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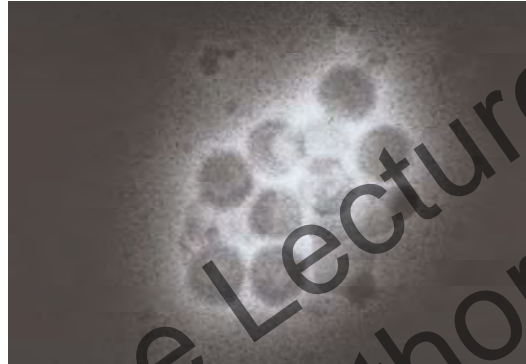
Varicella and pregnancy

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Varicella in pregnancy



- Rare : incidence 1 per 1000 pregnancies
- In temperate climates > 95% adult women protected
- Risk for the woman : severe varicella pneumonia < 1%
- Risks for child : Fetal varicella, Neonatal varicella (do not use confusing term of congenital varicella !)
- Zoster : no risk for fetus
- Breakthrough varicella : minimal risk (*Picone Prenat Diagn 2008*)
- Accidental vaccination : no major risk for fetus (*Wilson JID 2008*)

Chickenpox : a clinical diagnosis



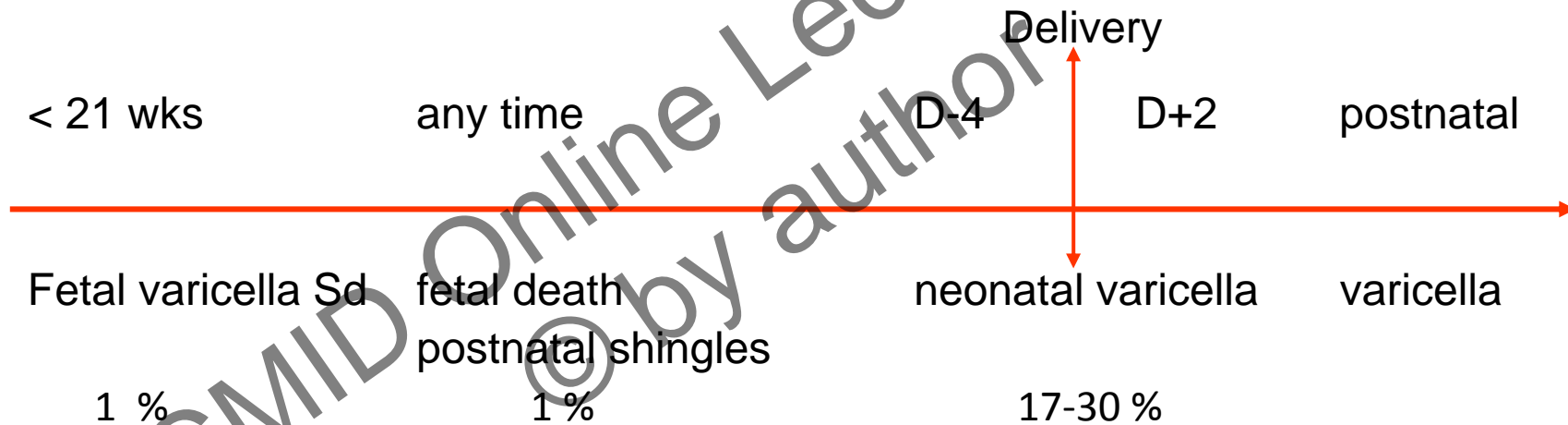
Risk for the mother

- Varicella pneumonia :
 - Incidence 1% as in non-pregnant
 - But higher risk of ARDS
- Risk factors :
 - 3d trimester
 - Immune deficiency
 - Smoking
 - Numerous lesions
- Mortality in varicella ARDS :
 - 20 to 45% before antivirals
 - 3 to 14% with antivirals



Varicella in pregnancy:

perinatal risk according to time of maternal rash



Breastfeeding

- Risk of postnatal contact with mother during acute varicella
- Breastfeeding is safe following postnatal vaccination
- After VZV vaccination, breast milk samples have failed to show any VZV DNA.

