Module 2: Diagnoses Associated with Prematurity and Developmental Implications

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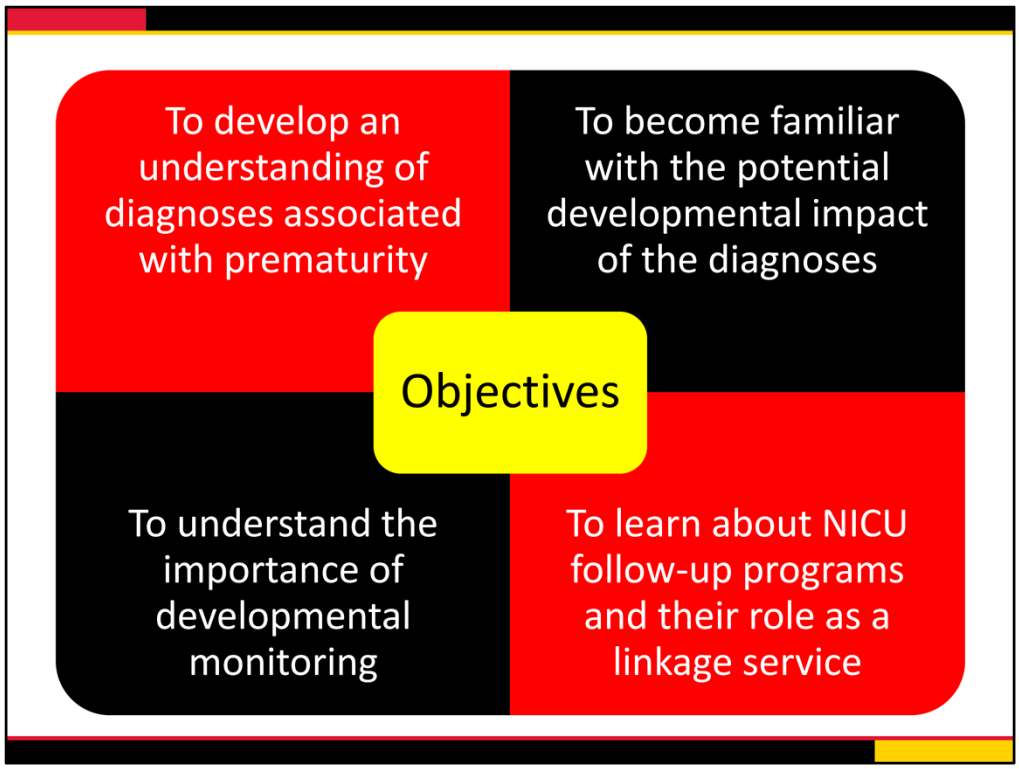
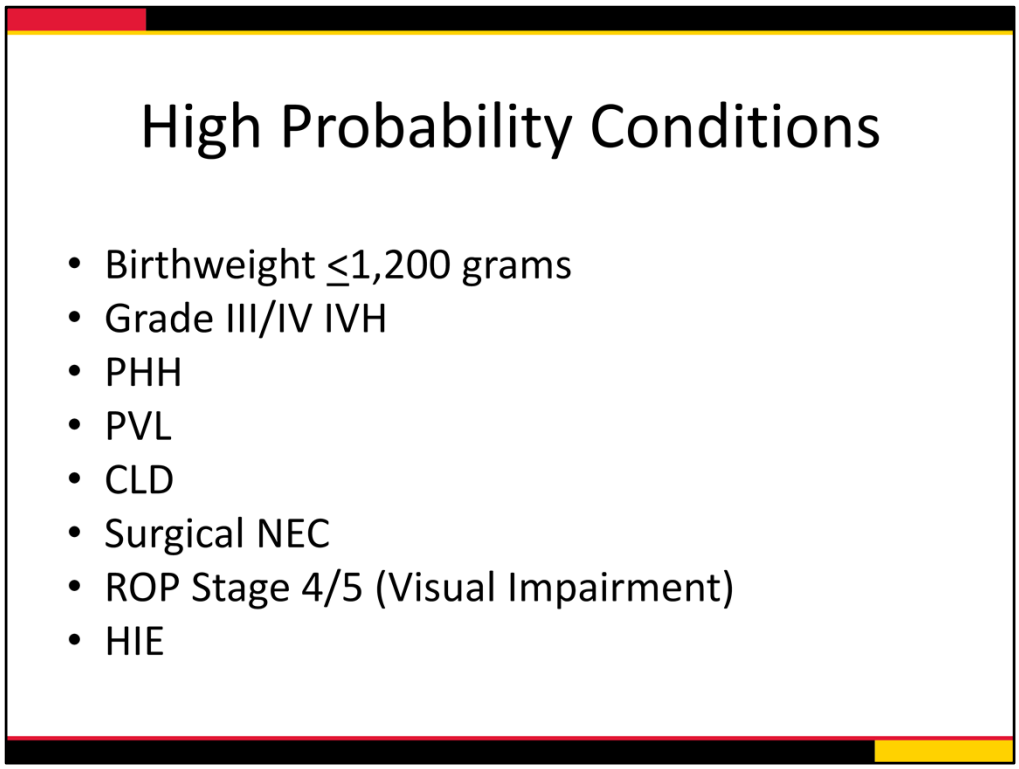
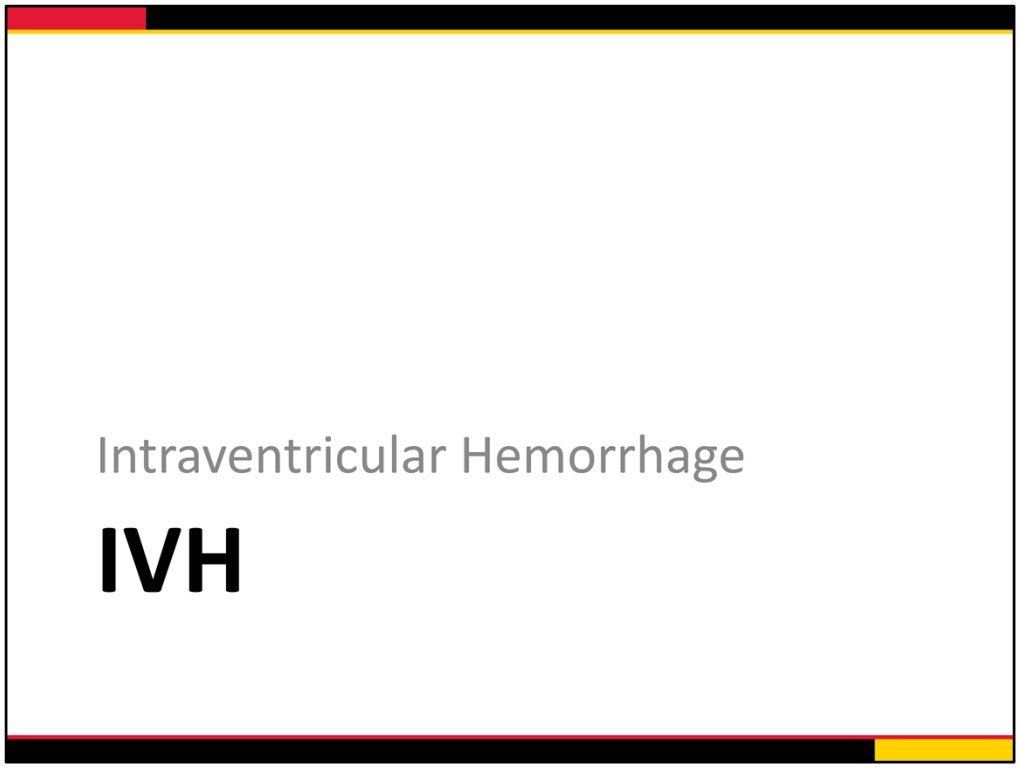
In this presentation, we will discuss diagnoses associated with prematurity and developmental implications. This is the second in a series of five modules relevant to infants and toddlers born prematurely.



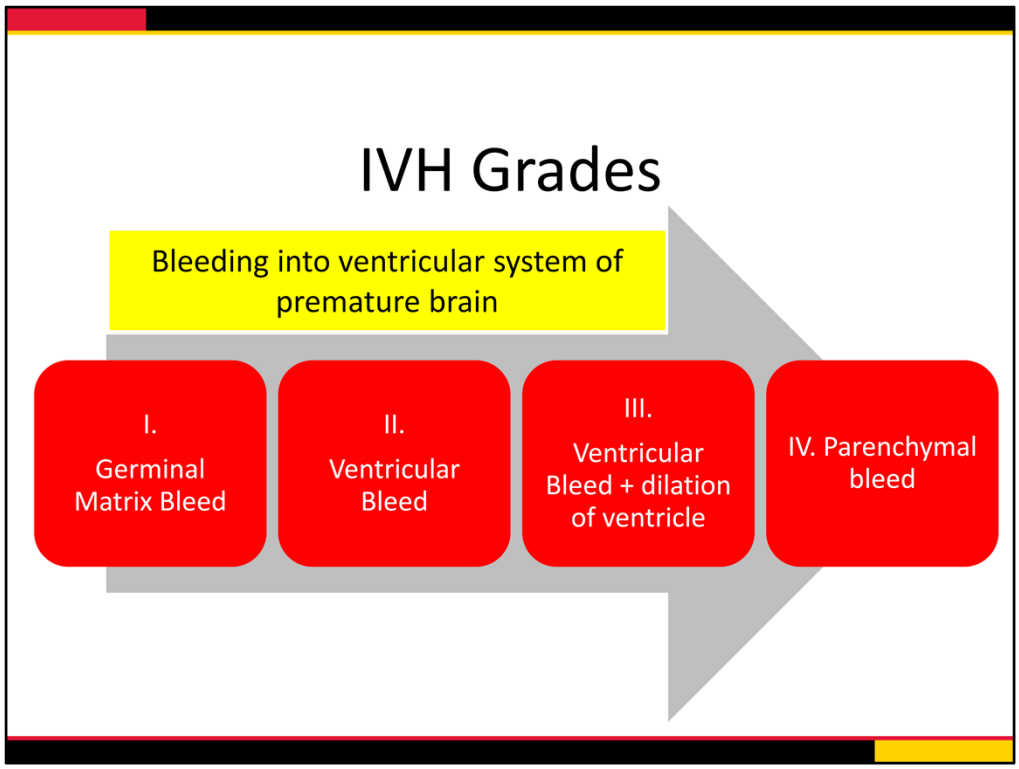
There are four objectives to this presentation. The first is to develop an understanding of diagnoses associated with prematurity. The second is to become familiar with the potential developmental impact of the diagnoses. The third is to understand the importance of developmental monitoring. The fourth and final objective is to learn about NICU Follow-Up programs and their roles as a linkage service.



In this presentation, we will learn about eight high probability conditions seen in infants hospitalized in a neonatal intensive care unit (also known as a NICU). Seven of these high probability conditions are seen in infants born prematurely: a birthweight of less than 1,200 grams, a Grade III and IV Intraventricular Hemorrhage (also known as IVH), Post Hemorrhagic Hydrocephalus, Periventricular Leukomalacia, Chronic Lung Disease, Necrotizing Enterocoitis requiring surgery, and Retinopathy of Prematurity Stage 4 and 5. The eighth high probability condition, Hypoxic Ischemic Encephalopathy, is seen in full-term infants hospitalized in the NICU.



Let's begin with intraventricular hemorrhage or IVH. IVH is the most common brain injury seen in premature infants. The incidence is higher and it is most severe in those born at the youngest gestational ages. IVH occurs in about half of infants born weighing less than 1,000g and most frequently occurs in the first 3 to 4 days of life. IVH rarely occurs in babies born after 34 weeks gestation.



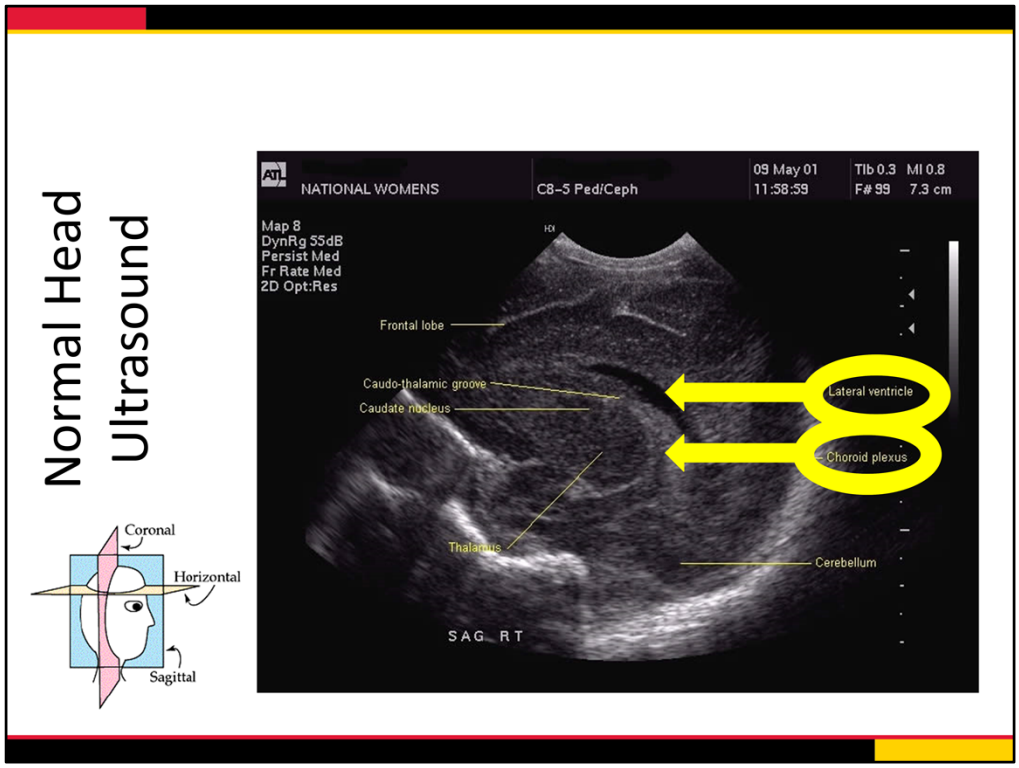
IVH involves bleeding into the ventricular system of the premature brain that begins in the germinal matrix. The germinal matrix is a layer of the premature brain adjacent to the lateral ventricles. It is a highly vascular region where neurons differentiate and migrate out to the developing brain. The walls of the blood vessels are very thin and prone to rupture into the ventricles. There are four grades of IVH:

(1) Grade I IVH is a germinal matrix bleed,

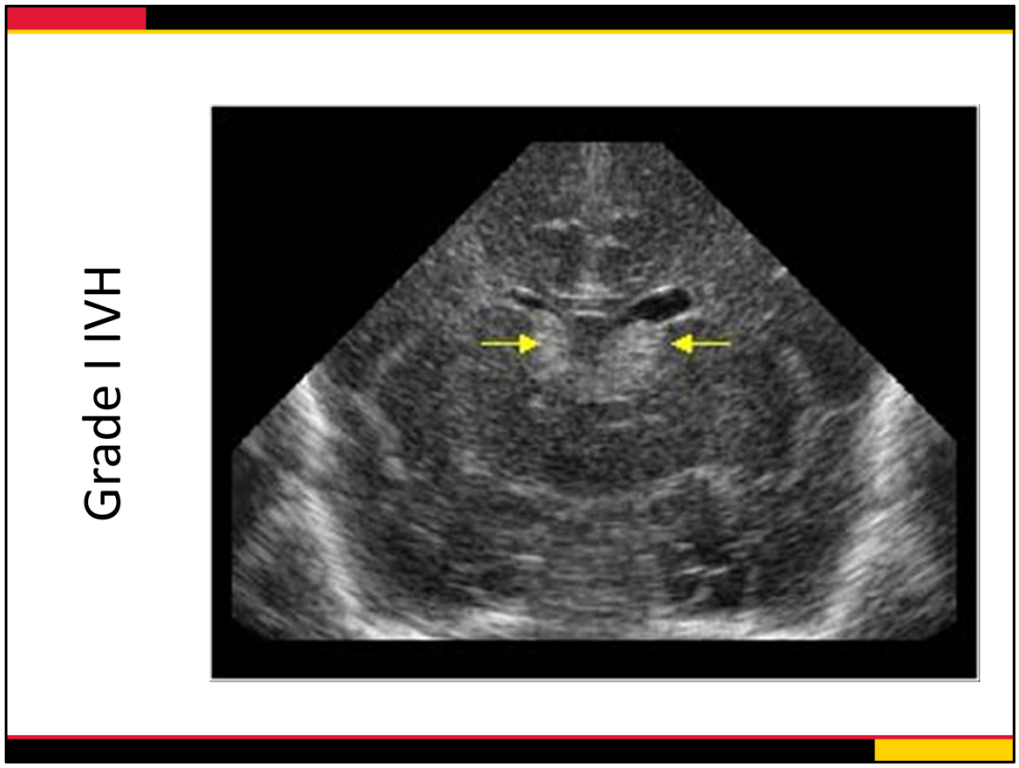
(2) Grade II IVH is a ventricular bleed,

