

“CELEBRATING 50 YEARS OF Rh DISEASE PREVENTION  
EXTENDING PROTECTION TO ALL RH NEGATIVE WOMEN IN NEED”

### Meeting Summary

The meeting consisted of a series of presentations and discussions (see attached agenda), leading to recommendations of work to be done in preparation for the final Columbia 50th celebration/CURhE meeting to be held in the Fall of 2018. At that meeting it is intended that items defined in the May 4<sup>th</sup> meeting will be discussed for implementation. A video of the meeting is available as follows, it includes all PowerPoint presentations.

*A link to the video file:*

[https://sickkidsca-my.sharepoint.com/:v/g/personal/grace\\_belayneh\\_sickkids\\_ca/EUYCHpmBnlNGghU6u8O53T0BZem4lLx\\_PGrgu-YHrzy1rA?e=S1rGnh](https://sickkidsca-my.sharepoint.com/:v/g/personal/grace_belayneh_sickkids_ca/EUYCHpmBnlNGghU6u8O53T0BZem4lLx_PGrgu-YHrzy1rA?e=S1rGnh)

PowerPoint presentations can be seen on the video. Separate Power Point videos can be obtained by request to Grace Belayneh at (grace.belayneh@sickkids.ca). A video presented by Richard Hendricks described Rh disease, the severity of the problem and its eradication by the great discovery of Rh immunoglobulin prophylaxis. A copy of the video can be obtained by request to Grace Belayneh (grace.belayneh@sickkids.ca)

*Fifty years of preventing Rh disease and the need to “complete the job”*

Steve Spitalnick provided an excellent and succinct review of the history of Rh disease which over 30 years led to an understanding of the nature of the disease and to its eradication: a unique and remarkable evolution from disease to eradication. It is a cause for celebration however as Dr Spitalnick stated in his final slide of the day: “Rh Disease: Are we done? Not yet!”

Work to be provided for presentation in the Fall celebration meeting:

- Summary of 50<sup>th</sup> celebration meetings of FIGO, as well as those held in Nigeria and New York.
- Plans for future Columbia-CURhE eradication initiatives

*The Consortium for Rh Disease Elimination (CURhE)*

Vinod Bhutani reviewed the problem of Rh disease placing it within the context of other causes of hemolysis and hyperbilirubinemia. He made the point that those countries with poor neonatal care (as evidenced by high neonatal mortality) are those countries which lack an Rh prevention program. He described the response to this problem by the establishment of CURhE whose goal was the elimination of Rh disease; he described CURhE links to the International Pediatric Association (IPA), the International Federation of Obstetrics and Gynecology (FIGO) and the International Confederation of Midwives (ICM). The rapid development of microtechnology has led to great potential for the

diagnosis, treatment and prevention of Rh disease. He also pointed out the response of a group of mothers concerned about kernicterus; they established a group advocating for improved care and concern about babies with neonatal jaundice; i.e. prevention of kernicterus. Accordingly he stressed the importance of education providing empowerment of women and of the community to solve the problem of Rh disease.

Work to be done for the Fall Meeting:

- The future role of CURhE in the global eradication of Rh disease.
- Microtechnology and point-of-care diagnosis in Rh disease.
- The role and commitment of international agencies to the eradication of Rh disease.(e.g.WHO, UN, Gates,etc.)

### *The Burden of Disease*

Alvin Zipursky stated that over 150,000 children annually die of Rh disease (still births, neonatal deaths) or permanent brain damage (kernicterus); mostly in low and mid income countries. These data were obtained indirectly from the global distribution of Rh immunoglobulin (i.e. a country that uses no immunoglobulin will have Rh disease the extent determined by birth rate, prevalence of Rh negativity etc). There is need to further define the burden of Rh disease.