Fetal varicella incidence

- **Transmission of VZV** to the fetus : 5% in 1st trimester, 10% in 2d trimester (25% in 3d trimester)
- **Incidence of Fetal varicella** syndrome 1% in case of maternal varicella between 8 and 21 (24) weeks gestation

Incidence (%) after maternal varicella < 24 WG	<i>Enders 1994</i> Retrospective 1300 infants	<i>IPP 2000</i> Prospective 358 prenatal diagnoses
Asymptomatic	12	5,6
Embryopathy	0,7	1,4
Postnatal zoster	0,8	1,1

Fetal varicella lesions

- Skin : vesicles, scarring, retractions
- Bones : Hypoplasia of limb
- Neurologic : Microcephalus, cranial nerve paralysis, bladder, Claude-Bernard. Horner Syndrome
- Eyes : Microphthalmia, optic nerve atrophy, corneal opacity, cataract, chorioretinitis
- IUGR : Intrauterine growth retardation
- *Manifestations can be isolated or associated*



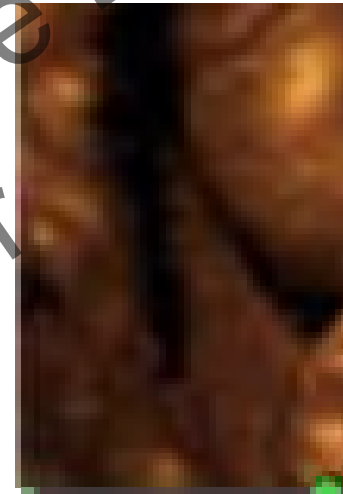
Table 1 Principal signs and symptoms of fetal varicella syndrome (n= 96 children) literature review.² Each child could have one or more symptom

Symptoms	Proportion of children (%)
Skin lesions (scars, skin loss)	76
Neurologic damage (cortical atrophy, spinal atrophy, limb paresis, seizures, microcephaly, Homer's syndrome, encephalitis, dysphagia)	60
Eye diseases (microphthalmia, chorioretinitis, cataract, nystagmus, anisocoria, optic atrophy)	51
Limb hypoplasia and other skeletal anomalies	49
IUGR	22
Muscle hypoplasia	21
Gastrointestinal abnormalities	15
Affections of internal organs	13
Developmental delay	12
Genitourinary abnormalities	12
Cardiovascular anomalies	8
Defects of other organs	7

IUGR, intrauterine growth restriction.

Case study 1

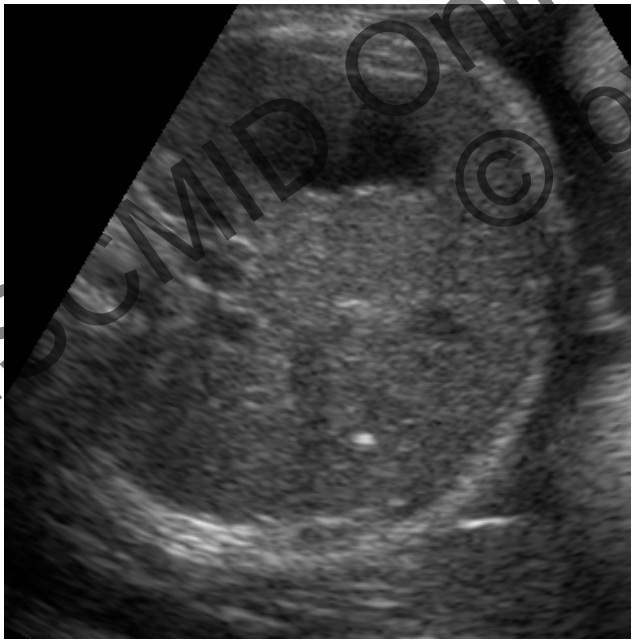
- Maternal varicella at 14 wks
- Transient pylectasis
- Talipes
- VZV PCR +



- Polyhydramnios and labor at 34 wks
- Abnormal CTG
- Neonatal death
- VZV encephalitis

Case study 2

- Maternal varicella at 17 wks
- Amniocentesis PCR+
- Transient hyperechogenic intestine
- Ultrasound follow-up and MRI normal
- No prenatal treatment