(3) Grade III IVH is a ventricular bleed with dilation of the ventricles, and

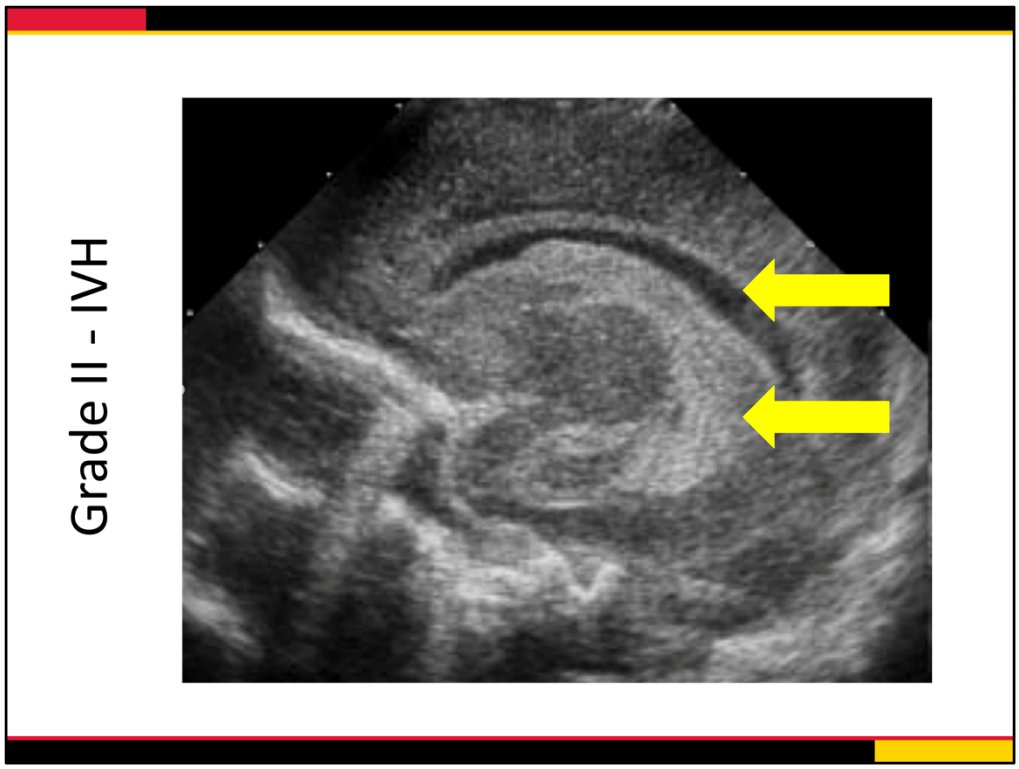
(4) Grade IV IVH is a parenchymal bleed, into the brain tissue.



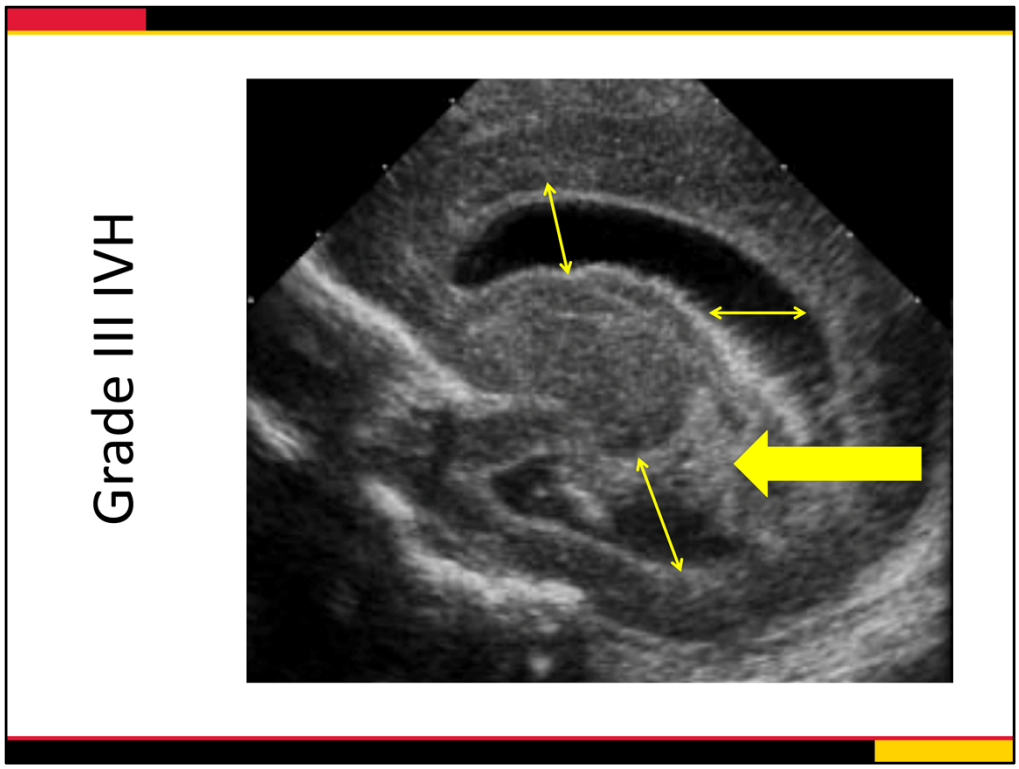
This is a right sagittal head ultrasound image of the neonatal brain showing a normal right lateral ventricle and choroid plexus. The choroid plexus is the location in the brain where cerebral spinal fluid is made. In this image, the ultrasound beam is going through the anterior fontanel; as the probe is moved around the head, different images are captured so you can look at the brain from various angles. Sagittal head ultrasound allow visualization of the left and right ventricles from the side, like a profile. Coronal views visualize the brain from front to back.



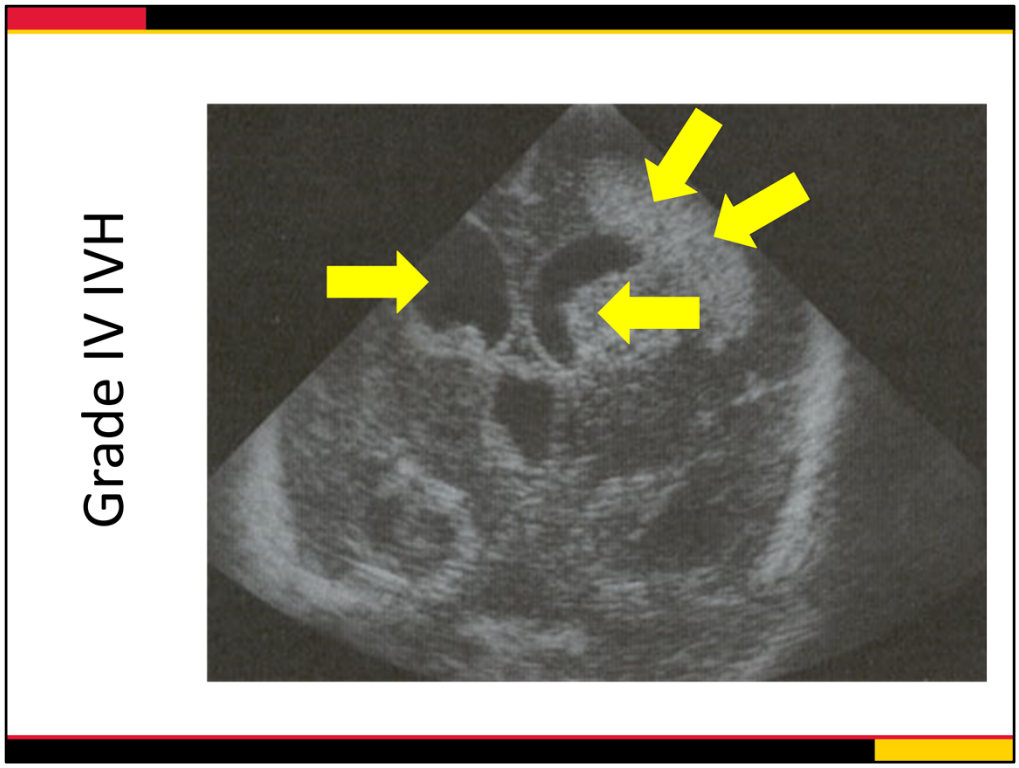
This is a coronal view of the neonatal brain demonstrating blood in the germinal matrix which is a grade I IVH. Of note, there is no blood in the lateral ventricles and the ventricles are not dilated.



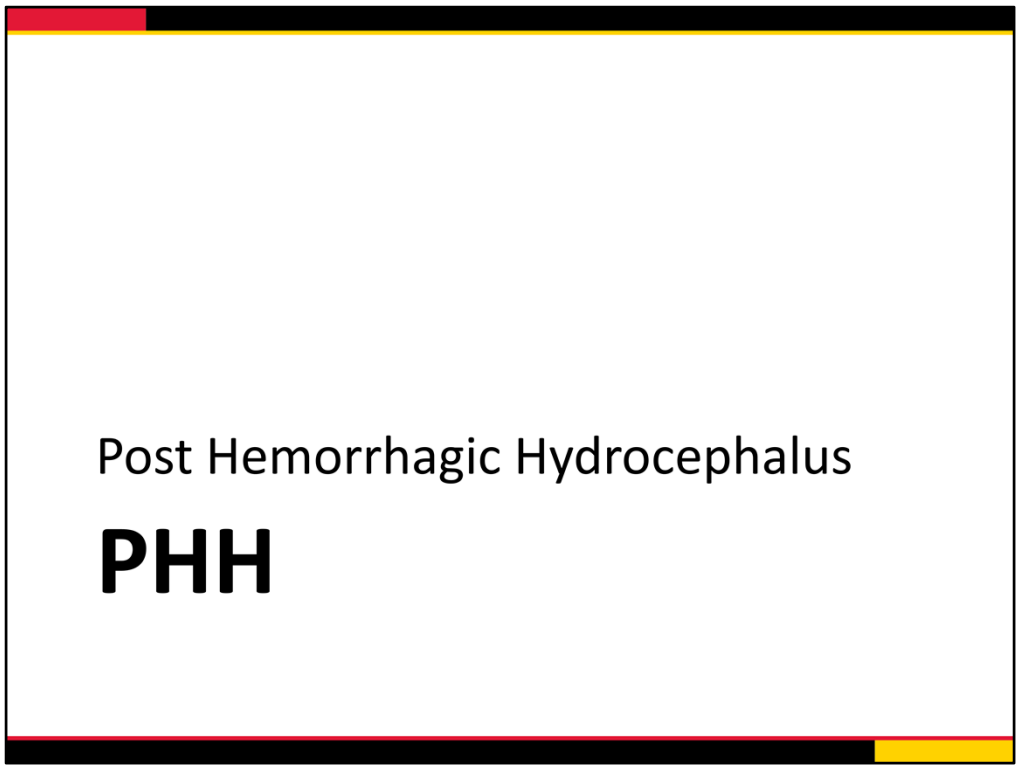
This sagittal view of the neonatal brain demonstrates blood filling the right lateral ventricle. This is classified as a Grade II IVH. The lucent or darker outline of the ventricle represents the part of the ventricle not filled with blood.



This sagittal view shows not only blood in the lateral ventricle, but a dilated ventricle consistent with a Grade III IVH. As a reminder, the bright white area depicts the bleed and the wide black area illustrates the dilated ventricle. The dilated ventricle pushes against the adjacent brain, this pressure may destroy some of the brain cells in the surrounding area.

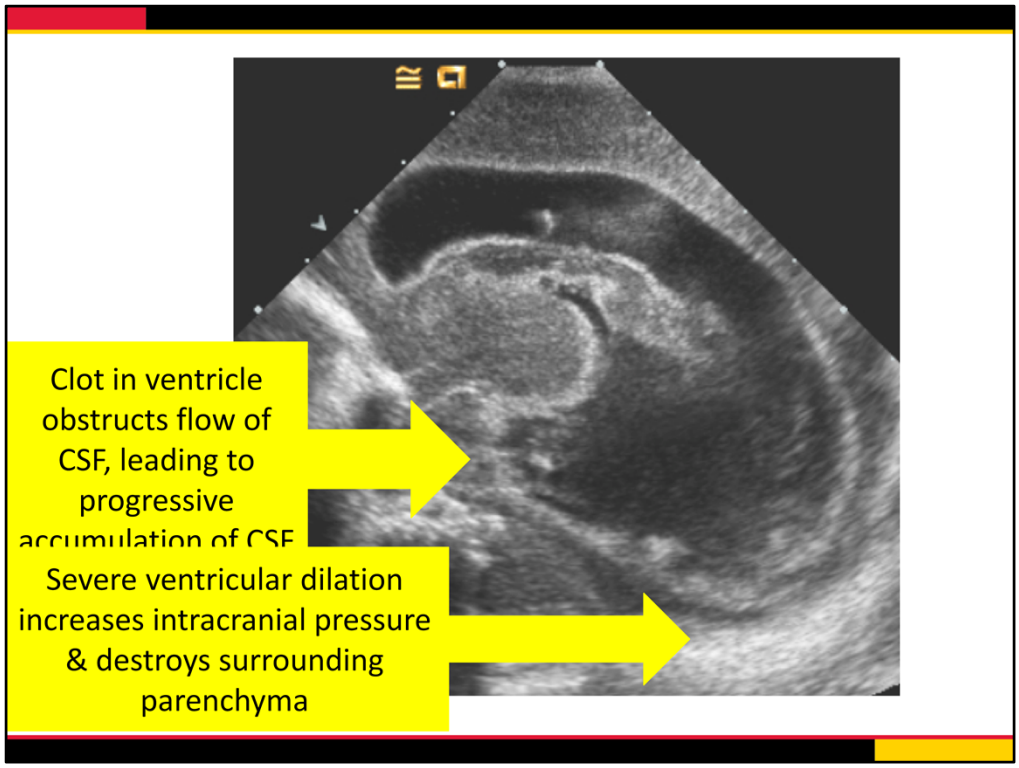


This coronal HUS shows blood in the left ventricle, and blood extending to the surrounding brain tissue on the left side. When there is bleeding involving the brain tissue, the cells are destroyed and eventually replaced with a cyst. On the right you can see a Grade III IVH.

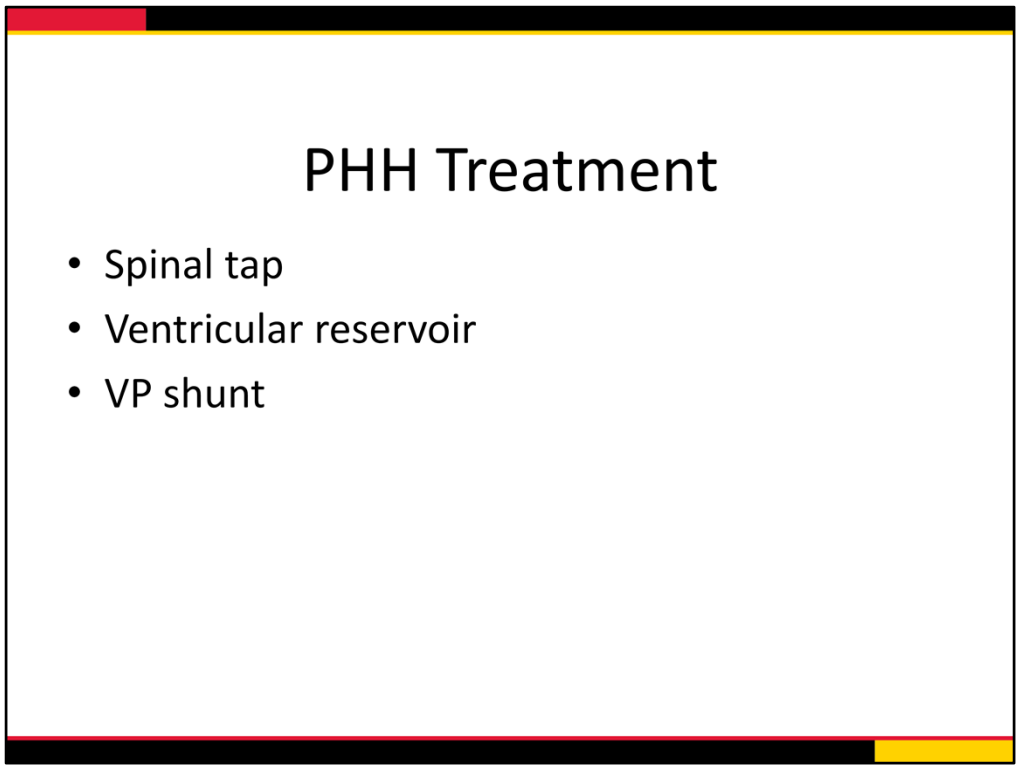


Post Hemorrhagic Hydrocephalus is a complication of IVH. It occurs most commonly after Grade III IVH, when blood clots in the lateral ventricles obstruct the normal outflow of CSF being made in the choroid plexus.

