Borderline or Mild Ventriculomegaly
Ilan Timor-Tritsch
“....the diagnosis of ventriculomegaly is easy, .....prenatal identification of the cause of the ventricular dilatation is a more difficult task.”

Vincenzo D’Addario
What is “ventriculomegaly”?

• A BIG bag of different diseases causing dilatation of different segments of the ventricular system.

• **Ventriculomegaly is NOT a diagnosis**

• Ventriculomegaly is a symptom or a sign

• The term ventriculomegaly should carry a diagnosis with it pertaining to the cause of the dilatation
Prevalence

- The prevalence of mild VM 10-15mm, based on current criteria, is estimated to be around 0.7%.

Definition

- The widely accepted definition of mild cerebral lateral ventriculomegaly is an atrial width of 10-15 mm on the transverse (BPD) plane.

Additional definitions

• VM is **severe** when the measurement of the ventricular width is $>15$ or $\geq 15$ mm (Den Hollander et al., 1998; Graham et al., 2001; Gaglioti et al., 2005; Breeze et al., 2007);

• It is defined **mild or borderline** when the measurement is $\leq 15$ mm (Cardoza et al, 1988; Wax et al., 2003; Wyldes and Watkinson, 2004).
Additional definitions

- Data would suggest to further divide borderline VM into *mild* (10–12 mm) and *moderate* (>12–15 mm) 

(Signorelli et al., 2004; Gaglioti et al., 2005; Salomon et al., 2006; Falip et al., 2007).
The measurement
Mesure at the occipito-parietal fissure

Reproduced from the International Society of Ultrasound in Obstetrics and Gynecology guidelines.
Data of Signorelli et al show normal neurodevelopment between 18 months and 10 years after birth in cases of MVM (10–12 mm), could provide a basis for reassuring counseling.
Width of the fetal lateral ventricular atrium between 10-12 mm: a simple variation of the norm?

- Retrospective study;
- 60 fetuses isolated MVM (10-12mm)
- Dilatation diminished in 18,
- Became NL in 9
- Dilatation stabilized in 42
- F/u info on 38 born up to 1997: NL neurodevel
- 22 born after 1998 were NL at 12 & 18 month

Conclusion: The NL neurodevelopment in this series should provide basis for reassuring counseling in cases of ventricles measuring 10-12mm, if isolated

Signorelli M et al, UOG 2004;23:14
Fetal cerebral ventriculomegaly: outcome in 176 cases

P. GAGLIOTI, D. DANELON, S. BONTEMPO, M. MOMBRÒ*, S. CARDAROPOLI and T. TODROS
Maternal-Fetal Medicine Unit and *Neonatal Unit, University of Turin, Turin, Italy

• Studied 176 fetuses with ventriculomegaly and evaluated neurodevelopmental outcome at 24 months.

• 3 groups
  – A (mild ventriculomegaly, 10 to 12 mm);
  – B (moderate, 12.1 to 14.9 mm) and
  – C (severe, 15 mm).
• When VM was an isolated finding, 97.7% of fetuses were alive at 24 months.

• The neurodevelopmental outcome was normal in 93% of fetuses with MV

• Results suggest that the definition of borderline or mild VM should be limited to ventricular width below 12 mm.

• Cases with measurements above this value are more often associated with malformations and have a normal neurodevelopmental outcome less frequently.
Fetal cerebral ventriculomegaly: Outcome in 176 cases

- 176 fetuses with ventriculomegaly
- Outcome measure: neurodevelopment at ≥24 month
- Ventricular size –
  - **Group A**: Mild 10-12mm
  - **Group B**: Moderate 12.1-14.9mm
  - **Group C**: Severe ≥15mm

• **Results:**

• 1. VM more often an isolated finding:
  – if Gr. A (mild):...................... 44/75 = 59%
  – than if Gr. B (moderate):  10/41 = 24.4%
  – or Gr. C (severe):.............. 24/60 = 40%

• 2. If V-M isolated, :
  – Gr. A (mild):97% of NN were alive @ ≥24 m
  – Gr. B (moderate):  80% -””-
  – Gr.C (severe):........33.3% -””-

Borderline Ventriculomegaly

1.11 cm

1.10 cm
Borderline Ventriculomegaly
Borderline Ventriculomegaly
Prevalence

- **0.7-1% of fetuses (pooled literature).**
- Enlargement of the cerebral lateral ventricles is not an anomaly *per se*.
- The clinical significance of this finding is that it *alerts* to the possibility of associated anomalies, of the brain or other organs.
- The final *prognosis* depends more on such anomalies than on the degree of ventricular dilatation.