Work to be done for the Fall Meeting

- AABB through Christine Bales and the global program of AABB is to ask blood banks in low income countries to determine the prevalence of Rh isoimmunization in blood samples.
- Gerry Visser, Chair of the maternal child health committee of FIGO has been asked to consider providing a FIGO questionnaire survey of members of the extent of Rh isoimmunization and Rh disease.
- Dr. Michael Sgro and Dr. Jillian Baker (see below) have developed a successful surveillance program with members of the Canadian Pediatric Society. They are to consider whether surveillance programs can be established through pediatric or obstetric groups in low and middle income countries. Further does CURhE have a role in establishing surveillance systems in countries with an Rh prevention program (surveillance of compliance of postpartum prevention, of antenatal and first trimester prophylaxis; of fetal DNA testing).

Vinod Bhutani described the current state of Rh disease in the following countries (Brazil, Mexico, Iraq, Egypt, India, China and Nigeria). In India there are several hospital-based programs and community programs for Rh prevention. A cost-effectiveness study has been undertaken in Chandigarh. In China there have been no Rh prevention programs. Although the prevalence of Rh disease is low in China, Rh disease occurs and plans are underway to develop Rh prevention programs. In Nigeria physicians in six centres committed themselves to establishing programs for the elimination of Rh disease. They met with officials of state governments who were strongly supportive of an initiative to establish Rh prevention programs in their regions. That led to a meeting, organized by Dr. Bhutani with the Federal Ministry of Health of Nigeria. They too were supportive, however neither the state governments nor the Federal governments could provide funds.

With the help of the Danish Embassy in Nigeria meetings were held with several African philanthropic groups (the Dangote foundation, MTN Foundation (Communications) and the European Union Office in Nigeria). They were responsive to the needs and the potential to provide funds for programs in each of the six centres. Those involved are Henry Akinbi of Cincinnati (a native of Nigeria), Dr. Audu Lamidi of Abuja, Kasper Juul Hedegaard of Eldon (Denmark) and Mrs. Funmi Banire of Lagos.

Work to be done for the Fall meeting

- Presentation of India cost-effectiveness study and its significance in Rh program development in low income countries
- Current status of Rh prevention program in Nigeria.
- Rh prevention programs in India and China
- A review of Rh disease globally

#### *Implementation of postpartum Rh prophylaxis*

Alvin Zipursky and Isaac Odame described a model program for Rh prevention is to be established in the Korle Bu Hospital in Accra, Ghana. An administrative team is in place. Annually there are 500 Rh negative deliveries. Planning for this program will involve, CURhE, Korle Bu Team and hospital administration, International agencies (WHO) and philanthropic groups. The model program is to be followed by a community based program in rural Ghana. A similar program is planned for Pakistan (see Below)

A community – based Rh prevention program (Rhesus Solution Initiative) was described by Mrs. Funmi Banire, the Founder and Director of the program. She described via PowerPoint the program in Nigeria which has identified and provided Rh prophylaxis for over 1500 Rh negative women, using privately donated funds. This amazing program was clearly described on PowerPoint slides and can be found on YouTube (“Rhesus Solution Initiative”).

Work to be done for the Fall meeting

- Expansion of Rhesus Solution Initiative programs into other communities
- Communication of RSI “story “to communities globally
- Results of proposed RSI 50<sup>th</sup> anniversary celebration in Nigeria, August 2018
- Detailed description of the Ghana model program in hospital with reference to planning for community-based programs.

#### *Anti D Production and Distribution*

This was described by Giorgi Gioacchino. Globally only 50% of Rh negative women receive postpartum prophylaxis. In Europe and North America it is near 100%, however in Russia (28%), South America (46%), Asia (34) and Africa (19%). There is minimal available data on antenatal and first trimester prophylaxis. Both industry and the medical community have responsibility to ensure distribution of Rh immunoglobulin to those in

need at the lowest cost. This will require effective distribution eliminating excessive and unregulated mark-ups and accommodating legal and administrative barriers. A formal demand-supply gap study is now underway by a commercial firm in collaboration with CURhE. It is suggested that planning for Rh programs in a country might be developed along lines similar to the GAVI program for childhood immunization. This would involve collaborative planning by industry, countries in need, international agencies and CURhE. An example of the effect of a supply-demand gap study was carried out in Russia; this was followed by a rise in Rh immunoglobulin utilization from 100,000 vials annually to 150,000.