Cerebral spinal fluid that is made in lateral ventricles travels through the ventricular system to the subarachnoid space where it protects and cushions the brain and spinal cord. After an intraventricular hemorrhage, particulate blood clots may clog this system. When this occurs, cerebral spinal fluid accumulates in the lateral ventricles.



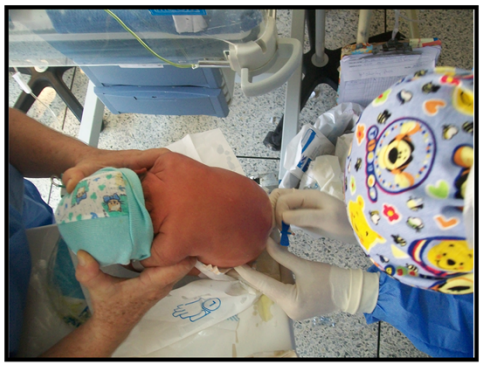
This sagittal head ultrasound shows a very dilated lateral ventricle with organized blood clots. Severe ventricular dilation increases intracranial pressure and destroys the surrounding brain tissue.



PHH is treated initially with serial spinal taps or a ventricular reservoir until the clots in the ventricle resorb. Some infants with persistently dilated ventricles require a ventriculoperitoneal (VP) shunt.

PHH Treatment

- Spinal tap
- Ventricular reservoir
- VP shunt

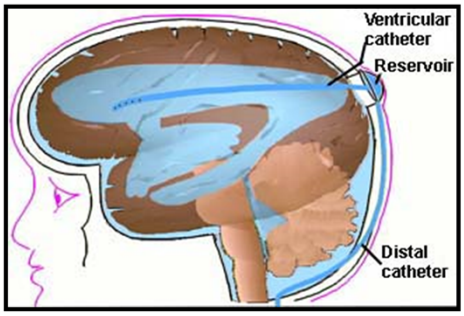


http://upload.wikimedia.org/wikipedia/commons/3/3e/New_born_spinal_tap.JPG

In a spinal tap, a needle is placed in the back to remove cerebral spinal fluid from the spinal canal to relieve the pressure.

PHH Treatment

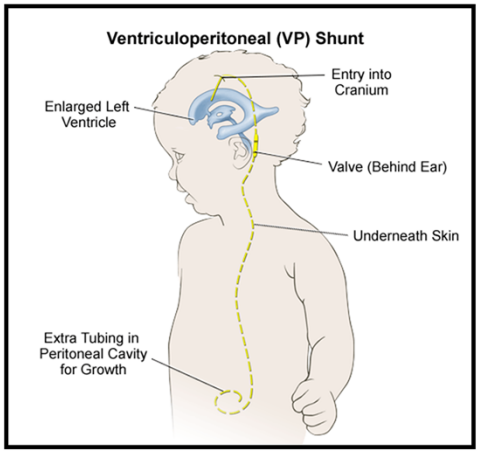
- Spinal tap
- Ventricular reservoir
- VP shunt



A ventricular reservoir is placed by a neurosurgeon. It is a temporary tube placed directly into the ventricular space that drains cerebral spinal fluid to a reservoir under the skin until the clots reabsorb.

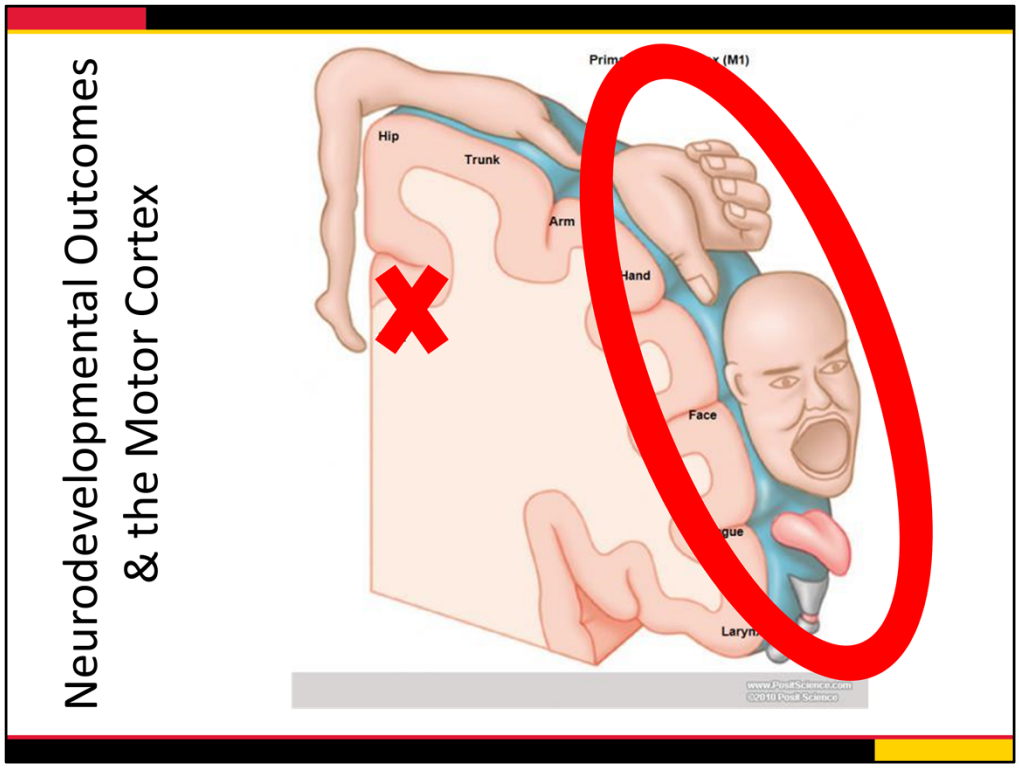
PHH Treatment

- Spinal tap
- Ventricular reservoir
- VP shunt

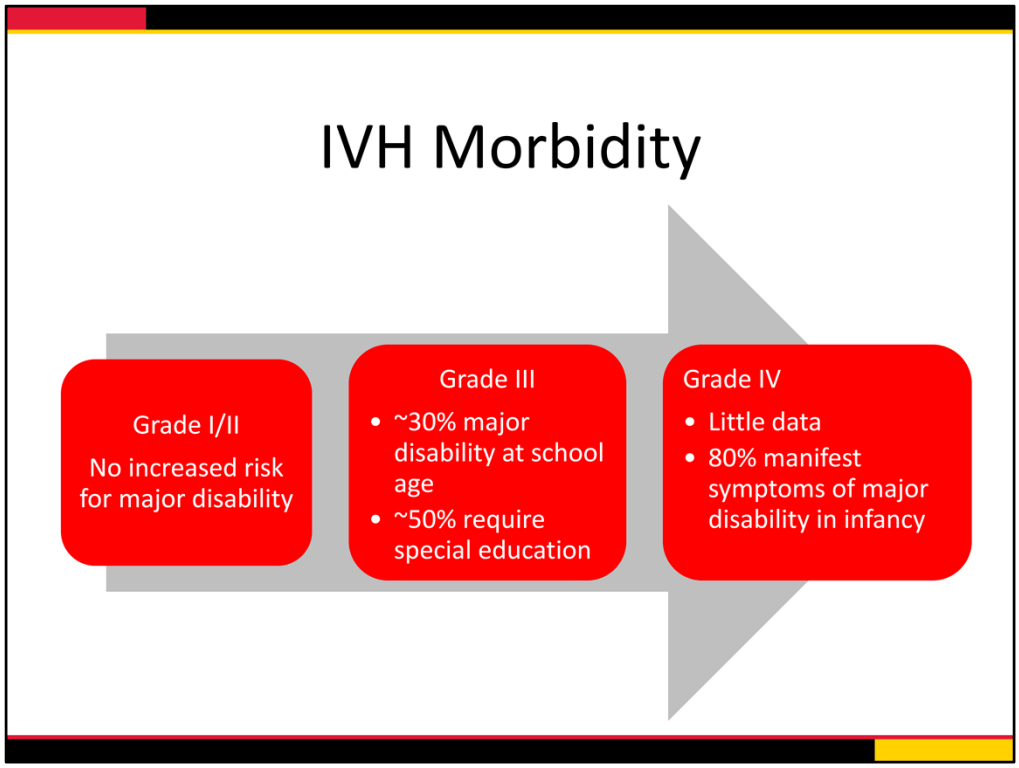


http://www.yalemedicalgroup.org/stw/images/161397.jpg

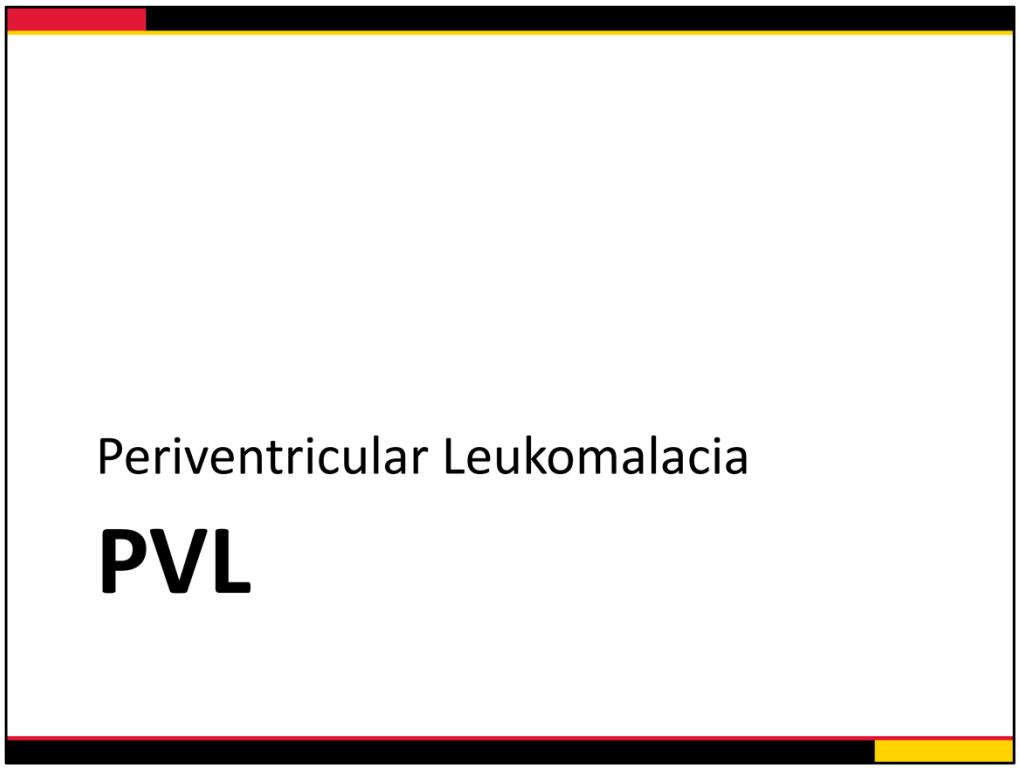
A VP shunt is a tube that connects the ventricular space to the peritoneal space in the abdomen to drain the cerebral spinal fluid. With infants born prematurely, the surgeon has to wait until the baby is big enough and strong enough to survive the surgery before placing a VP shunt.



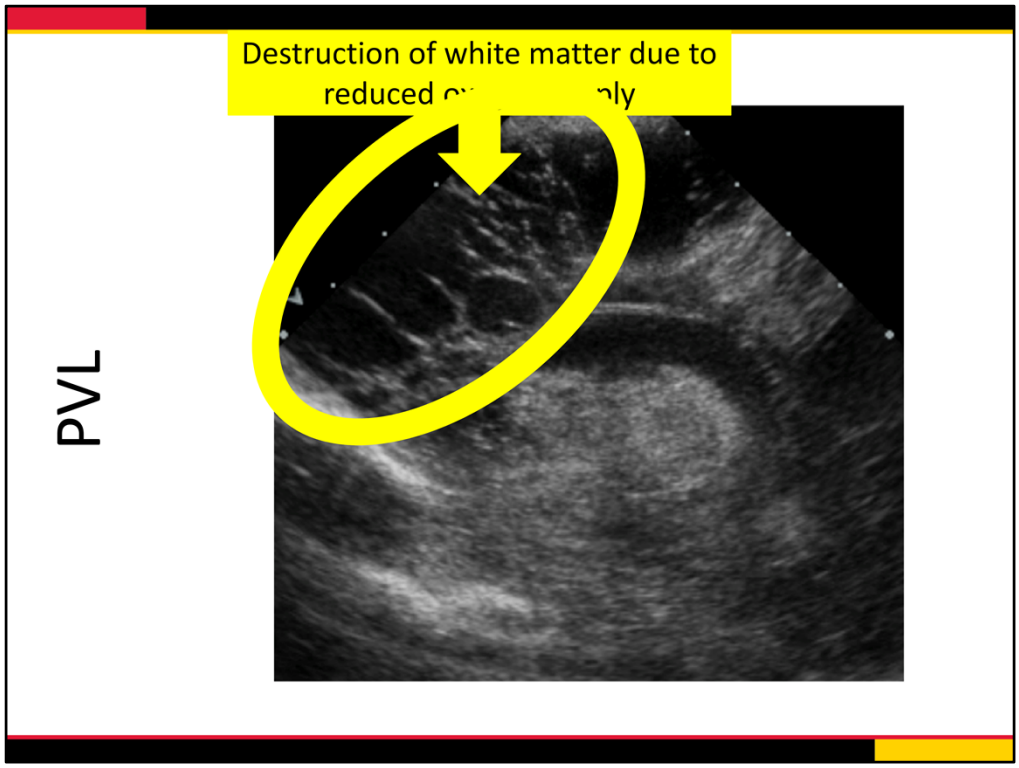
This figure is known as a homunculus. It depicts the distribution of motor signals coming from the brain as they move from the center of the brain outward. Notice that the motor fibers that control the lower extremities of the body are closest to the ventricle. This explains why spastic diplegia is the most common sequelae of IVH. The larger parts of the homunculus show parts of the body that require more motor control from the brain.



IVH Grades I and II are not associated with increased risk for major disability. Approximately 30% of children with a Grade III IVH will have a major disability at school age; the most common is spastic diplegia. Spastic quadriplegia may occur when the bleed is more severe. Approximately 50% of children with a Grade III IVH require special education services in elementary school; the most common reasons are cognitive, neurosensory, and neuromotor disabilities. There is less data regarding the outcomes associated with a Grade IV IVH because these bleeds occur less frequently and there is a higher rate of mortality. 80% of children with a grade IV IVH manifest the symptoms of a major disability in infancy; the most common sequelae is contralateral motor dysfunction, which may lead to hemiparesis and depending on the size of the bleed, cognitive and neurosensory impairment also may occur.



Periventricular leukomalacia (or PVL) is a condition caused by limited blood flow to the developing white matter of the brain that occurs most commonly in infants born prematurely.

