***Guidelines to be followed by centres, services and units in order to be designated as Reference Centres, Services and Units of the National Health System as agreed by the Interterritorial Board.***

## 10. ADVANCED RETINOPATHY OF PREMATURITY

Retinopathy of prematurity (ROP) is a retinal vascular disease which may lead to blindness. It is directly related to gestational age and birth weight. There are different degrees depending on its extent and location.
Prevalence of blindness due to ROP seems to increase in spite of appropriate screening programs, probably due to the higher number of premature babies with low weight surviving these days.

*Treatment* for stage 1-2 and 3 ROP consist of destruction of the peripheral avascular retina by means of transpupillary laser photocoagulation in order to generate abnormal vascular tissue involution before retinal detachment occurs. Once the treatment has been prescribed it must be started within the following 72 hours. It may be carried out in the same neonatal unit, with the infant sedated by a neonatologist, or in an operation theatre with the patient under supervision of an anaesthetist. When laser is used in high risk prethreshold stage, the recovery rate is 90-95%. It has been shown to be not as effective in later ROP stages (AP-ROP or zone I ROP) and more than 50% of these cases require additional vitreoretinal surgery.

Retinal detachment occurs if there is a poor response, defining stages 4 and 5 of the ROP. In some cases in stage 4 and very rarely in stage 5 the disease may be controlled by *extrascleral surgery* (placement of a 2.5 solid silicone band, with or without evacuation puncture). In most cases, *vitreoretinal* surgery will be required, a high specialized technique which provides variable results according to different publications.

### A. *Rationale for the proposal*

<table>
<tr>
<td>► Epidemiological data on retinopathy of prematurity (incidence and prevalence).</td>
<td>General incidence of ROP (any stage) is 26% of the infants examined. Percentages for severe cases of ROP (AP-ROP, stages 3-4 and 5): 2-7% for stage 4 ROP and 0.2-1% for stage 5.
<table>
<tr><td>Birthweight</td><td>ROP IV</td><td>Blindness</td></tr>
<tr><td><1000 gr.</td><td>22-44%</td><td>5-11%</td></tr>
<tr><td>1000-1500 gr.</td><td>0.7-3.7%</td><td>0.3-1.1%</td></tr>
<tr><td>>1500 gr.</td><td>0.2%</td><td>0%</td></tr>
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| | In 2005 a total of 465,616 babies were born in Spain. From the total, it is estimated that 1.5% weight <1500 gr. An estimate of 7,000 infants a year show risks of suffering the disease.<br>*Incidence in Spain of this condition varies among hospitals*, between 26.2% and 29%. These are mostly mild cases of ROP, tending to spontaneous recovery.<br><br>Focusing on more severe cases, the figure for severe ROP requiring treatment decreases to 3-7%.<br>When the disease reaches a "threshold ROP" stage (zone I or II, stage 3 ROP with plus disease) it is estimated that a 50% will develop stages 4 and 5. Treatment at this stage decreases significantly adverse response (stage 4 and 5) and the risk of blindness.<br>Nowadays, laser is used in "high-risk prethreshold ROP".<br>The current incidence of stages 4 and 5 in Spain, despite treatment with laser in the acute phase, is estimated to be 0.2-1%. In other words, in Spain there are 70 infants reaching stage 4 or 5 ROP per year.<br><br>*American statistics:*<br>-9,000 preterm infants, out of 14,000-16,000 preterm babies born in the U.S. less than 1,500 gr., develop ROP (50%). 9% require laser treatment and 3% will be legally blind[1].<br>- Despite the high effectiveness of the laser treatment, 12% of the infants with high-risk prethreshold ROP develop stage 4 and 5[2].<br>- Vitreoretinal surgery is required in 0.5% of the preterm infants[3].<br>- In a period of 6 years, the Baylor College of Medicine in Texas, American national reference centre, performed 108 surgeries to patients with stages 4A and 4B ROP[4].<br>- Countries where low weight babies survive, zone I ROP (or AP-ROP) incidence has increased. In this type or retinopathy laser results are poor, and 64% of the cases develop retinal detachment[5].<br><br>*Statistics on Chile:* 45% of the newborns less than 1,500 grams and/or less than 32 weeks GA show ROP and, out of these, 5% reached a threshold ROP with risk of blindness with 2% |

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| | developing blindness[6].<br><br>*Other references on stage 4 and 5 ROP*<br>- ROP incidence >3 has decreased along the years; however, there is great variability in incidence when comparing some centres to others. This variability depends on multiple factors: differences in clinical practice (screening differences; differences in laser use; pre-threshold stage versus threshold stage; differences in neonatal care, for example exhaustive oxygen saturation monitoring in order to avoid fluctuations, etc...) [7,8,9,10,11].<br><br>Whichever the statistic considered, stage 4-5 ROP incidence is higher in developing countries (Latin America, Asia, Eastern Europe) but also in developed countries where survival rates for extreme low weight babies, who more frequently develop AP-ROP, have improved[5]. |
| ► Data on the use of vitrectomy in children. | -Early vitreoretinal surgery (stage 4A ROP) in experienced hands has acceptable results[12,13,14]. Vitreoretinal surgery for stage 5 ROP or AP-ROP (ROP or zone I ROP) has variable results[15,16,17,18,19,20,21,22,23]. Anatomic success varies from 13% to 76% but functional results are usually poor[24,25].<br>-Limited research, recently published, shows that vitreoretinal surgery with laser, associated or not to angiogenic therapy, is the treatment preferred for zone I ROP (posterior ROP or AP-ROP) [26,27,28,29]. |

