Universal leukoreduction in the Netherlands

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In 1998 the Council of Health reporting to the Minister of Health, Welfare and Sports concluded that there was at that moment no reason to consider universal leukoreduction.

In 1999 the National Foundation for the Blood Supply Sanquin asked an expert group to reconsider implementation of universal leukoreduction. Calculation of costs should be included. The conclusion of this committee was, that leukoreduction of red cells and platelets is indicated for certain patient groups. Accepted indications being prevention of HLA allo-immunization, non-hemolytic febrile transfusion reactions and CMV transmission. Furthermore pre-storage leukoreduction of red cells and platelets improves the quality of the product. The studies on the effect on immunomodulation were still considered inconclusive.

The costs were calculated on upscaling of the methods in use: pre-storage filtration of red cells with filters connected with a sterile connection device (on-line filters) and pre-storage filtration of platelet rich plasma derived from pools of buffy coats. The number of leukoreduced apheresis platelets is very low. The estimated costs were 40 million Dutch guilders, about 11 million English pounds.

Another important conclusion of the expert group was that at least 3 months were necessary for upscaling leukoreduction of the platelets, whereas 9 months would be needed for the red cells. The Minister of Health decided that first a cost–benefit analysis should be made. To investigate immunomodulation a clinical study on the effect of transfusion of leukoreduced vs. buffy coat reduced red cells in vascular and orthopedic operations is going on now.

To anticipate an unexpected quick decision, Sanquin initiated a project group for preparing ULR with members from all blood bank divisions. The project group consists of a steering committee and at first two, later three, working parties. The first working party should investigate methods to count low residual leukocytes, the second should define a quality program to be tested for clearing filters, validation and process monitoring. The third working party started later than the other two and investigated bag systems with in-line filters for red cells.

The working party on counting reported in July 2000 that after comparing the Nageotte hemocytometer method with various flowcytometric methods the Nageotte was the least accurate and precise in the range of 3.3 WBC/µl corresponding with 1 × 10⁶ leukocytes in a 300 ml product.

Further investigation of flow cytometers revealed that the best results were obtained when the reagents of the manufacturers were applied on the flowcytometer of the same brand. Use of reagents of a different brand gave less accurate results.

The working party on in-line filters first determined to draw up a protocol containing require-
ments for blood collection, centrifugation, separation into blood components, and subsequently filtration of the red cells. The protocol was discussed and agreed upon with Fresenius NPBI, Maco Pharma, Pall Med Sep and Baxter. Requirements were amongst others Top and Bottom Systems for collection of 500 ml of whole blood with an in-line filter leaving less than $1 \times 10^6$ leukocytes when red cells were filtered at ambient temperature. Flow rate should allow filtration within 30 min.

All nine blood bank divisions participated in the pilot study to investigate whether all four brands in-line systems fitted on collection equipment in centrifuge-cups and on separation equipment. The results of this pilot study revealed that collection equipment only needed (small) adaptations; this was also the case with separation equipment. A larger problem was met with the centrifuges. In centrifuges with round buckets only few systems fitted. In other types centrifuges with oval single or double pack buckets some systems hardly fitted and it was suggested that rotors with larger buckets or new centrifuges would be necessary.

Next in four blood bank divisions 30 units of whole blood were collected in Top and Bottom Systems with in-line filters, and all blood components were evaluated. The results of these investigations are not yet available. One of the preliminary remarks from all divisions was that the handling and packing of the bag systems with in-line filters required extensive training. However, the overall conclusion was that the in-line systems were to be preferred over on-line systems.

Despite these drawbacks Sanquin now advocates to go for in-line filters instead of upscaling the method that is in use at present.

In the autumn of 2000 the Minister of Health again asked advice from the Council of Health on the subject of universal leukoreduction. In February 2001 the Council decided that universal leukoreduction of red cells should be compulsory. The ultimate decision of the Minister is expected in May 2001; the costs are still a problem.

Regarding plasma the fractionation institute for the Netherlands as yet does not accept filtered plasma because it is not clear what the effects of filtration are on clotting factors and complement.