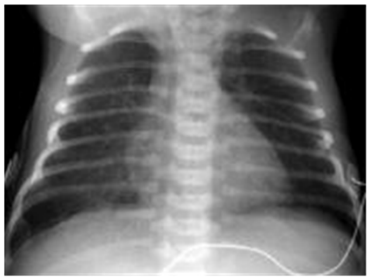


Like IVH, PVL commonly affects the brain parenchyma closest to the lateral ventricles. It is also most common in the sickest and most premature infants. PVL is seen on HUS towards the end of the first month of life. PVL involves destruction of the white matter of the brain due to reduced oxygen supply. After the brain parenchyma is destroyed, affected areas are replaced by cysts. This left sagittal HUS shows multiple cysts in the brain parenchyma, giving a Swiss cheese like appearance. After brain parenchyma is destroyed, infants may develop neurodevelopmental, neurocognitive and neurosensory impairments that correlate with the degree of injury. This image represents a severe case of PVL.

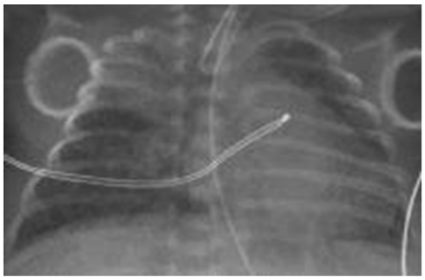
Chronic lung disease is a condition that typically affects premature infants that require prolonged treatment with a mechanical ventilator and oxygen to breathe. In chronic lung disease, immature lung tissue may trap air, collapse, or fill with fluid. Infants with chronic lung disease are often discharged from the NICU on oxygen. They are prone to develop severe breathing problems with upper respiratory infections and many develop asthma. However, as they grow and develop, their lung function typically improves. Chronic lung disease is also known as bronchopulmonary dysplasia, or BPD.

CLD

- Need for oxygen on DOL #28
- Need for oxygen at 36 weeks PCA



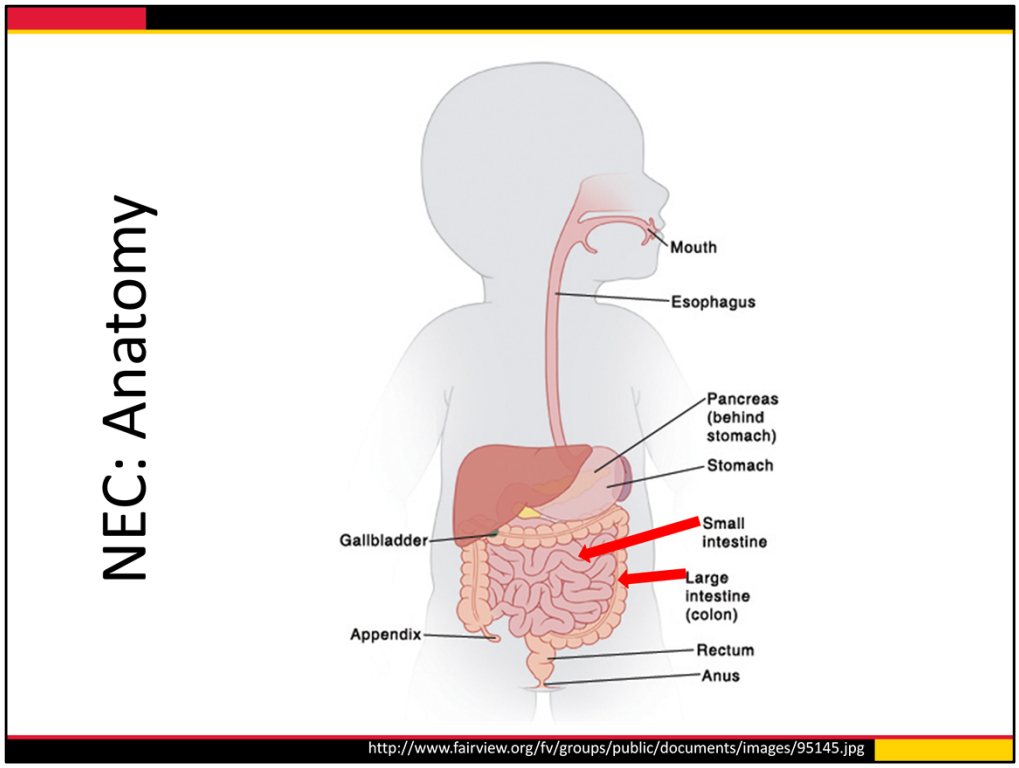
Normal lung x-ray



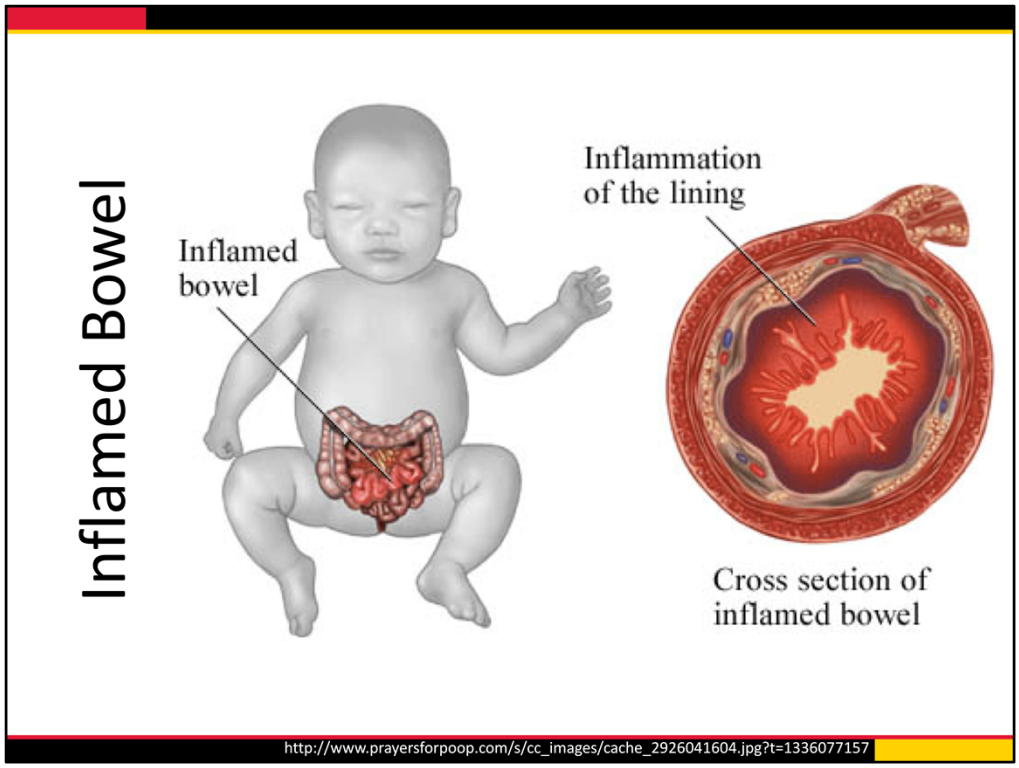
X-ray depicting CLD

Chronic lung disease is defined in two ways: the first is the need for oxygen on day of life number 28, the other is the need for oxygen at 36 weeks post-conceptual age. This image shows the appearance of normal lungs and heart in a premature infant on chest x-ray. The image on the right shows an infant with an endotracheal tube in place, and focal areas of inflammation and collapse of the lung. In a study conducted at the University of Maryland School of Medicine, the diagnosis of chronic lung disease, regardless of birthweight, was highly correlated with the receipt of early intervention services.

Necrotizing enterocolitis, or NEC, is the most common life threatening disease affecting the gastrointestinal tract of premature infants. Like IVH, its incidence directly correlates with the degree of prematurity.

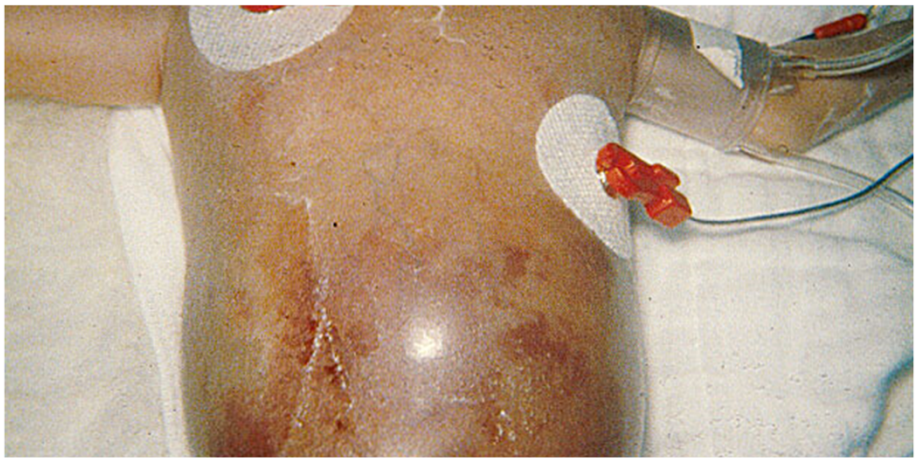


NEC develops after the introduction of feedings and is thought to be due to the combination of overproduction of bacteria and a poorly functioning immune system in premature babies. NEC can affect any segment of the small intestine or large intestine. Milder cases can be managed by resting the bowel and antibiotics. More severe cases require surgery.



When infants develop NEC, inflammation occurs within the bowel wall that may lead to thinning, destruction of bowel tissue, and perforation of the bowel. When the bowel perforates, contents spill into the abdominal (or peritoneal) cavity and surgery is required to remove damaged sections of bowel and repair the bowel.

Premature Infant with NEC



This image shows distension and discoloration of the abdominal wall due to damaged and perforated bowel in an infant with NEC. Infants in this condition require emergent surgery and long term antibiotic therapy. Those infants with more severe cases requiring surgery may develop liver dysfunction (due to prolonged IV nutrition), short bowel syndrome (which occurs when too much of the intestine needs to be removed), and failure to thrive (when there is not enough bowel remaining for digestion). Infants with surgical NEC are at risk for neurodevelopmental sequelae.

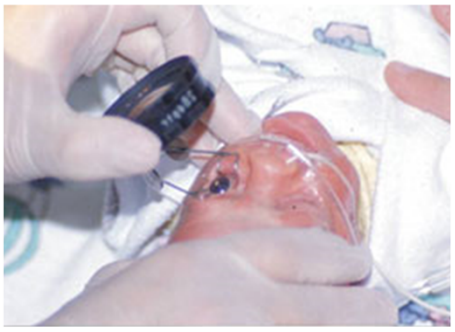
Breastmilk

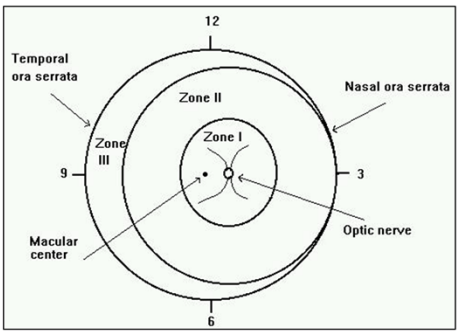
http://www.fda.gov/ucm/groups/fdagov-public/documents/image/ucm335265.jpg

Breastmilk is the only known protective factor against NEC.

Retinopathy of prematurity, or ROP, is a progressive eye disease that occurs in premature infants. The incidence of ROP is directly correlated with the degree of prematurity and use of oxygen therapy in the NICU. The blood vessels of the retina normally finish growing several weeks before babies are born. In premature infants, the blood vessels are not finished growing until after the baby is born, and may grow abnormally. ROP begins with mild changes in the blood vessels of the retina and may progress to severe changes and scarring. Scarring can lead to retinal detachment and blindness if severe ROP is not treated.