Implications for targeted examination: ULTRASOUND

• Exclude other neural and extra-neural malformations.

• I recommend careful multiplanar (3D!) examination of the fetal brain, performed if possible with a high resolution vaginal probe, and a detailed evaluation of the spine.

• Both lateral ventricles should be visualized & assessed as this condition can be unilateral.
Implications for targeted examination: ULTRASOUND

• A detailed evaluation of the entire fetal anatomy, including echocardiography should also be performed.

• These examinations may be incomplete or limited during the 3rd trimester.
Implications for targeted examination: MRI

- MRI has also been used*, HOWEVER, when following the protocol suggested (next side), the role of fetal MRI remains limited to those cases in which technical issues impaired US visualization.

Based on 179 fetal MRI exams (mean GA: 26 w)

**Results:** In 49/179 cases, MRI & US results differed,

Only in 2 of these cases did MRI studies provide clinically consistent additional information.

In 130/179 cases, MRI confirmed US findings.

**Conclusion:** In a selected group with isolated, mild VM and no risk factors, MRI may not be indicated in the prenatal imaging protocol.

Prenatal Diagnosis **2012**, 32, 752–757
• OBJECTIVE:

• Assessed the accuracy of expert neurosonography (two- and three-dimensional NSG) in characterizing of major fetal CNS anomalies seen at a tertiary referral center and to report the differential clinical usefulness of MRI used as a second-line diagnostic procedure in the same cohort.
**METHODS:** Retrospective analysis of 773 fetuses with confirmed CNS abnormalities

The following variables were analyzed:

- gestational age,
- NSG and MRI diagnoses,
- diagnostic doubt;

- indication for MRI (confirmation of NSG findings;
- search for possible additional brain anomalies),

- association with other malformations,

- diagnostic accuracy of NSG vs MRI (no additional clinical value for either MRI or NSG;

- additional information with clinical/prognostic significance on MRI relative to NSG;

- additional information with clinical/prognostic significance on NSG relative to MRI, NSG and MRI concordant but incorrect) and final diagnosis, which was made at autopsy or postnatal MRI/surgery.
• **RESULTS 1:** CNS malformations were associated with other anomalies in 372/773 (48.1%) cases
• Isolated in the remaining 401 (51.9%) cases.
• NSG alone established Dx in 647/773 (83.7%)
• MRI was performed in 126 (16.3%) cases.
• **Indication for MRI** was: to confirm NSG Dx in 59 (46.8%); diagnostic query (in the case of inconclusive/ uncertain on NSG) in 20 (15.9%); Search for possible additional brain anomalies in 47 (37.3%) cases.
• **RESULTS 2**: NSG and MRI were concordant & correct in 109/126 (86.5%) cases.

• Clinically relevant findings were evident **on MRI alone** in 10/126 (7.9%) cases (1.3% of the whole population) and

• **on NSG alone** in 6/126 (4.8%) cases; in all six of these cases, MRI had been performed at < 24 weeks of gestation. In one case, both NSG and MRI diagnoses were incorrect.

• The main type of malformation in which MRI played an important diagnostic role was space-occupying lesions, MRI identifying clinically relevant findings in 42.9% (3/7) of these cases.
• CONCLUSIONS:
  
  (1) In a tertiary referral center with good NSG expertise in the assessment of fetal CNS malformations, MRI is likely to be of help in a limited proportion of cases;
  
  (2) MRI is more useful after 24 weeks;
  
  (3) the lesions whose diagnosis is most likely to benefit from MRI are gross space-occupying lesions.
Flowchart for investigation of VM

Posterior fossa NL?

NO

ONTD

DWM

NO

SOD/ASP

ACC

HPE

YES

CC & CSP NL?

NO

CH

YES
Insults? 

- YES 
  - Infection 
  - Hemorrhage 
  - Tumor 

- NO 

Malf. Cort. Dev.? 