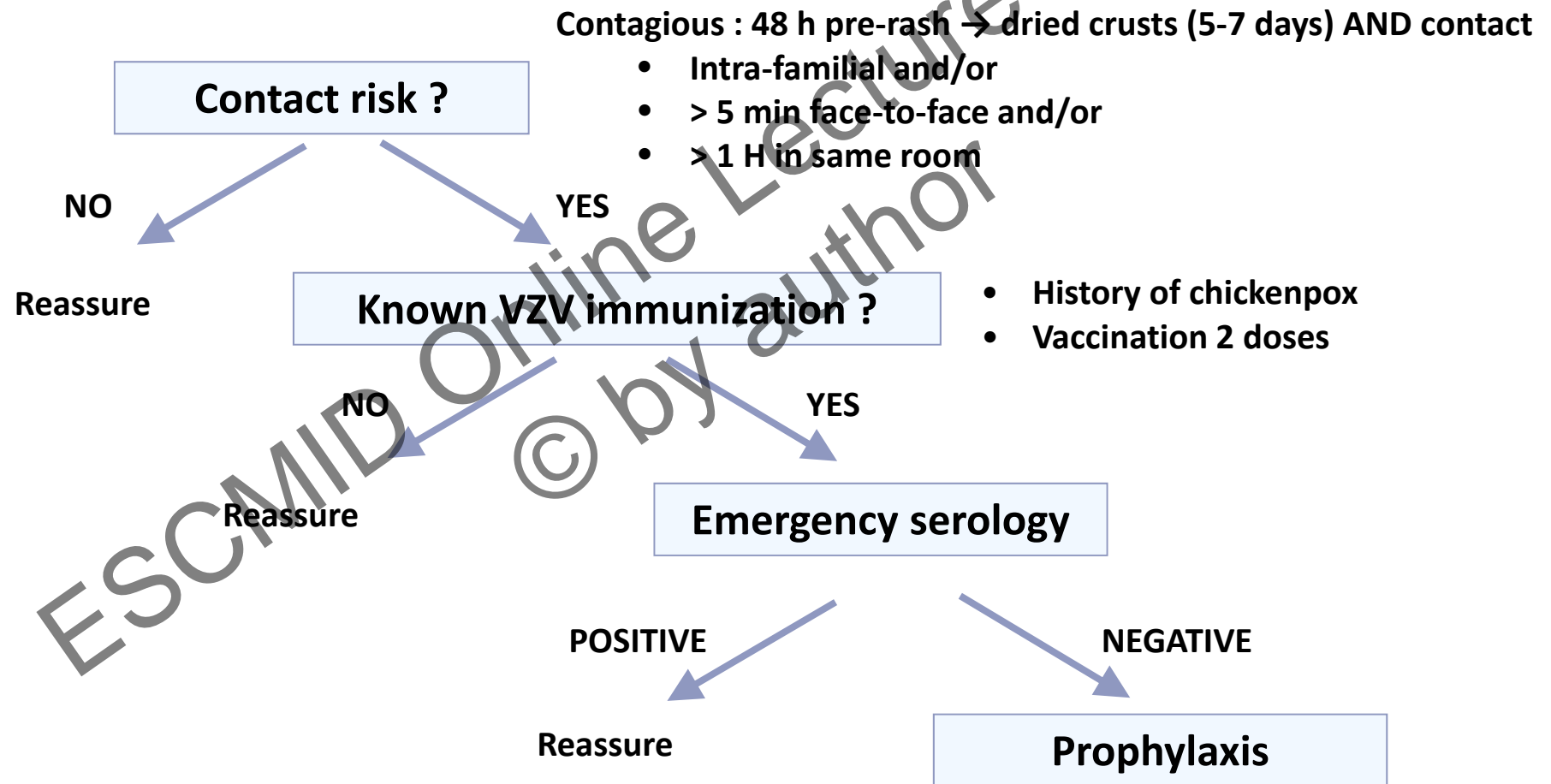
- At birth : inguinal ulceration and muscle dehiscence
- After treatment and graft at 6 months

Mme V



- 2G1P, 16 weeks gestation, normal pregnancy
- Brings her son to pediatric emergency for chickenpox
- She thinks that she never had chickenpox
- She is worried
- The pediatrician is worried
- What do you do ?