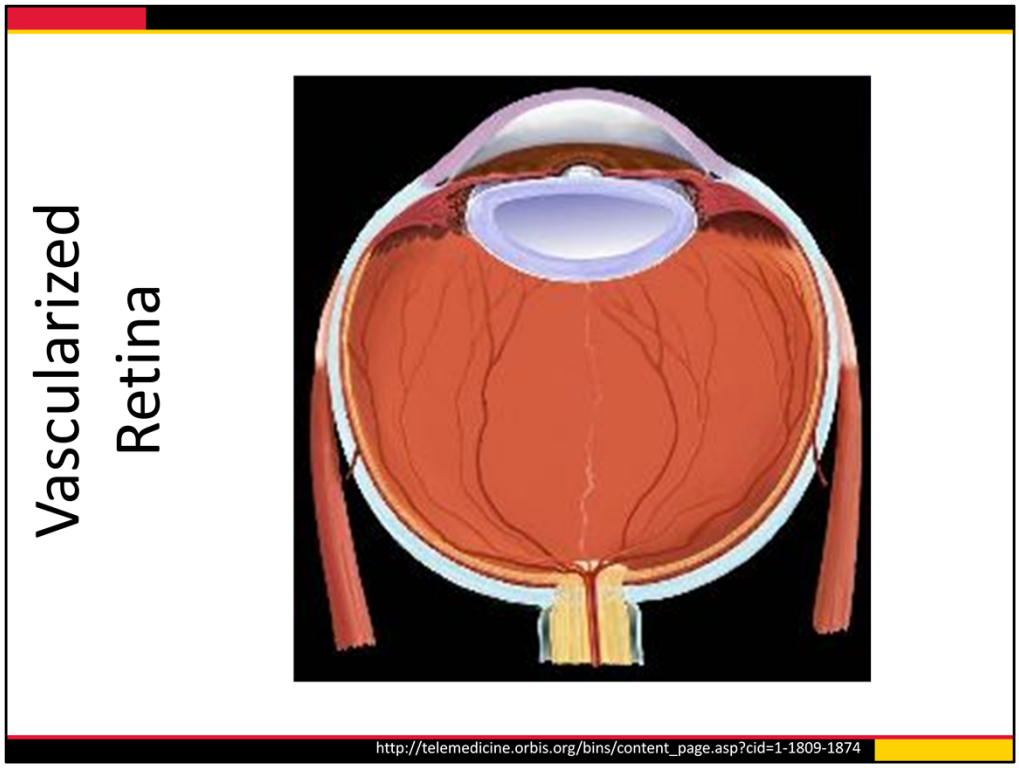
Diagnosing ROP



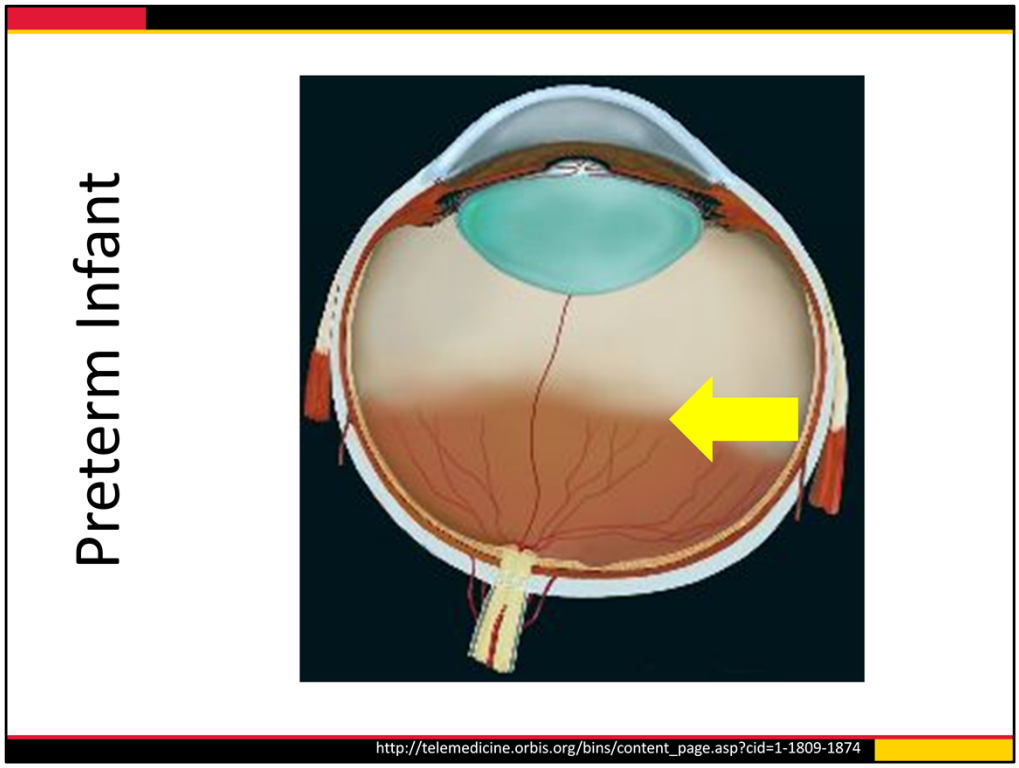


http://www.aapos.org/client_data/files/2011/_135_retinopathy1.jpg

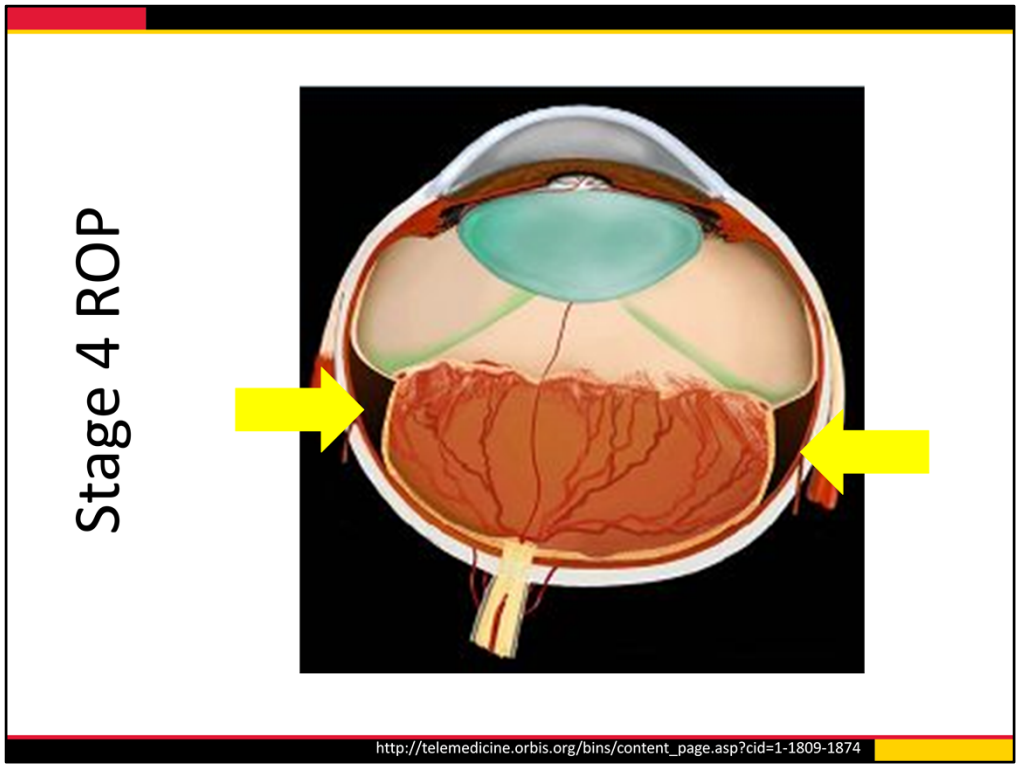
ROP is diagnosed by an ophthalmologist who examines the eyes after dilating them with eye drops. The retinal blood vessels begin to grow at the center of the retina next to the optic nerve. The zones in the picture above describe the location of the immature blood vessels around the optic nerve. If ROP develops in the lower zones nearer to the optic nerve, it may have a greater impact on vision than in the more peripheral zones. The stage of ROP describes abnormal retinal blood vessel formation that may lead to scarring and retinal detachment.



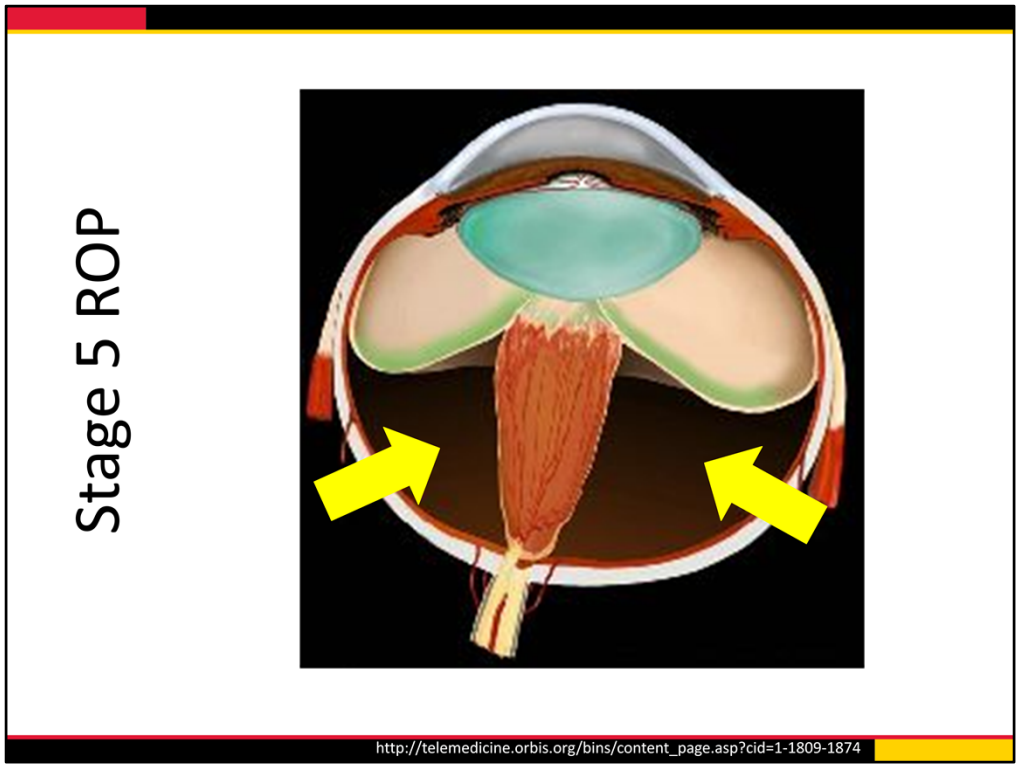
This image depicts the retina of a full term infant with the retina blood vessels fully developed.



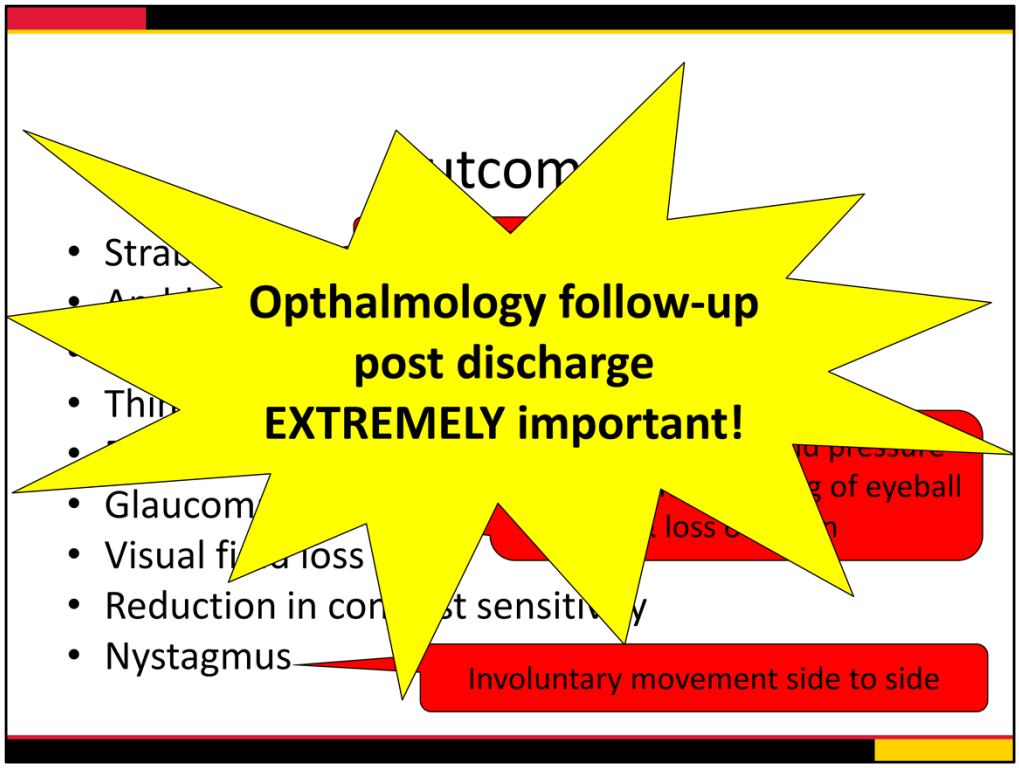
This image depicts the retina of a preterm infant that is not fully vascularized. Here the blood vessels have developed in the back of the eye only.



Concerns exist if infants develop what is termed threshold disease, in which an infant has a 50% chance of developing retinal detachment. Serial eye exams are performed in the NICU, and if threshold disease is reached laser surgery is performed to prevent Stage 4 (or partial retinal detachment) or Stage 5 (retinal detachment). This image shows Stage 4 ROP or partial retinal detachment. The yellow arrows indicate the areas of detachment of the retina from the supporting layers of the eye.



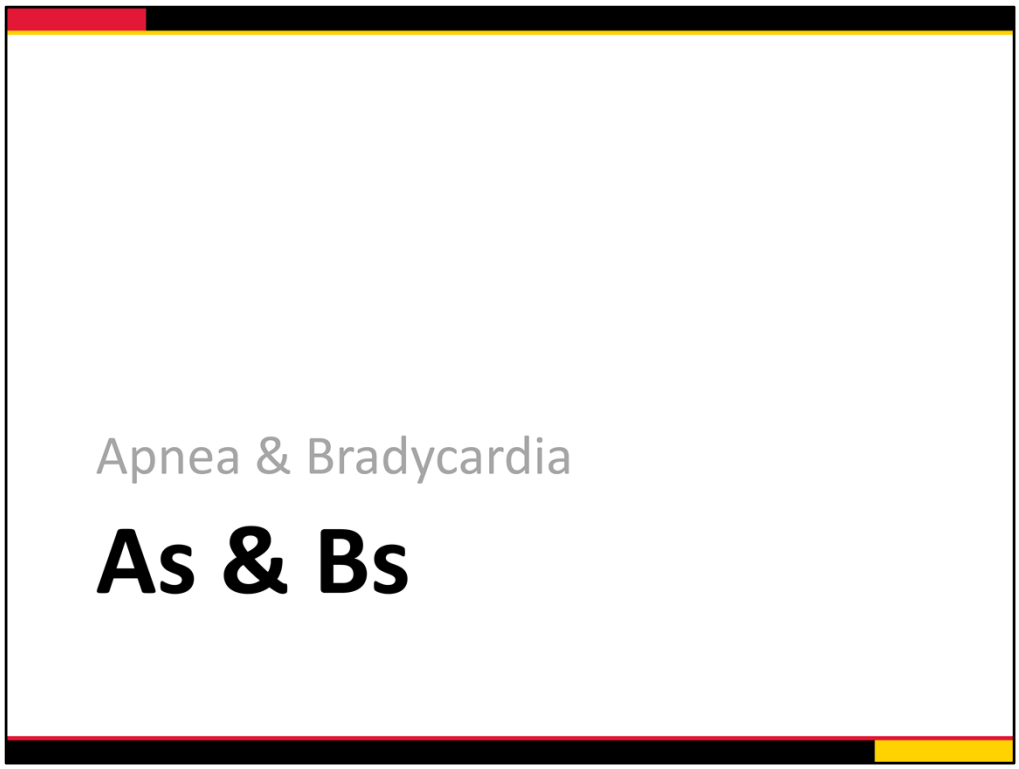
In Stage 5 ROP, there is complete retinal detachment. In Stage 5 ROP, infants usually have no useful vision, even if surgery is performed to repair the detachment.



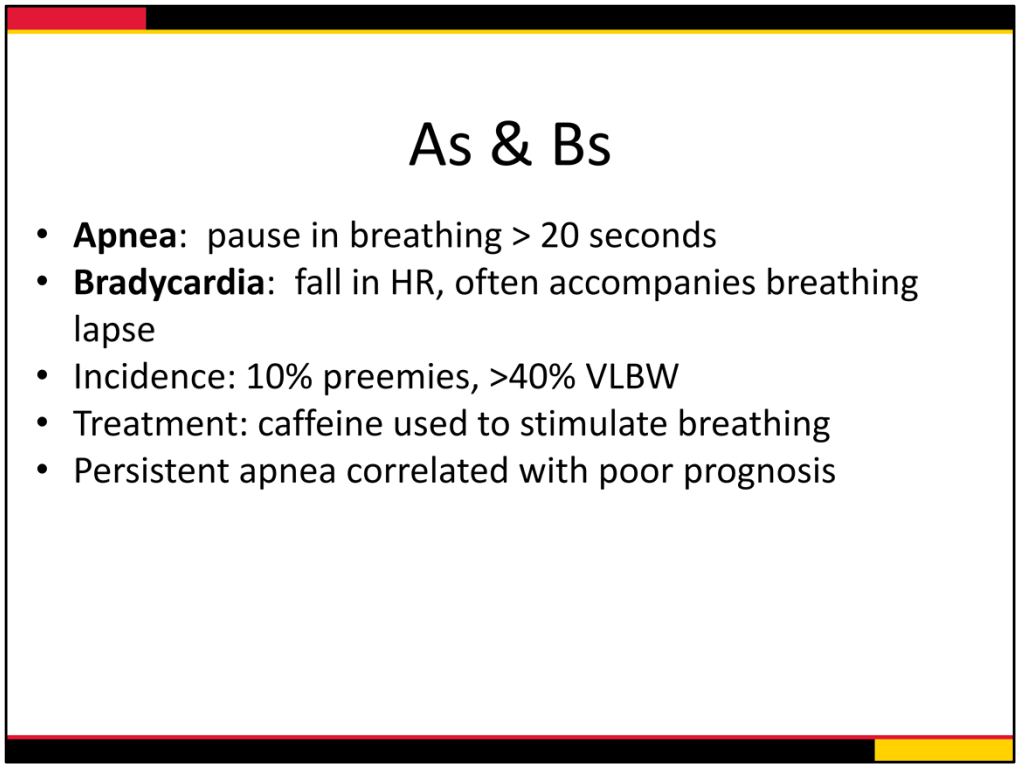
Possible outcomes of ROP include strabismus:

- (crossed eyes or lazy eye) or amblyopia
- (vision in one eye is reduced because the eye and brain are not working together), myopia
- (nearsightedness), thinning of the retina, retinal tears, glaucoma
- (abnormally high fluid pressure in the eye that may cause loss of vision), reduced visual acuity, visual field loss, reduction in contrast sensitivity, and nystagmus
- (involuntary movement of the eye side to side).

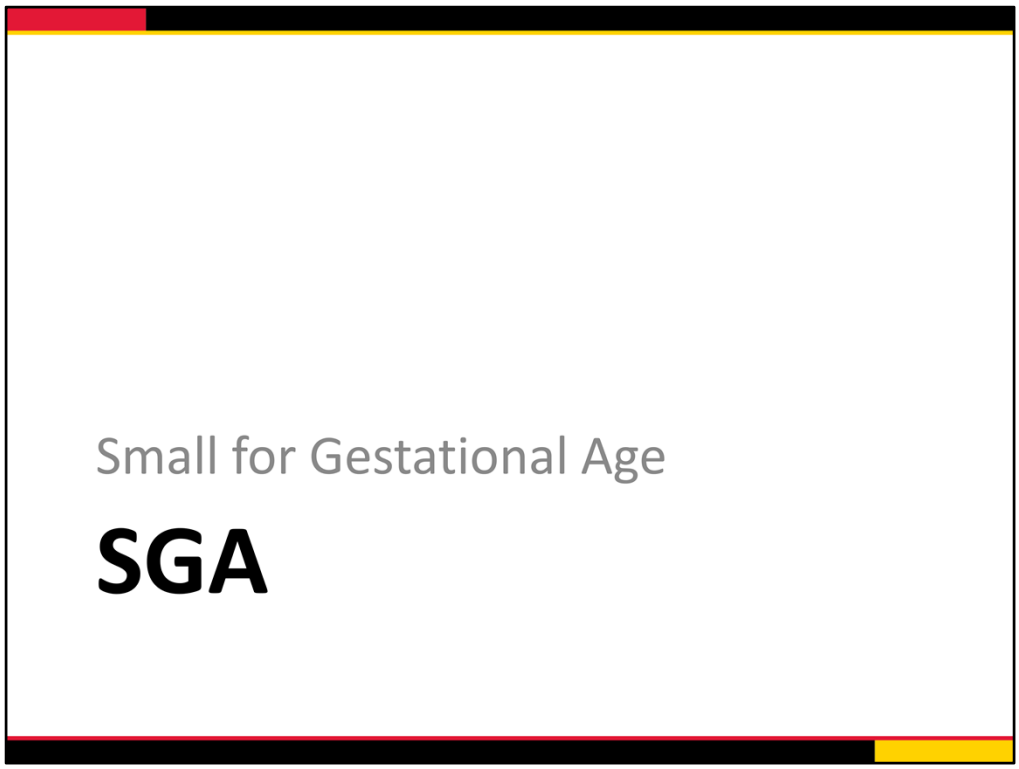
Infants with ROP require close ophthalmology follow-up post discharge, so that threshold disease is diagnosed and retinal detachment can be prevented. Regular appointments will be required until the infant's retinas are fully vascularized. Ophthalmology appointments will then become intermittent. ROP follow-up, when needed, should be included in the IFSP as a linkage service.