- YES 
  - Lissencephaly 

- NO 

Probably Isolated VM 

Measure head circumference 

- NL or large 
  - NL or Macrocephaly 

- Small 
  - Microcephaly/ T21
Pathogenesis and pathology:

- In many cases, it probably represents a normal variant. In other cases, mild enlargement of the lateral ventricles may be the only obvious epiphenomenon of heterogeneous cerebral anomalies.
Table 2—Malformations in fetuses with borderline ventriculomegaly (10–15 mm)

<table>
<thead>
<tr>
<th>Author</th>
<th>No. of cases</th>
<th>Malformations n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goldstein et al. (1990)</td>
<td>55</td>
<td>42 (76)</td>
</tr>
<tr>
<td>Bromley et al. (1991)</td>
<td>44</td>
<td>17 (38.6)</td>
</tr>
<tr>
<td>Patel et al. (1994)</td>
<td>37</td>
<td>6 (16)</td>
</tr>
<tr>
<td>Vergani et al. (1998)</td>
<td>82</td>
<td>34 (41.5)</td>
</tr>
<tr>
<td>Pilu et al. (1999)</td>
<td>31</td>
<td>3 (10)</td>
</tr>
<tr>
<td>Mercier et al. (2001)</td>
<td>26</td>
<td>4 (15.3)</td>
</tr>
<tr>
<td>Breeze et al. (2005)</td>
<td>30</td>
<td>9 (30)</td>
</tr>
<tr>
<td>Gaglioti et al. (2005)</td>
<td>116</td>
<td>59 (51)</td>
</tr>
<tr>
<td>Morris et al. (2007)</td>
<td>18</td>
<td>8 (44)</td>
</tr>
</tbody>
</table>

(10-12mm!!)
<table>
<thead>
<tr>
<th>Author</th>
<th>No. of cases</th>
<th>No. of isolated cases</th>
<th>Aneuploidies n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bromley <em>et al.</em> (1991)</td>
<td>44</td>
<td>27</td>
<td>0</td>
</tr>
<tr>
<td>Patel <em>et al.</em> (1994)</td>
<td>37</td>
<td>31</td>
<td>1 (3.2)</td>
</tr>
<tr>
<td>Tomlinson <em>et al.</em> (1997)</td>
<td>46</td>
<td>46</td>
<td>3 (6.5)</td>
</tr>
<tr>
<td>Vergani <em>et al.</em> (1998)</td>
<td>82</td>
<td>48</td>
<td>2 (4.16)</td>
</tr>
<tr>
<td>Pilu <em>et al.</em> (1999)</td>
<td>31</td>
<td>28</td>
<td>0</td>
</tr>
<tr>
<td>Graham <em>et al.</em> (2001)</td>
<td>35</td>
<td>35</td>
<td>5 (14.2)</td>
</tr>
<tr>
<td>Mercier <em>et al.</em> (2001)</td>
<td>26</td>
<td>22</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Gagliotti <em>et al.</em> (2005)</td>
<td>116</td>
<td>57</td>
<td>3 (5.2)</td>
</tr>
</tbody>
</table>
# Neuro-developmental outcome 10-12mm

**Table 4—Long-term neurodevelopmental outcome in fetuses with different degrees of ventriculomegaly**

<table>
<thead>
<tr>
<th>Author</th>
<th>Type of study</th>
<th>Degree of Ventriculomegaly</th>
<th>No. of cases</th>
<th>Months of FU</th>
<th>Mode of FU</th>
<th>Normal outcome (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signorelli et al. (2004)</td>
<td>Retrospective</td>
<td>10–12</td>
<td>38</td>
<td>&gt;36 m</td>
<td>Detailed interviews</td>
<td>100</td>
</tr>
<tr>
<td>Signorelli et al. (2004)</td>
<td>Prospective</td>
<td>10–12</td>
<td>22</td>
<td>18 m</td>
<td>Griffiths</td>
<td>100</td>
</tr>
<tr>
<td>Gaglioti et al. (2005)</td>
<td>Retrospective</td>
<td>10–12</td>
<td>43</td>
<td>≥24 m</td>
<td>Structured interviews</td>
<td>93</td>
</tr>
<tr>
<td>Falip et al. (2007)</td>
<td>Prospective</td>
<td>10–11.9</td>
<td>51</td>
<td>≥24 m</td>
<td>Brunet–Lezine; McCarthy; Wechsler</td>
<td>94</td>
</tr>
</tbody>
</table>

- **10-12mm**
- **n=150**
- **18-36months**
- **NL: 100-93%**

*Prenat Diagn 2009; 29: 381–388.*
Does uni- or bilateral MVM affect outcome?