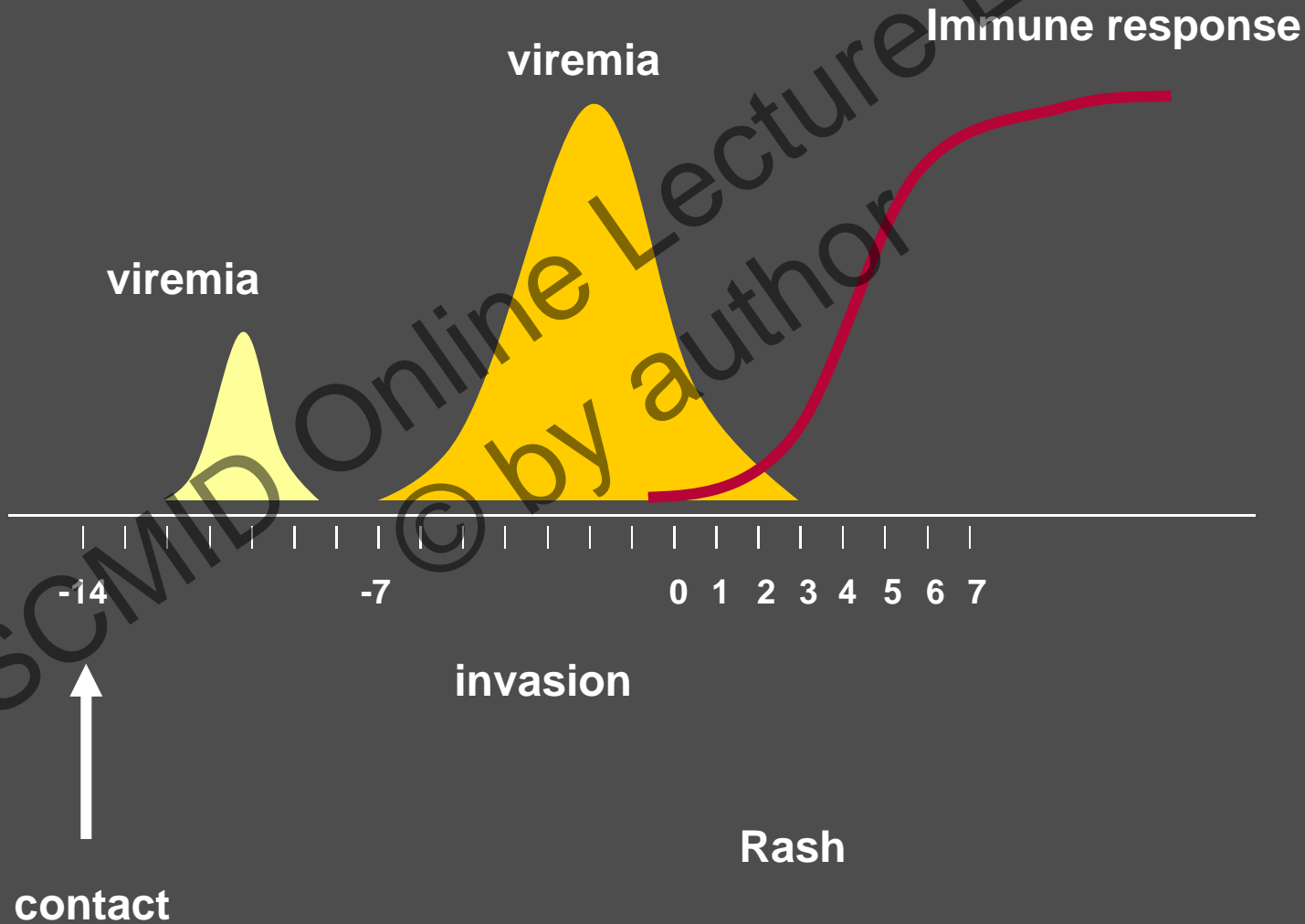
Management of exposure



Mme V

- Referred to adult emergency (not maternity !)
- Emergency serology returns negative
- anti-VZV immunoglobulin
 - As soon as possible (10 days at latest) Varitect® (25 UI /ml) 1 to 2 ml/kg (special dispensation protocol)
 - Preventive if injected within 4 days of exposure (before 1st viremia)
 - Efficacy in pregnant women : varicella incidence 29% vs 70% (*Wallace, 1992*)
 - Enders: 97 patients with VZVIG: no congenital varicella (*Lancet, 1994*)
 - If exposure > 10 days before : Valaciclovir prophylaxis ? *No study*

Varicella in pregnancy : natural history



***Mme V returns one week later at 17 WG for a generalized maculo-papulo-vesicular rash :
What do you do ?***

1. Isolate from other pregnant women and neonates
2. Direct home, inform on symptoms which require emergency care (adult) : rash > 7 days or hemorrhagic, persistent fever, respiratory symptoms , neurological symptoms
3. Treat with valaciclovir 1g , 3 tid for 7 to 14 days
4. Offer prenatal diagnosis with ultrasound and amniocentesis
5. Schedule 2 weeks later for evaluation

***Mme V returns one week later at 17 WG for a generalized maculo-papulo-vesicular rash :
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3. *(Treat with valaciclovir 1g , 3 tid for 7 to 14 days)*
4. Offer prenatal diagnosis with ultrasound and amniocentesis
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Objectives of prenatal therapy for varicella

1. Maternal health : the only proven indication
2. Treat infected fetuses in utero ?
3. Prevent mother-to-child transmission (MTCT)
by reducing viremia ?

Fetal varicella : prenatal diagnosis

- **Serial expert ultrasound (monthly)**
- Amniocentesis with VZV PCR ? :
 - When ?
 - After maternal lesions disappear
 - Check for negative viremia (*Mirlesse BJOG*)
 - What does it add ?
 - Reassure if negative
 - Better ultrasound follow-up ?
 - Discuss fetal MRI (32 WG) : value not evaluated
 - Neonatal follow-up
 - Potential treatment with (val)acyclovir ?
 - Discuss benefits/risks/limitations with couple