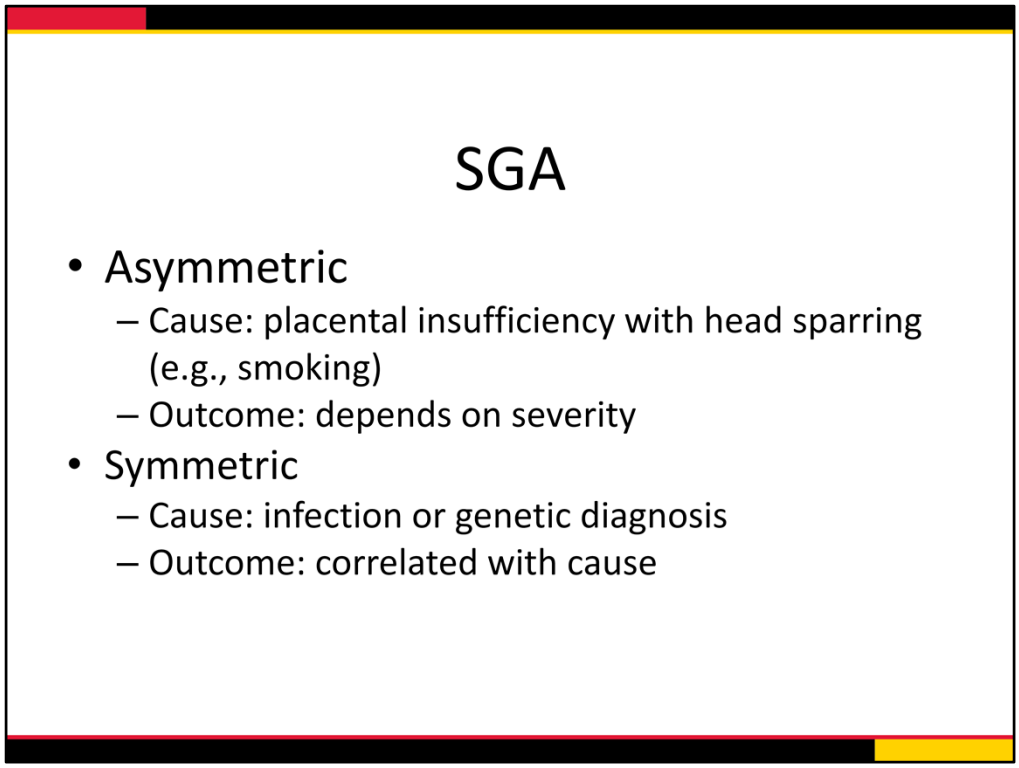
Apnea of prematurity may be referred to as apnea and bradycardia, or A's and B's. While not a high probability medical condition, A's and B's happen frequently in infants born prematurely.



Apnea of prematurity is a pause in breathing greater than 20 seconds commonly associated with a reflexive fall in HR. Apnea of prematurity occurs frequently in infants less than 32 weeks gestational age; A's and B's are seen in 10% of all infants born prematurely and in over 40% of very low birthweight infants. Apnea of prematurity typically resolves by 34 weeks post conceptual age and is treated with caffeine to stimulate breathing while infants are in the NICU. Some infants with very mild A's and B's may be discharged on a home monitor. Persistent severe apnea is correlated with poor prognosis.

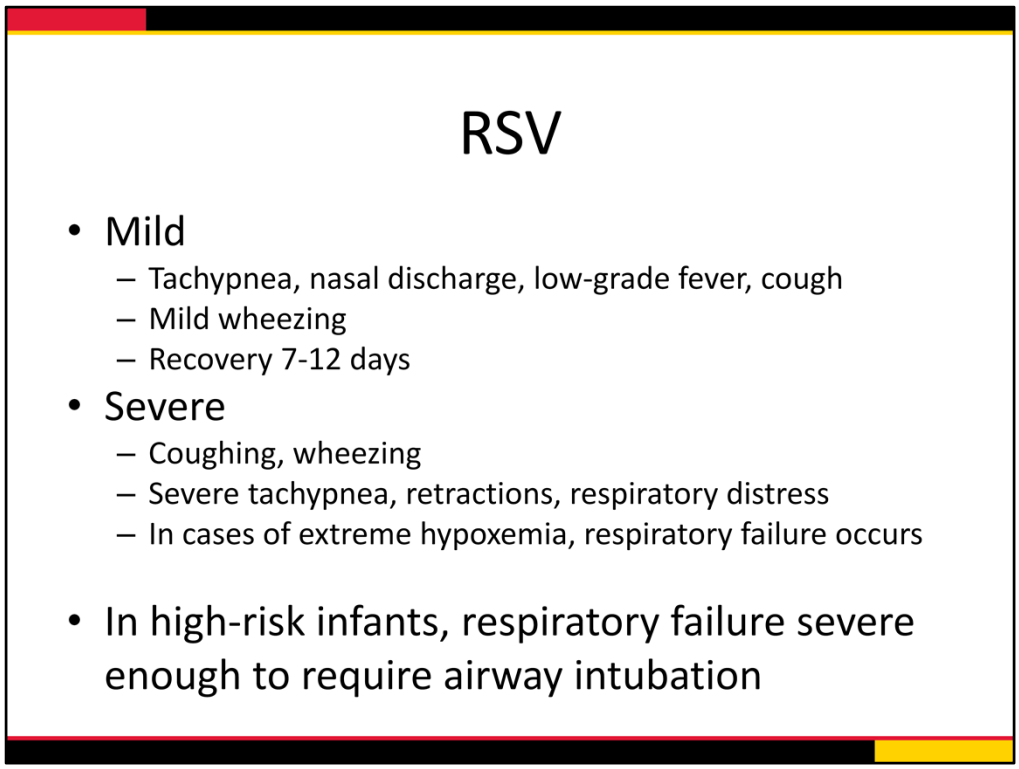


Newborns with a birthweight that plots at less than the 10th percentile for their gestational age are considered SGA or small for gestational age. Maternal cigarette smoking is a known cause.



There are two types of SGA: asymmetric and symmetric. Asymmetric SGA is usually caused by placental insufficiency with head sparing. Outcome depends on the severity of placental insufficiency. Symmetric SGA is typically a result of a viral infection (often known as TORCH) during early pregnancy or genetic diagnoses. With symmetric SGA, outcome is related to the cause.

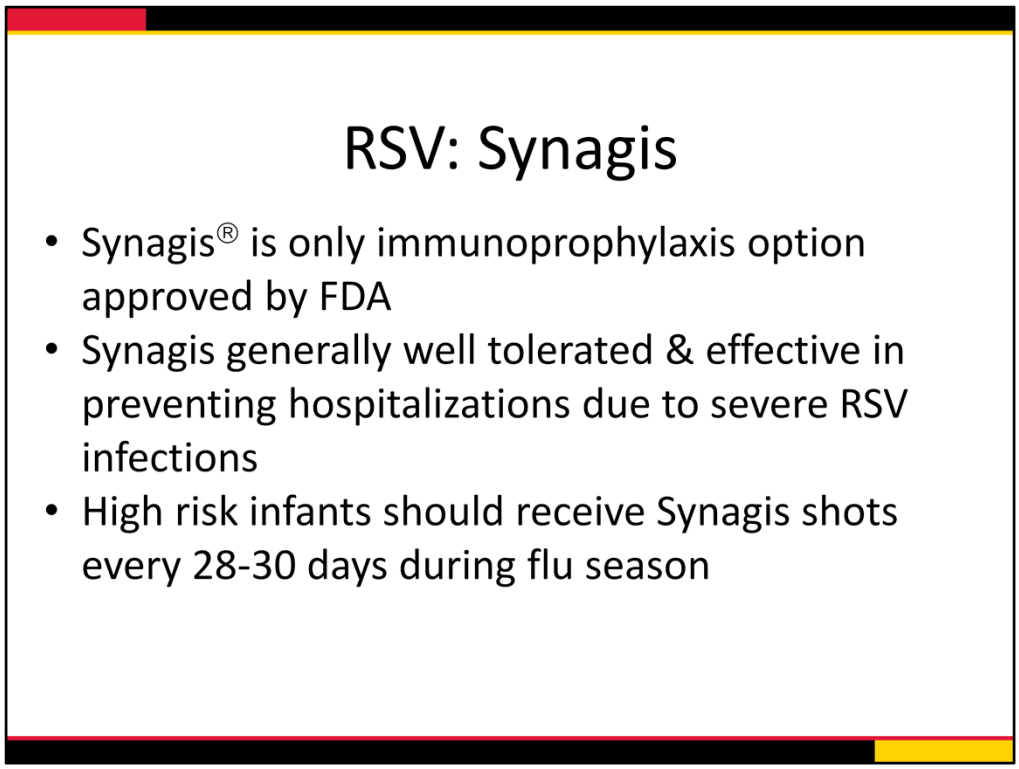
Respiratory syncytial virus, or RSV, is a very contagious respiratory virus. RSV is transmitted by droplets via sneezing or coughing. Fomites can transmit RSV; the virus can survive up to 12 hours on hard, nonporous surfaces. Most children are exposed to RSV prior to 2 years of age. Many of those exposed only get an upper respiratory infection from RSV. Some babies, especially those born prematurely with chronic lung disease, may develop serious lower respiratory infections. RSV is the leading cause of hospitalization in infants less than 1 year of age.



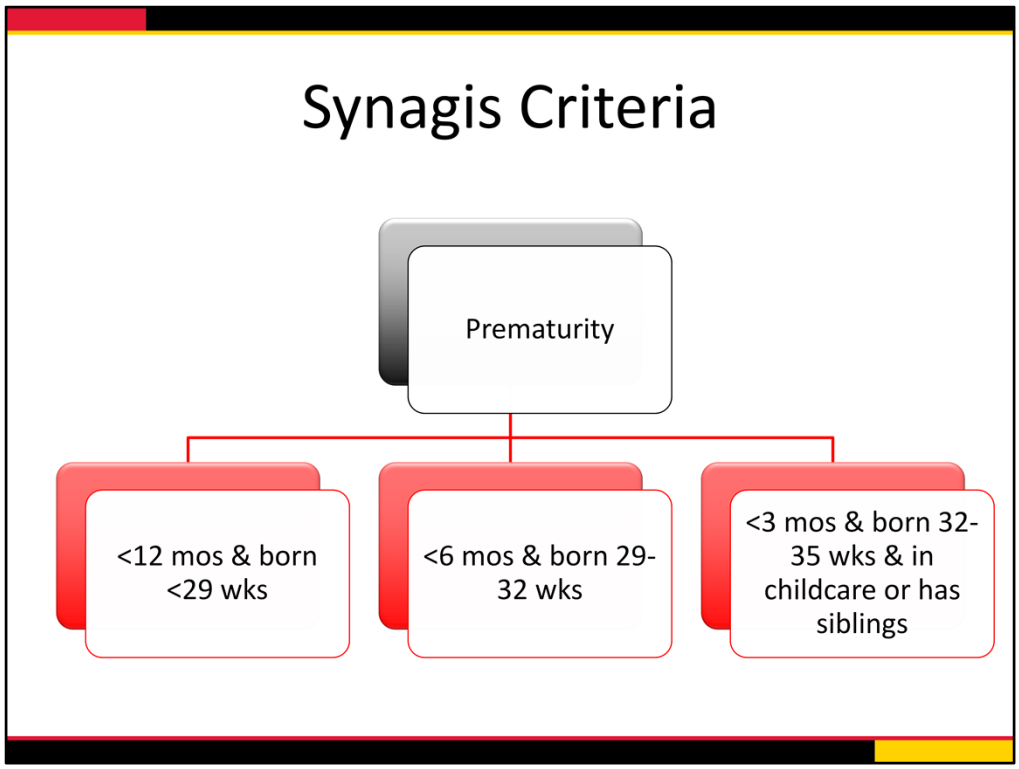
Symptoms of mild RSV include tachypnea, or rapid breathing, nasal discharge, mild wheezing, cough, and low-grade fever. Those with mild RSV usually recover in 7 to 12 days. Severe RSV may lead to coughing, wheezing, severe tachypnea, and respiratory distress. In some cases, respiratory failure may occur that can be severe enough to require intubation.

Families and early interventionists can help prevent RSV by:

- careful hand washing,
- cleaning toys and surfaces that the baby may touch,
- avoiding crowds or anyone with a cold or fever, and
- keeping the baby away from smokers because tobacco smoke can increase the risk of severe RSV disease.

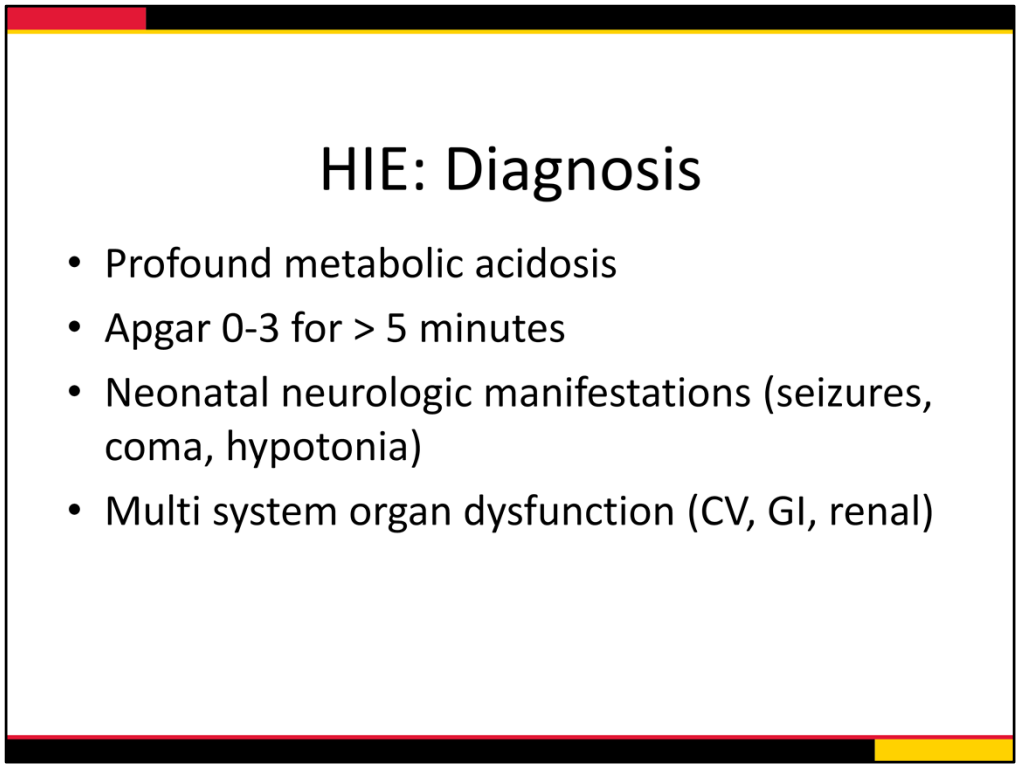


Synagis is the only FDA approved immunoprophylaxis option for RSV. Synagis is generally well tolerated and effective in preventing hospitalization due to severe RSV infections. High-risk infants should receive Synagis shots every 28 to 30 days during flu season.