• Bilateral or unilateral does not affect outcome

  • (Lipitz et al., 1998;
  • *Senat et al.*, 1999;
  • Durfee et al., 2001;
  • Kinzler et al., 2001;
  • Sadan et al., 2007).
Are there differences in degree of VM in male or female fetuses?

• **Prevalence** of male fetuses with VM and better neurodevelopmental outcome reported in male than female fetuses*

• This finding would suggest that male fetuses have slightly larger atrial width compared to female**

• Others*** found no difference between sexes or found differences that were statistically, but not clinically, significant.

• **These data, therefore, should be** used with caution when counseling prospective parents in cases of VM.

*Pilu et al. 1999; Gaglioti et al. 2000  **Patel et al., 1995; Nadel; Benacerraf, 1995
*** Haddad et al., 2001; Kramer et al., 1997
Objectives

This is a systematic review and meta-analysis.

To assess the prevalence of neurodevelopmental delay in cases of isolated mild fetal ventriculomegaly.

To assess false-negative rate of prenatal imaging for the Dx of associated abnormalities in patients referred for isolated mild ventriculomegaly.
• **Methods:**

  • Definition of MVM: between 10 - 15 mm.
  • Neurodevelopmental delay was defined as an abnormal quotient score, according to the test used.
• Results 1:
• The search yielded 961 citations;
• 904 were excluded
• Full manuscripts retrieved for 57 studies,
• 20 were included with a total of 699 cases of isolated MVM.
• Results 2

• Overall prevalence of neurodevelopmental delay was 7.9% (95% CI, 4.7–11.1%).

• Of the 20 studies 9 reported data on postnatal imaging, showing a prevalence of previously undiagnosed findings of 7.4% (95% CI, 3.1–11.8%).
Reported rates of neurodevelopmental delay in cases of truly isolated ventriculomegaly

7.9% (95% CI, 4.7–11.1%)
• Conclusions:

• The false-negative rate of prenatal imaging is 7.4% in apparently isolated fetal VM of ≤15 mm.

• The incidence of neurodevelopmental delay in truly isolated VM of ≤15mm is 7.9%.

• As the latter rate is similar to that noted in the general population, large prospective cohort studies assessing the prevalence of childhood disability, rather than subtle neurodevelopmental delay, are required.
In this Review we aim to provide up-to-date and evidence based answers to the common questions regarding the diagnosis of isolated mild fetal ventriculomegaly (VM). 7–11.1%
Should women with IMVM be sent to a referral center for a detailed anomaly scan?

• IM VM is a diagnosis of exclusion.

• Since prognosis can be altered drastically depending on coexisting anomalies, expert US examination is needed.

• Women would therefore benefit from referral to a center with a high level of expertise in fetal US assessment.
Should MRI be considered as a part of assessment of IMVM?

- **Maybe!**
- IM VM can be associated with abnormal cerebral development which may be better seen by MRI.
- Some say: *only* when US is inadequate or *if* there is a suspicion of an associated brain abnormality.
- Others say: routine use in all fetuses, since it adds important info in 6–10% of cases.
- Take into account resource allocation and only if there is sufficient technical expertise.
Should MRI be considered as a part of assessment of IMVM? If yes, WHEN?

• Between 30-32wks

• The optimal time remains unclear.

• As the main advantage is analysis of gyration, MRI examination between 30 and 32 wks may be the most appropriate.
Should a transvaginal scan be performed in order to assess the fetal brain?

• Detailed fetal neurosonographic evaluation should be performed in each fetus with MVM;

• Whether this is obtained with a transvaginal or transabdominal scan depends on the fetal position and the preference of the patient and the operator.
Should prenatal karyotyping be offered?

• **Most probably YES!**

• The likelihood ratio for trisomy 21 is about 9 and invasive testing for chromosomal analysis should be offered.

• Nevertheless, given the strength of the association between mild VM and chromosomal abnormalities, it is likely that the risk will be high in the majority of cases regardless of a previous low-risk result.
Should screening for congenital infection be performed?