**B.** ***Guidelines to be followed by Centres, Services and Units in order to be designated as Reference Centres, Services and Units treating advanced retinopathy of prematurity.***

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| ► Experience of the Reference Centres, Services and Units:<br><br>- Activity:<br><br>• Number of procedures in children that | At least 40 vitrectomies per year. |

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| should be performed in a year to ensure an adequate care of the advanced retinopathy of prematurity. | |
| • Number of procedures that should be performed in a year of techniques, technologies and procedures similar to those specific to the designation requested. | At least 15 laser therapies per year. |
| - Other data: research on the subject, postgraduate teaching, continuing training, etc. | - Accredited postgraduate teaching.<br>- Participation in research projects and publications in the field[a].<br>- Continuing training programs[a]. |
| ► Specific resources of the Reference Centres, Services and Units: | |
| - Human resources required for the adequate care of advanced retinopathy of prematurity. | - Two ophthalmologists.<br>- 24 hour continuous ophthalmic care, given the need for postoperative monitoring and the possibility of complications during the first hours.<br>- Nursing staff, surgical auxiliaries and technicians. |
| Professional experience[b]: | - Ophthalmologist with more than 3 years experience performing ROP screening, diagnosis and treatment and using laser in preterm infants, as well as in children's ophthalmic pathology.<br>- Ophthalmologist with more than 5 years experience in vitreoretinal surgery in preterm babies.<br>- Nursing staff with experience in premature babies and eye pathologies. |
| - Specific equipment required for the adequate care of advanced retinopathy of prematurity. | - Established ophthalmic operating theatre in order to avoid movement of high sophisticated equipment.<br>- Laser: Mobile laser equipment with head to perform indirect photocoagulation and with |

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| ► Resources from other units and services besides those belonging to the Reference Centres, Services and Units required for the adequate care of advanced retinopathy of prematurity. | endolaser fibre connection.<br>- Vitrectomy equipment:<br>▪ High speed vitrectomy cutter (higher than 1000 cpm) with air pump system, silicone injection, two light sources, electric surgical scissors kit.<br>▪ Specific equipment for vitroretinal surgery.<br>▪ Ability to perform 25G vitrectomies.<br>▪ Surgical microscope which enables wide visual field system, both contact and non-contact mode, with lenses set.<br>▪ Lens system for panoramic, wide field of vision for corneal contact surgery.<br>▪ Disposable material (light probes with irrigation systems and 2.5mm infusion cannulas).<br>-Adjuvant treatments: antiangiogenic drugs.<br><br>- Neonatology.<br>- Anaesthesia services with experience in paediatric patients[b].<br>- Intensive care unit with experience in paediatric patients[b]. |
| ► Procedure and clinical results indicators of the Reference Centres, Services and Units [c]: | **The indicators will be agreed with the Units that will be designated.** |
| ► Existence of an adequate IT system:<br>(Type of data that the IT system must include to allow identification of the activity and evaluation of the quality of the services provided) | - Filling up the complete MBDS of hospital discharge.<br><br>- The unit must have a *registry of patients* with advanced retinopathy of prematurity which at least must include:<br>- Medical record number.<br>- Date of birth.<br>- Sex.<br>- Admission date and discharge date.<br>- Family history (mother, siblings, multiple births...). |

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| | - Neonatology data (gestational age, weight at birth, other risk factors, other procedures ...).<br>- Diagnosis procedures performed to the patient (ICD-9-CM).<br>• Number of ophthalmologic examinations performed.<br>• Other diagnosis procedures.<br>- Main diagnosis (ICD-9-CM).<br>• Clinical situation at the time of diagnosis (ROP stage).<br>- Number and type of therapeutic procedures provided to the patient (ICD-9-CM):<br>• Laser.<br>• Vitrectomy.<br>• Other therapeutic procedures.<br>- Treatment results.<br>• Retinal detachment.<br>- Complications.<br>- Patient's progress.<br><br>- The unit must have the required data which should be sent to the Spanish National Health Service Reference Centres, Services and Units Appointment Commission Secretariat for yearly reference unit monitoring. |

[a] *Criteria to be assessed by the Appointment Commission.*
[b] *Experience will be accredited by certification from the hospital manager.*
[c] *Clinical results standards, agreed to by the experts group, will be assessed, initially by the Appointment Commission, while in the qualification process, as more information from the Reference Centres, Services and Units is being obtained. Once qualified by the Appointment Commission, the Quality Agency will authorize its compliance, as for the rest of guidelines.*

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