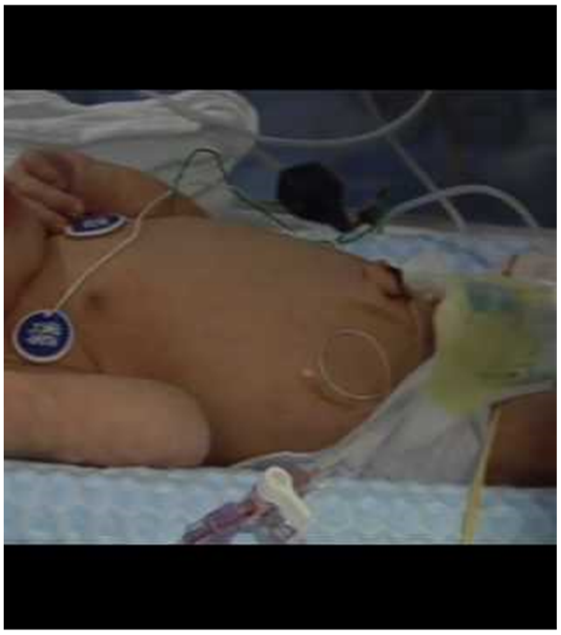
Infants who were born prematurely are eligible to receive Synagis if they are currently under 12 months of age and were born at less than 29 weeks gestation, or they are currently under 6 months of age and were born between 29 and 32 weeks gestation or they are currently less than 3 months of age and were born at 32 to 35 weeks gestation and they are in childcare or have siblings. Parents of infants meeting these criteria should talk with their primary care physician about Synagis. Parents of infants and toddlers with a history of chronic lung disease or congenital heart disease should also discuss Synagis with their primary care physician as their children may also be eligible for Synagis.

Hypoxic ischemic encephalopathy is also known as HIE. HIE is a form of neonatal brain injury caused by lack of oxygen to the brain. It is most common in full-term infants and is a type of neonatal encephalopathy.



Criteria for the diagnosis of HIE includes profound metabolic acidosis which is a build up of acid in the blood; Apgar scores of less than 3 for more that 5 minutes; the presence of neonatal neurologic manifestations such as seizures, coma or hypotonia; and multi-system organ dysfunction involving the cardiovascular, gastrointestinal, and/or renal system.

Treatment: Therapeutic Hypothermia



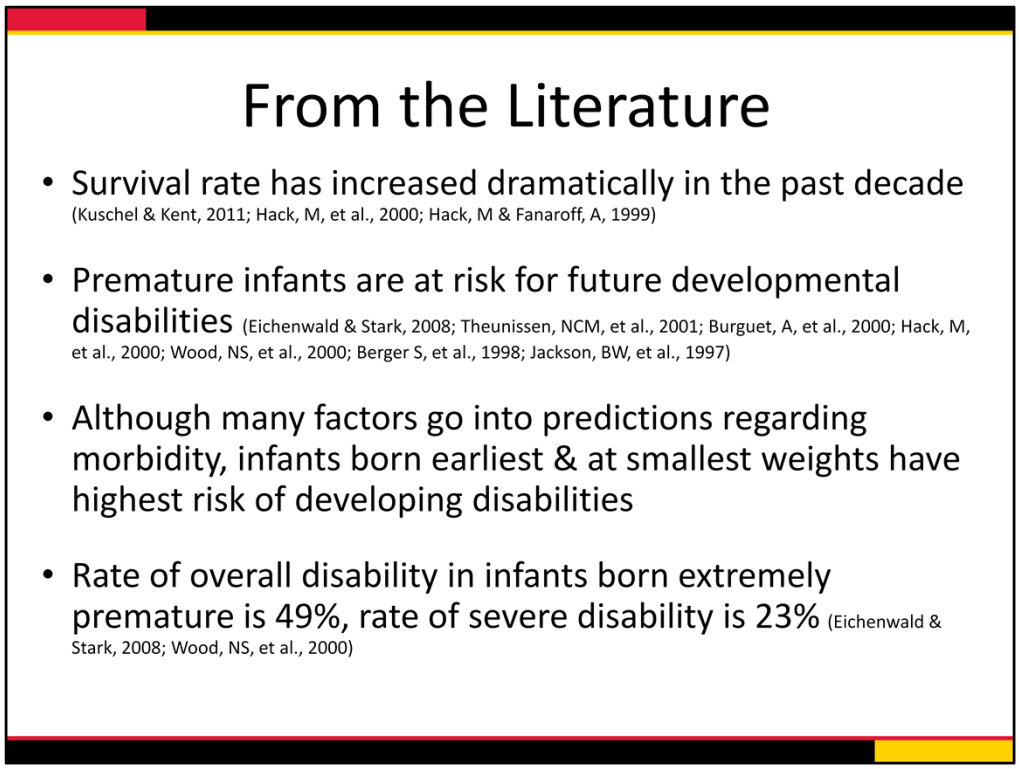
Therapeutic hypothermia is a neuroprotective therapy that slows the injury process to the brain resulting in improved neurodevelopmental outcome in those with moderate to severe HIE.

Rationale from the Literature

UM Study

MONITORING THE DEVELOPMENT OF CHILDREN BORN PREMATURELY

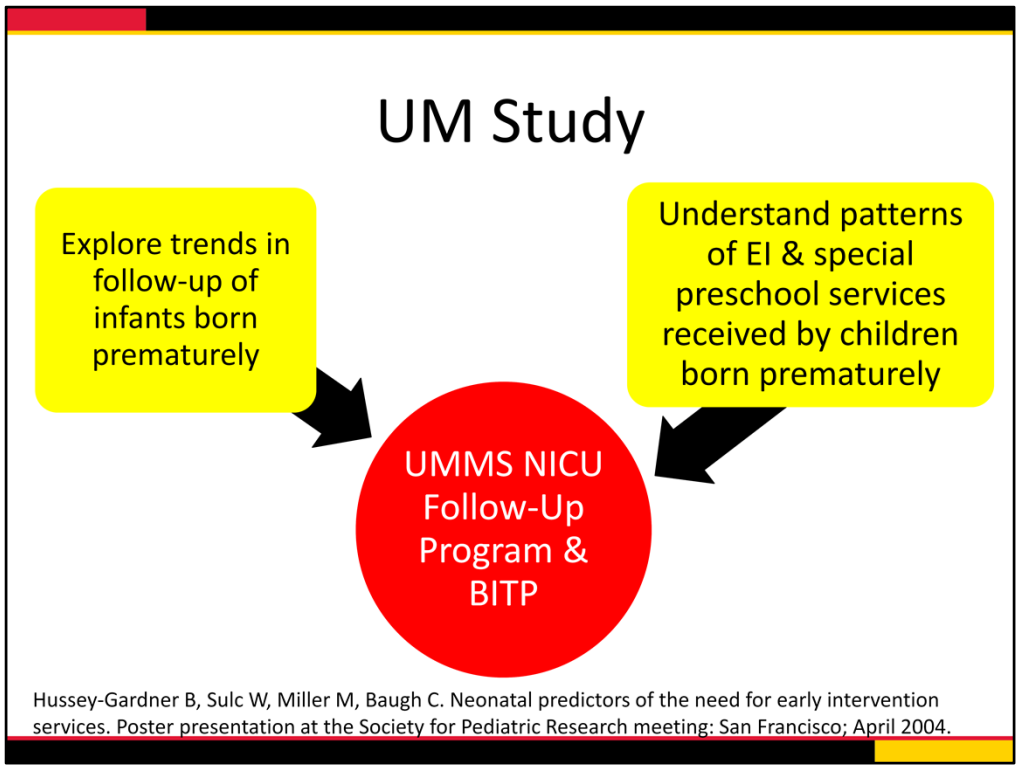
Now, let's discuss the importance of monitoring the development of children born prematurely.



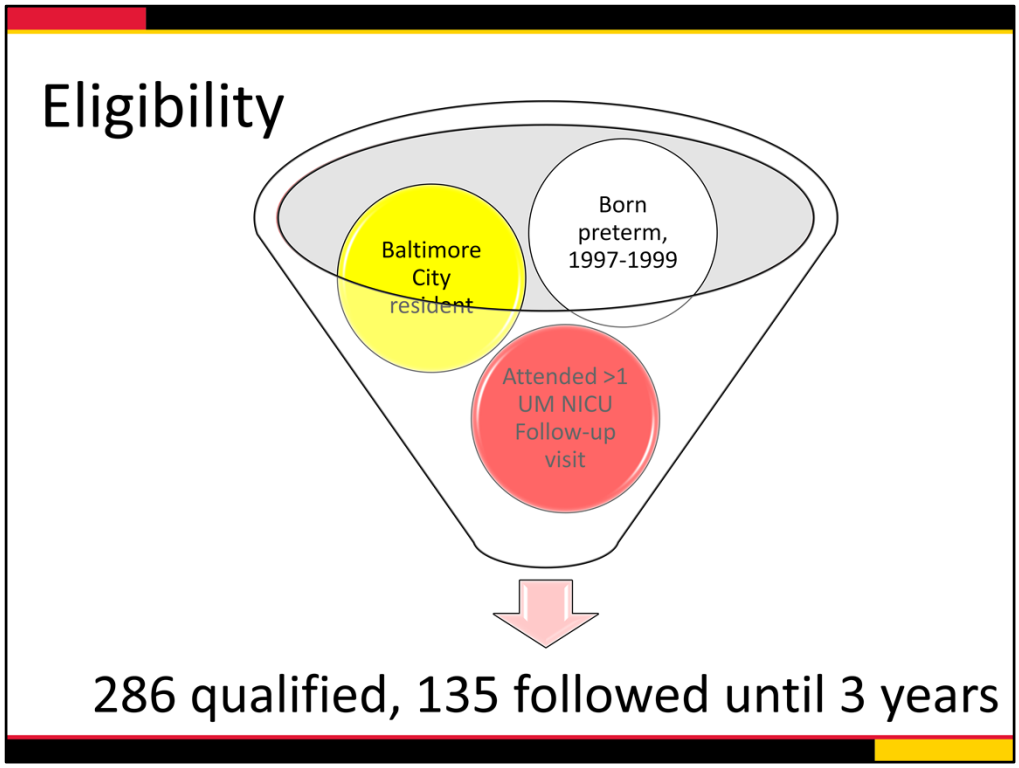
Researchers indicate that the survival rate of infants born prematurely has increased dramatically in the past decades. Their studies demonstrate that premature infants are at risk for future developmental disabilities. Although many factors go into predictions regarding morbidity, infants born at the earliest ages and at the smallest weights have the highest risk of developing disabilities with approximately half of infants born extremely premature having a disability and approximately one-fourth having a severe disability.

UM Study Exploring Trends In Early Intervention Services Received By Birthweight & Common Perinatal Diagnosis

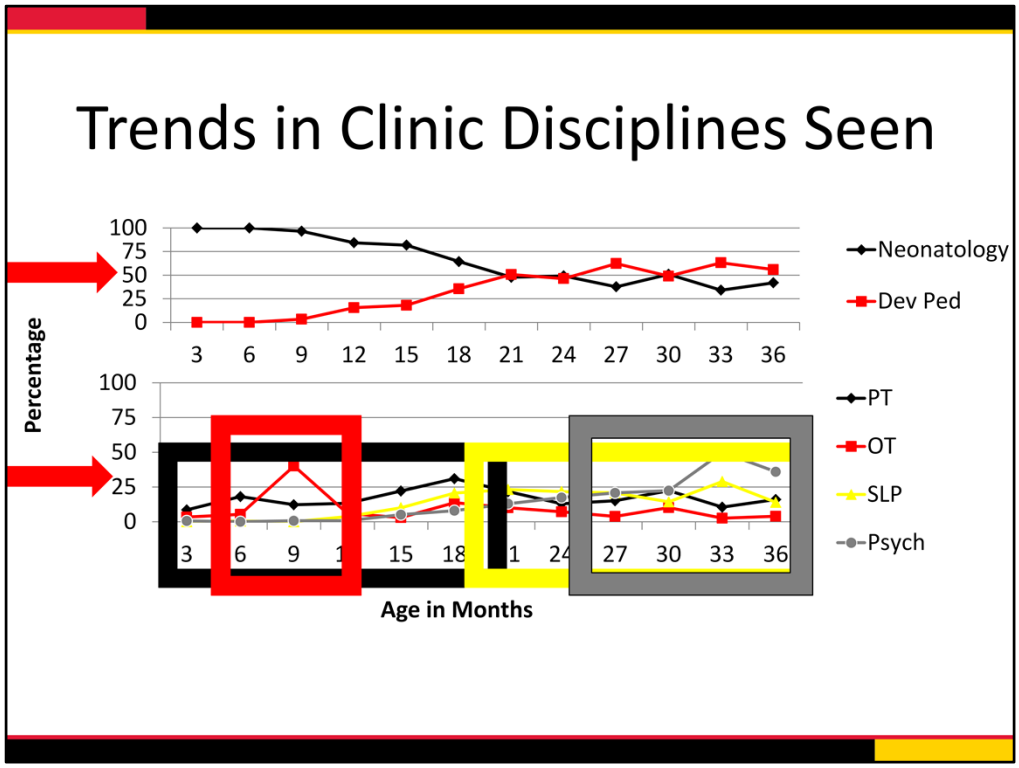
Researchers with the University of Maryland, Division of Neonatology, explored the trends in early intervention services received by birthweight and common perinatal diagnosis.



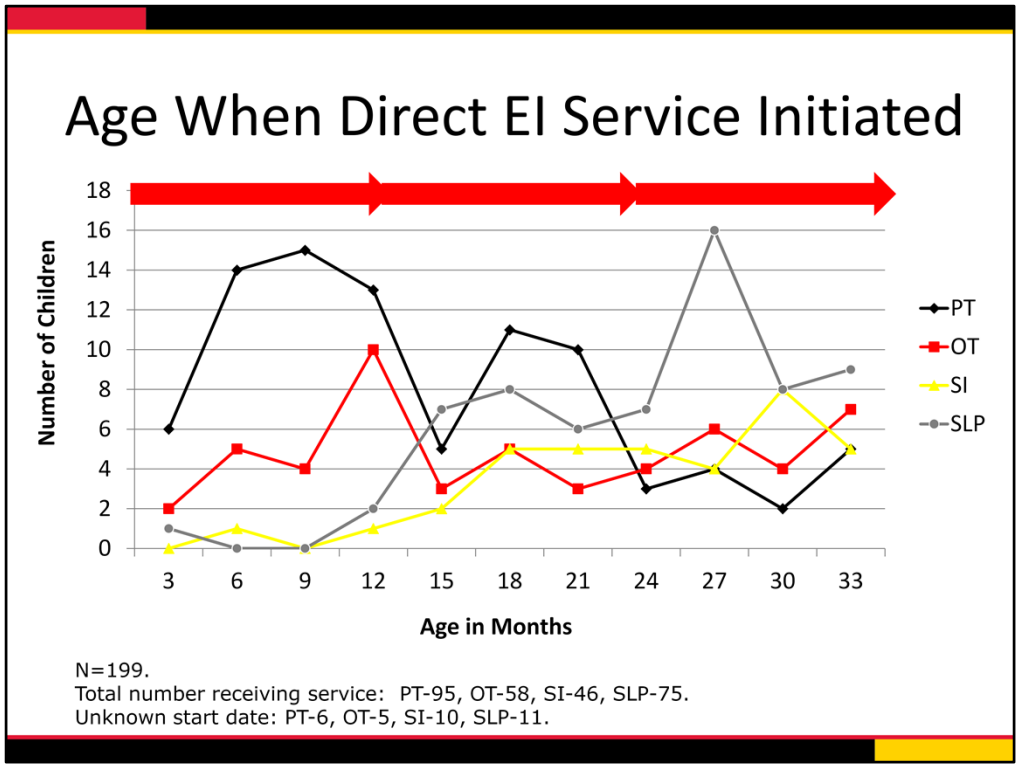
This study was a collaborative effort between the University of Maryland NICU Follow-Up Program and the Baltimore City Infants and Toddlers Program. The purpose of the study was to explore trends in the follow-up of infants born prematurely to better understand patterns of early intervention and special preschool services received by children born prematurely.



This study involved retrospective reviews of the University of Maryland NICU Follow-Up Clinic and BITP databases. Preterm infants born in 1997, 1998 or 1999 were included in the study if they were Baltimore City residents who attended at least one University of Maryland NICU Follow-Up appointment. 286 infants were included in the study; 135 of these infants were followed until three years of age.