- **YES!**

- Maternal serum CMV & Toxoplasma studies should be considered, and test for measurement of anti-HPA antibodies may be justified if there is a suspicion of ICH.

- Given the simplicity, safety and relatively low cost of the screening tests, the above studies should be considered.
Cytomegalovirus infection
Should screening for platelet allo-antibodies be performed?

• Even if Feto-Neonatal AIT may be treatable if detected promptly, this condition is rarely found in association with apparently isolated mild VM; therefore, a search for anti-HPA antibodies may be justified only if there is a suspicion of ICH on imaging.
What is the risk that the mild ventriculomegaly is not truly isolated?

• The rate of false-negative cases (Ave 7.9% in Pagani’s review) depends on the antenatal protocol used at the time of the initial assessment.

• The parents should be informed that there are limitations in the capability of US imaging in differentiating truly IMVM from that associated with initially occult abnormalities; this is in the region of 13%
What is the neurological outcome of children with prenatal diagnosis of MVM?

• There is wide variation in the reported incidence of neurodevelopmental delay, but pooled data* suggest this is around 11% (48/439)

• Few studies have used objective measures or assessed long-term follow-up**


Which factors influence the prognosis of fetuses with IMVM?

- **Fetal gender:**
  - It has been reported that, there is a male predominance among fetuses with MVM & that female gender significantly correlates with a worse neuro-developmental outcome*.
  - **BUT:** Others found no differences between male and female * infants.


Which factors influence the prognosis of fetuses with IMVM?

- Symmetrical vs. asymmetrical bilateral MVM?

- Infants with asymmetrical bilateral mild VM may have higher rates of neurodevelopmental anomalies (50% higher, 4/8)*, but the small number of cases of asymmetrical mild VM must be highlighted.

Asymmetric VM
Asymmetric VM

Asymmetric Venticulomegaly
Which factors influence the prognosis of fetuses with IMVM?

- **Progression:**
  - The most important prognostic factors are:
    - the association with other abnormalities not detected at first examination (about 13%),
    - the progression of ventricular dilatation (about 16%) both of which are retrospective diagnoses.

- Therefore, follow-up US and/or MRI in the 3rd Δ should be considered.
What postnatal management and type of follow-up are recommended?

- Postnatal assessment by an expert pediatrician to identifying prenatally undetected disorders.
- Further postnatal follow-up according to the diagnosis at birth.
- Some authors suggest that long-term postnatal follow-up and MRI should be arranged, regardless of spontaneous resolution of the finding.
Did we overlook something in the fetal brain when we assess the lateral ventricular atrium, that may prove to be a “game-changer”

Yes!
We should evaluate the “frONTAL complex”, namely the anterior horns of the lateral ventricles
Significance of *anterior horn dilatation* at diagnosis in mild ventricular abnormalities

**Aim:** evaluation of the effect of frontal horn dilatation (FHD) in cases of mild MV (10-15mm) and borderline VM (8-10mm)

**M&M:** n=104 (39 non dilated & 65 dilated FH)

**Definition of FHD** → >3.5mm

**Results:** “FHD >3.5mm was associated with remarkably poorer outcome (p=0.001) regardless of GA, atrial width and should be considered for the prognosis and f/U”

Eixarch E et al -Abstract #OC 15.05 ISUOG 2014
Fetal v-megaly/hydrocephaly

Signs of poor prognosis

- Extracranial malformations
- Association w. chromosomal defects
- Intracranial malformations or tumor
- Signs of infection (brain calcifications, ascites, hydrops)
- Severe IUGR, Microcephaly
- Extreme ventriculomegaly (cortex?)
- Fast progressing ventriculomegaly
- Large spinal defect & hydrocephaly
Ventriculomegaly/hydrocephaly is a SIGN of pathology - NOT A Dx!!

Any dilatation of the lateral ventricles has to be evaluated by detailed anatomy scan

Karyotyping, infectious, genetic workup strongly suggested

If vertex, TVS is good, however……

3D TVS neuroscan: best tool
Summary & conclusions

• If you have good US and use TVS, MRI is mostly redundant
• MRI effective in selected cases and mostly after 28 weeks
• Uni-or bilateral, isolated, mild (10-15mm) ventriculomegaly = good outcome
• Definition of v-megaly should be changed: dilatation of 10-12mm is benign
• Counseling is extremely hard and should be individualized based upon multiple parameters