#### Work to be done for Fall meeting

- A report of the demand-supply study
- Report on global programs for antenatal and first trimester prophylaxis
- Description of a formal plan for Rh prevention in a country employing industry, international agencies, CURhE and countries in need.
- Inclusion of all producers of Rh immunoglobulin in the global program for Rh prevention.
- Planning for programs in collaboration with WHO

*Strategies for funding of a global Rh prevention program* As described above it will be the responsibility of communities/countries to develop their own programs. During discussion reference was made to the importance of the World Health Organization (WHO) in advocating for Rh prophylaxis. Dr. Ornella Lincetto (Senior Medical Officer Newborn Health, WHO) sent a letter indicating the interest and importance of WHO and its intended involvement in the global prevention of Rh disease. Dr. Lincetto wrote:

”Updated WHO antenatal care guidelines provide recommendations on antenatal anti-D immunoglobulin prophylaxis state that anti-D after childbirth should be given.

- The WHO model list of Essential Medicine includes immunoglobulins.
- WHO will include anti-D immunoglobulin prophylaxis after childbirth in the list of interventions recommended by WHO for the benefit package that countries should put in place to reach universal health coverage. This will facilitate the discussion with Ministry of Health in countries.
- WHO will include the anti-D immunoglobulin prophylaxis after childbirth among the recommendations in the next version of the Guidelines on postnatal care for the mother and newborn.”

Dr. Lincetto added:

“Personally I believe WHO should engage in efforts to address the burden of Rh- diseases. One option is to gather support to launch an initiative for *elimination* of Rh- disease in LMICs, given the burden, similarly to the initiatives for tetanus elimination or congenital syphilis elimination. However this will require careful thinking on the definition of elimination, how to measure it, how to certify the countries, etc.,

Looking forward to continuing our collaboration”

#### Work to be done for Fall meeting

A detailed description of planning for community programs involving: WHO, producers of Rh immunoglobulin, countries in need, CURhE, and international funding sources.

### *Cost-effectiveness of preventing Rh disease*

Post-partum prophylaxis in India – Unfortunately Professor Kumar could not attend. The Indian study of cost effectiveness will be further developed in coming months for presentation in the 50<sup>th</sup> celebration meeting in the Fall.

The availability of monoclonal anti-D was raised. Alvin described the studies that had been done and the consensus that no monoclonal anti D has been substantially proven to prevent Rh disease. However a monoclonal preparation, Rhoclone was produced and used in India and more recently available in many other countries in the world.

Concern was expressed in the New York 50<sup>th</sup> celebration meeting about the effectiveness of Rhoclone. As a result Alvin is corresponding with the manufacturers of Rhoclone and a full report will be presented at the Fall 50<sup>th</sup> celebration. Also it was suggested that CURhE might arrange to meet with the manufacturers of Rhoclone.

Antenatal prophylaxis — Alvin Zipursky presented evidence that alloimmunization can occur antenatally and that Rh immunoglobulin prophylaxis can prevent that. However it is clear that antenatal immunization is ten times as expensive as postpartum prophylaxis, therefore should it be recommended for Rh prevention programs in low and mid income countries? There was considerable discussion about this point. WHO has recommended that antenatal prophylaxis not be included in programs for low and mid income countries. On the other hand since antenatal prophylaxis is recommended for all “rich” countries why should universal Rh prevention programs not include antenatal prophylaxis? It was concluded that all global programs should provide postpartum prophylaxis; if funds, organization and health care priorities in a country warrant antenatal prophylaxis it should be included.