Neonatal varicella



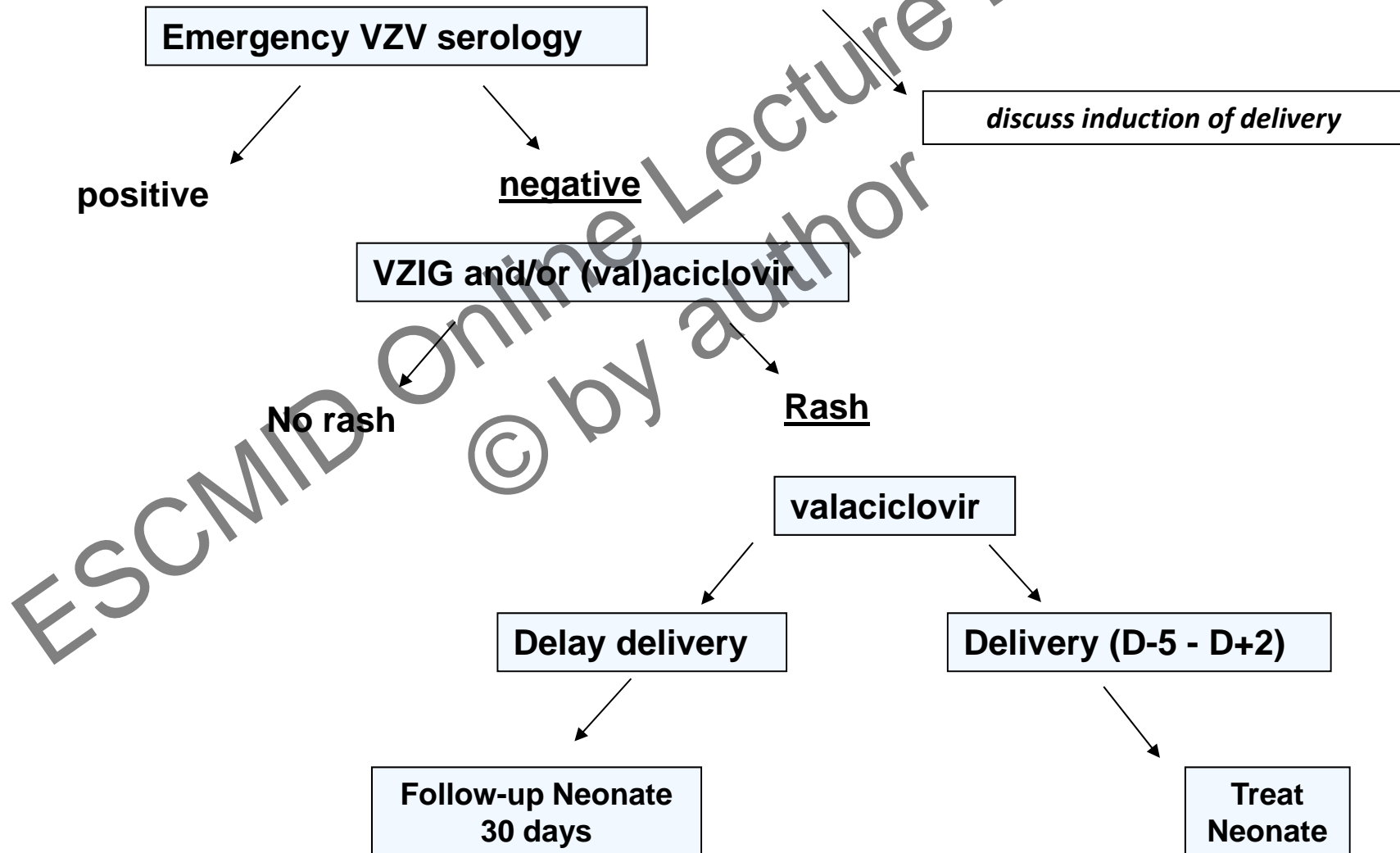
Neonate with varicella acquired from the mother in perinatal period :
skin lesions, pneumonia, hepatitis, encephalitis and severe
coagulopathy resulting from liver failure and thrombocytopenia

From C.K. Smith, A.M. Arvin. Seminars in Fetal & Neonatal Medicine (2009)

Neonatal varicella

- May occur when maternal disease occurs within an 1-wk period from 5 days before delivery until 2 days after delivery
- Onset of symptoms in the first 10 days postnatally
- Neonatal intensive care, acyclovir : survival >95% of term NN
- Prevention at birth with VZIG (or IVIG if VZIG not available)

Exposure in late pregnancy in a mother without VZV history



Primary prevention of fetal and neonatal varicella : vaccination

Various policies :

- Routine universal vaccination
- Screen and vaccinate women of (pre)-reproductive age or pre-conceptionally
- Healthcare workers who deal with pregnant women
- Routine antenatal screening (history and selective serotesting) and postpartum vaccination of seronegative women prevents 1/2 of VZV cases

(Morgan-Capner P, Commun Dis Public Health 2002)

Summary : management of varicella during pregnancy

- Up to 21 weeks:
 - Risk of fetal varicella syndrome about 1%
 - Ultrasound monthly
 - Discuss amniocentesis
 - Consider treatment with valacyclovir
- Third trimester
 - No significant risk for fetus
 - Treat mother with valacyclovir
- Peripartum:
 - Risk of neonatal varicella (-5,+2) +++
 - Immunoglobulin + valacyclovir
 - Try to delay delivery
 - Neonatal VZIG and acyclovir

Take-home messages

- Neonatal varicella is a high risk in case of maternal infection near delivery
- Antiviral therapy is justified by maternal risk in 3d trimester and neonatal risk if perinatal varicella
- Fetal varicella syndrome (FVS) is a rare, but serious complication which can occur between 8 and 20 weeks gestational age
- Prenatal diagnosis of FVS can be performed with serial expert ultrasound and amniocentesis
- Perspectives for prenatal antiviral therapy warrant further research