The top chart depicts the percentage of children, by age, which received a developmental screening from a neonatologist and the percent that received an assessment by a developmental pediatrician. The bottom chart indicates the percentage of children, by age, which received an assessment by a physical therapist, occupational therapist, speech and language pathologist or psychologist secondary to a concern or need. The discipline most frequently involved in the assessment of children less than 21 months of age was the physical therapist with a unique increase in oral-motor and fine motor evaluations by the occupational therapist at 9 months of age. After 21 months of age the discipline most frequently involved in the assessment of children was the speech and language pathologist. As children approached three years of age, a higher percentage received an assessment by the psychologist to assist in obtaining cognitive levels for Part B eligibility determination.



This slide depicts that age when children first started to receive physical therapy, occupational therapy, special instruction, and speech and language therapy. In the fist year of life, the most frequently initiated service was physical therapy followed by occupational therapy. Between one and two years of age, physical therapy continued to be the most frequently initiated service but speech and language therapy now ranked second. From two to three years of age, speech and language therapy became the most frequently initiated service with occupational therapy and special instruction being the next most frequent.

Diagnoses Correlated with Specific Services

	Any	PT	OT	SI	SLP
CLD	.254**	.182**	.194**	.186**	.162**
PHH	.002	.061	.124*	.129*	-.079
Hypothyroidism	.152*	.045	.054	.083	.156*
IVH III-IV	.245**	.239**	.230**	.101	.144*
SNEC	.151*	.144*	.180**	.116	.178**
PVL	.085	.089	.183**	.192**	.105
ROP	.259**	.238**	.234**	.166**	.157**
Seizures	.088	.122*	.061	-.038	-.053
Tone Abnormal	.087*	.132*	.105	.041	.081

*Significant at the .05 level. ** Significant at the .01 level.

This table displays the correlation between neonatal diagnoses and specific early intervention services. Each of these diagnoses (chronic lung disease, post-hemorrhagic hydrocephalus, hypothyroidism, intraventricular hemorrhage Grades III and IV, necrotizing enterocolitis requiring surgery, periventricular leukomalacia, retinopathy of prematurity, seizures and tonal abnormalities at the time of discharge) was significantly correlated with one or more early intervention services.

Diagnoses Predicting Services, Above & Beyond Birthweight (<1200g)

	Any	PT	OT	SI	SLP
CLD	X		X		
PHH				X	
IVH III-IV	X	X	X		
SNEC			X		X
PVL			X	X	
ROP		X	X		
Seizures		X			
Tone Abnormal	X	X			

X denotes multiple regression significant at $p < .05$.

As a birthweight of less than 1,200 grams is a high probability condition in Maryland, we wanted to see if any of the diagnoses warranted high probability in children over 1,200 grams. Each of the diagnoses presented in this table was significant for predicting receipt of one or more early intervention services.

Transition at Age 3 (N=135)

Characteristic		Part B Eligible 43.9%	Not Eligible 55.3%
Sex	Male	63.8%	37%
	Female	36.2%	63%
Race	African-American	92.9%	93.1%
BW	Median	930 grams	989 grams
	Mean	1086.5 grams	1082.1 grams
GA	Median	27 weeks	27 weeks
	Mean	28.2 weeks	28 weeks

(Part B elig unknown N=1)

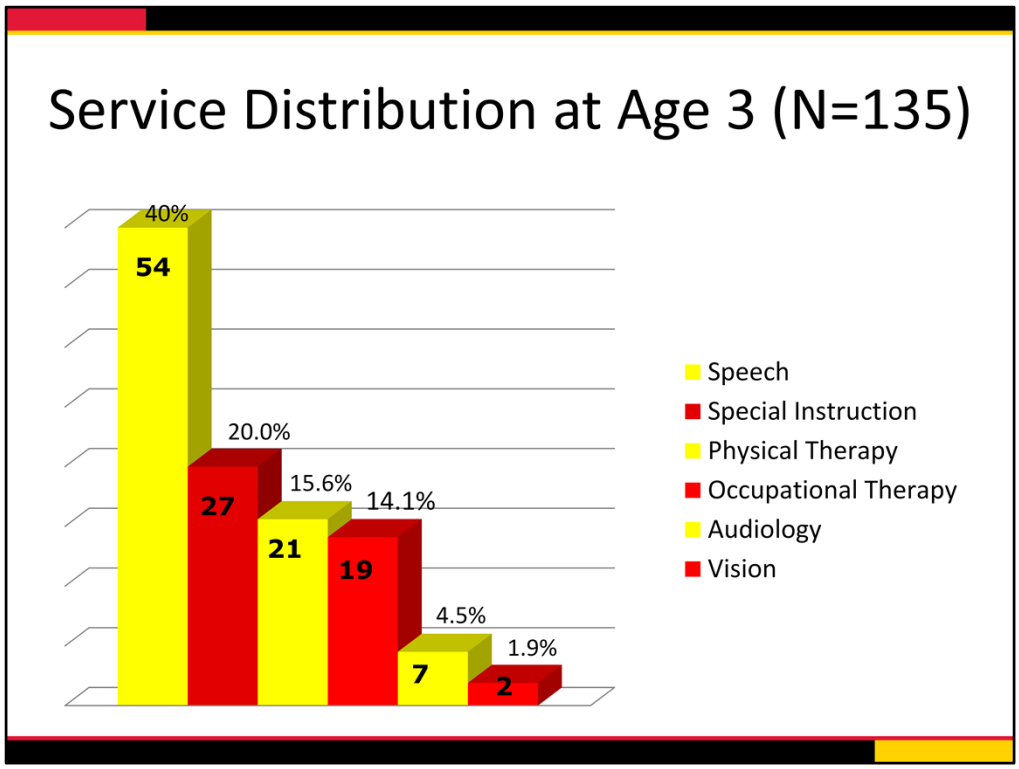
Next, we looked at Part B eligibility at age 3. Of the characteristics explored, gender was the strongest predictor of Part B eligibility with 63.8% of boys becoming eligible and only 36.2% of girls qualifying for Part B services.

Diagnoses Correlated with Part B Services at 3, Above & Beyond BW <1200g

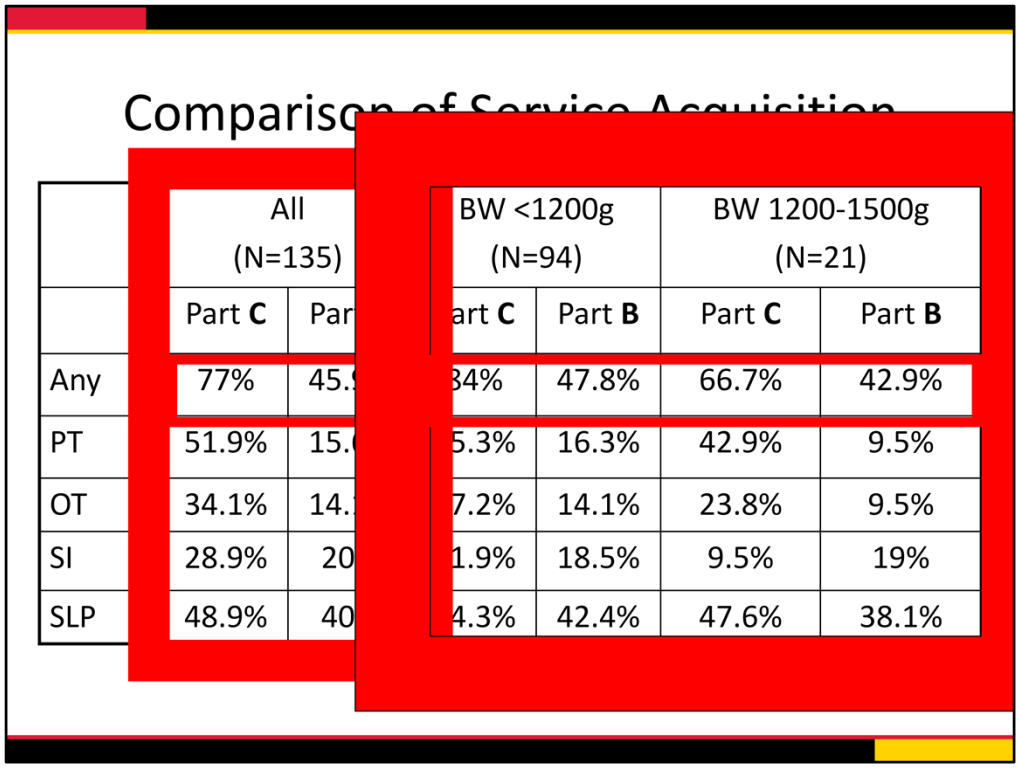
Diagnosis	PT	OT	SI
PVL	.380*		
HIE	.380*	.422**	
PHH	.408*		
Seizures	.380*	.422**	
Tone Abnormal	.544**	.606**	.423**

Significance Level *=.05, **=.01.
No significant correlations with diagnosis & SLP.

Then we looked at the correlation between perinatal diagnoses with Part B services at 3 years of age, after factoring out birthweight of less than 1,200 grams. PVL, HIE, PHH, seizures and tonal abnormalities continued to correlate with services.



At 3 years of age, speech and special instruction were the services that children most frequently qualified to receive with 40% qualifying for speech services and 20% for special instruction.

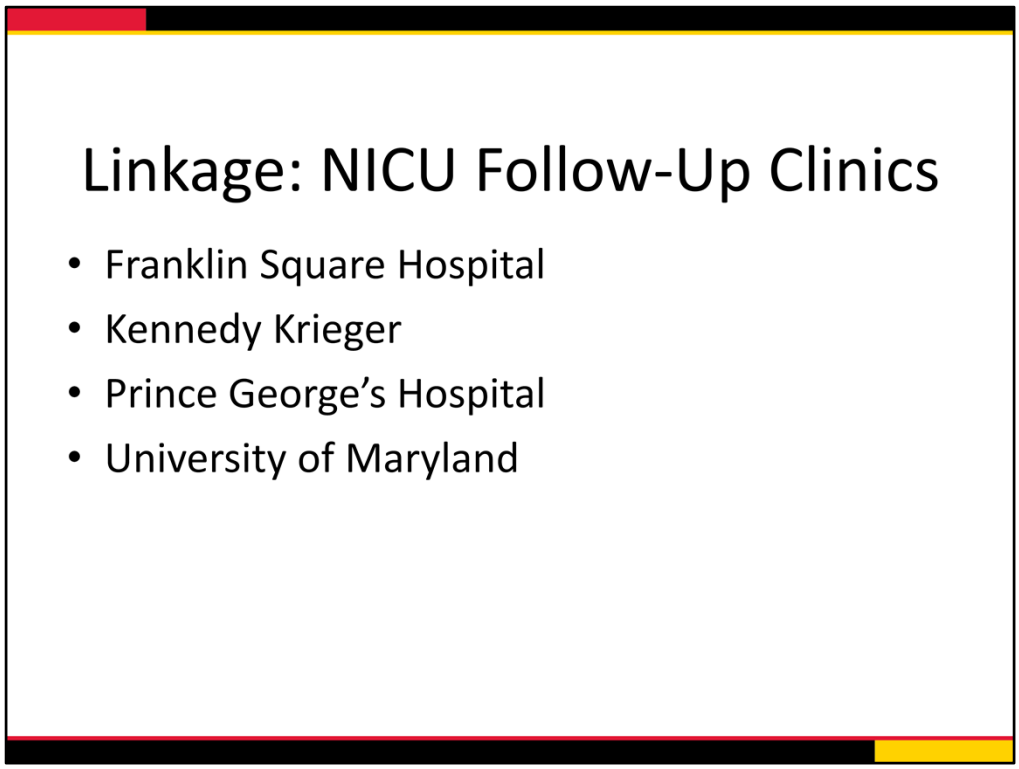


In our final analysis, we compared service acquisition by birthweight. When looking at all of the preterm infants followed until 3 years of age, 77% qualified for any direct early intervention service such as PT, OT, special instruction, or speech services and 45.9% qualified for Part B. This latter figure is very close to the 50% of children noted in the literature to receive special education services in elementary school. When comparing infants born weighing less than 1,200 grams and those born weighing 1,200 to 1,500 grams, we see that 84% of those with a birthweight less than 1,200 grams qualified for any direct early interventions service and 47.8% qualified for Part B services. Of those born at 1,200 to 1,500 grams, 66.7% qualified to receive a direct early intervention service and 42.9% were eligible for Part B services.

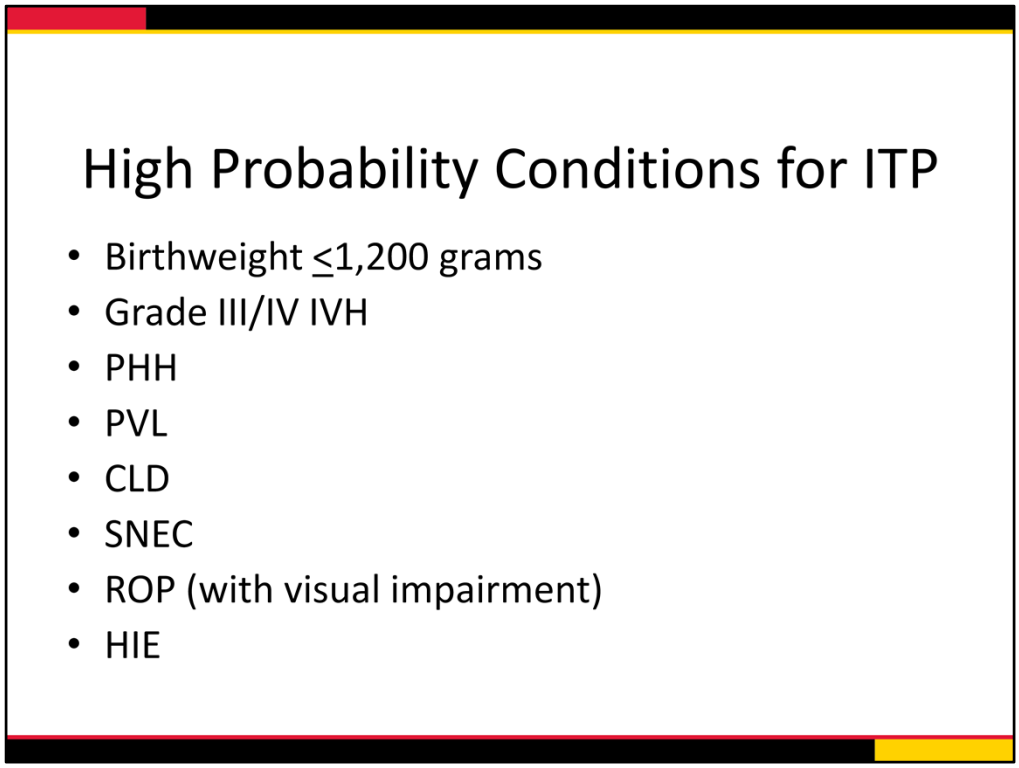
Conclusions

- Reinforces clinic policy of following infants born ≤1500g & all infants with high-risk medical conditions (e.g., CLD, SNEC) regardless of BW
- Emphasizes need to routinely screen all developmental domains until at least 3 years
- MITP inclusion of high probability conditions as eligibility criteria is supported by results of this study—CLD & SNEC was added to existing list.

In conclusion, the results of this study reinforces NICU Follow-Up Clinic policy of monitoring the development of all infants born weighing less than 1,500 grams and all infants with high-probability medical conditions regardless of birthweight. Findings also emphasize the need to routinely screen all developmental domains until at least 3 years of age. Finally, the Maryland Infants and Toddlers Program inclusion of Grade III/IV IVH, PHH, PVL and HIE as high probability conditions was supported; furthermore, the diagnoses of chronic lung disease and NEC requiring surgery were added to the list of high probability conditions.



Because infants and toddlers born prematurely and at very low birthweights are at very high risk for neurodevelopmental delays, it may be beneficial to have their development and medical status monitored by a NICU Follow-Up Program. There are currently four NICU Follow-Up Programs in Maryland (Franklin Square Hospital, Kennedy Krieger, Prince George's Hospital, and University of Maryland). If eligible, and if the parents are interested, NICU Follow-Up should be included as a linkage in the child's IFSP.



In summary, we reviewed the medical issues and developmental outcomes associated with high probability conditions related to prematurity in Maryland. All children born weighing less than 1,200 grams are automatically eligible for the Infants and Toddlers Program; as are those with a Grade III or IV IVH, PHH, PVL, CLD, surgical NEC, ROP with visual impairment or HIE.