Rh prophylaxis in first trimester: It is clear that in the first trimester Rh isoimmunisation can occur following spontaneous or induced abortion or any potential damage to the placental site. Rh immunoglobulin prophylaxis will prevent alloimmunization in the first trimester. This should be included in all Rh prevention programs.

Work to be done for Fall 50<sup>th</sup> celebration meeting

- Presentation of Indian cost-effectiveness study
- Definition of the role of antenatal prophylaxis in low and mid income countries, in the light of WHO recommendation
- Recommendation for Rh prophylaxis in first trimester.
- A report on the monoclonal product, Rhoclone.

### *Surveillance and Compliance*

Michael Sgro and Jillian Baker described a surveillance study in Canada to determine the incidence of Rh disease in a country with a comprehensive Rh prevention program. A total of 17 cases in one year/ (If no program were in place the numbers would be several thousand). Nine of the 17 cases were immigrants.

This study was successful because of the support of Canadian members of the Canadian Pediatric Society. It raises the question of whether similar studies could be undertaken in low and mid-income countries using resources of pediatric and/or obstetric societies, government agencies or other groups. One would have to be clear as to the questions to be asked.

Work to be done for Fall 50<sup>th</sup> celebration meeting

- Can Pediatric or Obstetric Societies in developing countries participate in surveillance studies
- Questions to be asked in surveillance studies
- Can surveillance studies be incorporated into country health priorities

### *Identification of Rh negative women at risk*

Shaun Morris described a research program supported by Grand Challenges Canada to study, in a rural community of Pakistan 2000 pregnant women to determine by point-of-care technology and cellphone-App technology to identify women who are Rh negative women and provide postpartum prophylaxis. Dr. Morris discussed the intention that success with this study could lead to model program in Pakistan for the provision of an Rh prevention program in a rural community

Kasper Juul of Eldon Biologicals sent information on the worldwide licensing of the Eldon card for point-of-care blood group determination.

Steve Spitalnick discussed the accuracy and acceptability of point-of-care technology for blood group determination especially in those situations where laboratory testing was not available.

Work to be done for Fall 50<sup>th</sup> celebration meeting

- Progress report of Pakistan study
- Experience with App for transmission of point-of-care blood group results.
- Feasibility of community –based Rh prevention program in rural Pakistan
  
- Advocacy and Education

A video prepared by Bob Fleck was shown. It can be found on YouTube at “Rh Disease Video –Broken Miracles”. It was clear to all that advocacy and education was a critical step in achieving global eradication of R disease. Several newspaper reports of CURhE and the global problem of Rh disease have been distributed on the web and are available globally. Additional reach to newspapers and social media worldwide is being assisted by the Global Reporting System of Vancouver.

Jillian Baker presented her plans for Rhap, a program involving Rh negative mothers who had received Rh prophylaxis as well as mothers who had had babies with Rh disease. They will constitute a powerful voice advocating for the global prevention of Rh disease.

Work to be done for Fall 50<sup>th</sup> celebration meeting

- Worldwide distribution of education and advocacy information via Global Reporting System
- Report of Rhap activities
- Use of all or portions of Fleck video and other videos for global distribution
- Distribution of Rhesus Solution message worldwide
- Distribution and impact of scientific publications

Dr. Spitalnick’s presentation. He reviewed the current situation regarding the study of the global problem of Rh disease. He made several specific points which deserve to be followed and perhaps discussed more completely in the final 50<sup>th</sup> celebration meeting which will be held in New York in early November, 2018.

Work to be done for the Fall 50<sup>th</sup> celebration meeting

- Creation of model or demonstration project in a low income country which would demonstrate the feasibility of effective Rh prevention programs
- Potential sources of funding of model/demonstration projects (? NICHD, Gates, Foundation, National Blood Foundation, AABB etc.)
- Possible involvement of Rh prevention with other Columbia initiatives:
  - Columbia-Bangladesh project
  - Columbia-Dominican Republic
  - Columbia South Africa
  - Columbia Mailman School of Public Health