyne Hospital NHS Trust, Newcastle, NE4 5NR

7Department of Sexual & Reproductive Health, Homerton Healthcare NHS Trust, Homerton Row, London, E9 6SR

8MSI Reproductive Choices, 1 Conway Street, Fitzroy Square, London, W1T 6LP

9National Unplanned Pregnancy Advisory Service (NUPAS), 5 Arthur Road, Edgbaston, Birmingham, B15 2UL

\*Corresponding author:

Dr Katherine Whitehouse

BPAS, Centre for Reproductive Research & Communication

30-31 Furnival St, London EC4A 1JQ

kate.whitehouse@gmail.com

**Word count** (800): 777

Since the 1960s, standard practice across the UK includes administration of anti-D immunoglobulin to Rh-negative pregnant patients to prevent sensitisation and future haemolytic disease of the newborn. Despite the ubiquity of this practice, few stop to consider what the production of anti-D entails: a limited pool of Rh-negative men (and some sterile women) are purposely sensitised and donate their plasma, from which the immunoglobulins are extracted. None of the anti-D used in the UK is locally obtained or made; it primarily comes from the United States (US) 1,2.

While national guidance has historically endorsed anti-D administration during first trimester abortion, the evidence is antiquated, weak, and with significant limitations. For example, these studies used Kleihauer-Betke tests, which can’t differentiate fetal from maternal cells and included sharp curettage abortions – an obsolete procedure that may increase likelihood of fetomaternal transfer. For their 2019 guidance on abortion care, NICE performed a systematic review on this matter. They found no evidence on anti-D prophylaxis for first trimester abortion 3. Relying on expert opinion, NICE recommended: do not offer for medical abortion up to 10 weeks of gestation, ‘consider’ for surgical abortion up to 10 weeks’, and offer to all over 10 weeks’ gestation 4. While the ‘consideration’ language allowed flexibility, it does not empower change in routine practice thus many services continue to offer it ubiquitously. Nonetheless, this pivotal change paved the way for important advancements in telemedical abortion care. During the COVID-19 pandemic, patients in England and Wales could access medical abortion at home up to 10 weeks’ gestation. Scottish patients could have medical abortions up to 12 weeks’ gestation at home without RhD typing or anti-D administration.

The momentum has continued: in 2022, the World Health Organization recommended against routine RhD typing and anti-D administration during medical or surgical abortion up to 12 weeks’ gestation 5. In 2023, American researchers published a landmark study evaluating RhD sensitisation during abortion up to 12 weeks’ gestation 6. Using high-flow cytometry, they determined how frequently maternal exposure to fetal red blood cells (fRBCs) exceeded the accepted threshold for sensitisation. None of the 506 participants had a newly elevated fRBC above the threshold. The authors concluded that medical and surgical abortion up to 12 weeks’ gestation are not risk factors for RhD sensitisation and therefore, ‘Rh testing and treatment are unnecessary.’

In the US, the Society of Family Planning and the National Abortion Federation endorsed these findings and recommended that providers forego RhD testing and treatment up to 12 weeks’ gestation 7,8. In Britain, the guidance is inconsistent: the recent RCOG ‘Best practice in abortion care’ only recommends anti-D from 12 weeks’ onward 9. A 2023 NICE update on miscarriage does not recommend anti-D for medical management up to 13 weeks. In the NICE abortion guidance, the rationale states that ‘…there is no evidence to distinguish surgical and medical abortion on this topic…’ 4. It references ‘theoretical concerns that greater fetomaternal haemorrhage could be possible in surgical procedures,’ and made a research recommendation prior to the landmark study publication (3).

RhD testing and anti-D administration have significant cost and resource implications. Although guidelines recommend 250 units of anti-D in the first trimester, most services can only access a 1500-unit dose, which is significantly more expensive. We calculate that the system could save over £0.5m per year in testing and treatment costs alone if national guidance endorsed these updated practices from 12 weeks onward. Besides the cost implications, anti-D immunoglobulin administration also carries the risk of drug reactions and transmission of infectious disease 10,11.

Rh immunoglobulin has important indications outside of pregnancy. It is also a treatment for immune thrombocytopenic purpura (ITP) and complications of incompatible blood transfusions. Health services worldwide have been facing global shortages of Rh immunoglobulins for years, citing ‘reduction of supply due to increase in demand 2,12.’ The European Directorate for the Quality of Medicines & Healthcare states that ‘the lack of self-sufficiency in anti-D plasma and products in Europe is of public health concern, with patients being put at risk in the event of a sudden plasma supply shortage when no current alternatives exist on the European market 1.’ By eliminating this superfluous use of Rh immunoglobulin during abortion up to 12 weeks’ gestation, we would protect continued access for those who truly need it.

Compelling new evidence, ethical issues of wasting blood products, burden to patients, and cost effectiveness concerns all speak for themselves: national guidance should no longer recommend RhD testing or anti-D administration for abortions up to 12 weeks’ gestation. We call on NICE to review and update their guidance so abortion services can deliver best practice in line with the latest evidence and WHO recommendations.

**References**

1. European Directorate for the Quality of Medicines & HealthCare. Anti-D Immunoglobulin: Exploring collection, production and alternatives. Published online 2023. Accessed June 20, 2024. https://www.edqm.eu/en/-/a-series-of-3-webinars-to-raise-awareness-on-the-lack-of-self-sufficiency-in-the-provision-of-anti-d-treatment-in-europe

2. NHS University Hospitals Sussex. Immunoglobulin Shortage. Published online 2021. Accessed June 20, 2024. https://www.bsuh.nhs.uk/wp-content/uploads/sites/5/2016/09/Immunoglobulin-shortage.pdf

3. Schmidt-Hansen M, Lord J, Hawkins J, et al. Anti-D prophylaxis for rhesus D (RhD)-negative women having an abortion of a pregnancy up to 13(+6) weeks’ gestation: a systematic review and new NICE consensus guidelines. *BMJ Sex Reprod Health*. Published online January 20, 2020:bmjsrh-2019-200536. doi:10.1136/bmjsrh-2019-200536

4. NICE. *Abortion Care (NG 140)*. National Institute for Health and Care Excellence; 2019. Accessed October 7, 2019. www.nice.org.uk/guidance/ng140

5. World Health Organization. Abortion care guideline. Published online 2022.

6. Horvath S, Huang ZY, Koelper NC, et al. Induced Abortion and the Risk of Rh Sensitization. *JAMA*. 2023;330(12):1167-1174. doi:10.1001/jama.2023.16953

7. Horvath S, Goyal V, Traxler S, Prager S. Society of Family Planning committee consensus on Rh testing in early pregnancy. *Contraception*. 2022;114:1-5. doi:10.1016/j.contraception.2022.07.002

8. National Abortion Federation. Clinical Policy Guidelines for Abortion Care (CPGs). Published online 2024. https://prochoice.org/providers/quality-standards/

9. Royal College of Obstetricians & Gynaecologists. Best practice in abortion care. Published online 2022. https://www.rcog.org.uk/media/geify5bx/abortion-care-best-practice-paper-april-2022.pdf

10. CSL Behring. Rhophylac Prescribing Information. Published online 2020. Accessed June 20, 2024. https://labeling.cslbehring.com/PI/US/Rhophylac/EN/Rhophylac-Prescribing-Information.pdf

11. Murdoch A. Irish mothers called for hepatitis C virus screening. *BMJ*. 1994;308(6929):613-614. doi:10.1136/bmj.308.6929.613a

12. US FDA. CBER-Regulated Products: Current Shortages. Published online 2024. Accessed June 20, 2024. https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/cber-regulated-products-current-shortages