Exposure to amniotic fluid in the pathophysiology of MMC

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No disclosures

Objectives

- Review amniotic fluid toxicity as it relates to pathology in MMC
- Examine data from animal models
- Consider data from human studies
- Discuss potential future therapies

Prenatal Diagnosis

WILEY

PRENATAL DIAGNOSIS

REVIEW OPEN ACCESS

Role of Amniotic Fluid Toxicity in the Pathophysiology of Myelomeningocele: A Narrative Literature Review

Yoann Athiel[1,2] | Jean-Marie Jouannic[1,3] | Matthieu Lépine[2] | Corentin Maillet[1,2] | Timothée de Saint Denis[4] | Jérôme Larghero[2] | Lucie Guilbaud[1,2,3]

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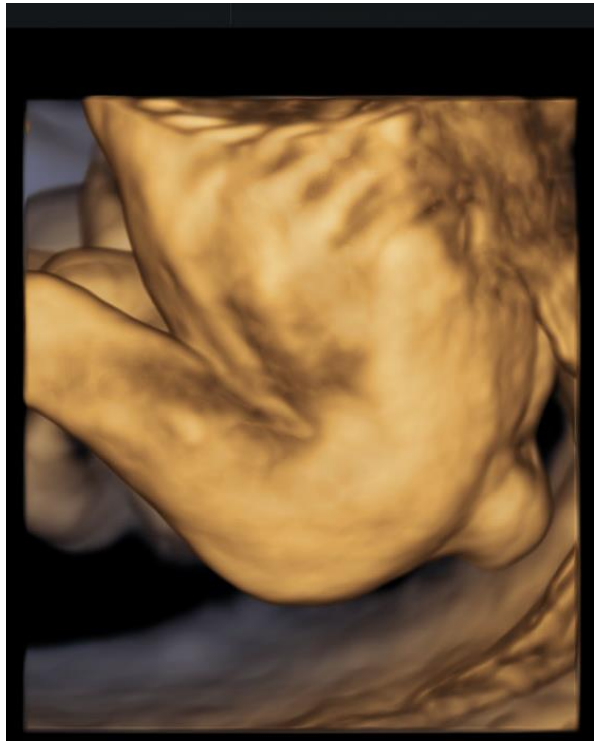
Mechanisms of injury

Mechanisms of injury

- Two-hit hypothesis – embryological defect and a second inciting event
- Mechanical trauma
- Chemical factors



Amniotic fluid toxicity

- Neuronal degradation
- Histological studies
  - Animal models vs human fetuses
- Clinical studies
  - Cytotoxic effect of AF → fluid exchange studies

JNS JOURNAL OF NEUROSURGERY
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Home COVID-19 Journals

Fetal spina bifida in a mouse model: loss of neural function in utero

Dorothea Stiefel M.D., Andrew J. Copp M.D., Ph.D., and Martin Meuli M.D.

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Page Range: 213–221
Volume/Issue: Volume 106: Issue 3
DOI link: https://doi.org/10.3171/ped.2007.106.3.213

RESEARCH ARTICLES | MARCH 07 2008

Quantitative Analysis of the Toxicity of Human Amniotic Fluid to Cultured Rat Spinal Cord

Subject Area: Neurology and Neuroscience , Surgery , Women's and Children's Health

Michael J. Drewek; Joseph P. Bruner; William O. Whetsell; Noel Tulipan

Pediatr Neurosurg (1997) 27 (4): 190–193.
https://doi.org/10.1159/000121250 Article history
PubMed:9577972

OBSTETRICS

Severe and progressive neuronal loss in myelomeningocele begins before 16 weeks of pregnancy

Check for updates

Selima Ben Miled, MD; Laurence Loeuillet, MD; Jean-Paul Duong Van Huyen, MD, PhD; Bettina Bessières, MD; Amel Sekour, MS; Brigitte Leroy, MD; Julia Tantau, MD; Homa Adle-Biassette, MD, PhD; Houria Salhi, MD; Maryse Bonnière-Darcy, MD; Aude Tessier, MD; Jelena Martinovic, MD; Frédéric Causeret, PhD; Julie Bruneau, MD, PhD; Yoann Saillour, PhD; Syril James, MD; Yves Ville, MD, PhD; Tania Attie-Bitach, MD, PhD; Ferechte Encha-Razavi, MD; Julien Stirnemann, MD, PhD

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REVIEW ARTICLES | JANUARY 10 2001

Amniotic Fluid Exchange for the Prevention of Neural Tissue Damage in Myelomeningocele:An Alternative Minimally Invasive Methodto Open in utero Surgery

Subject Area: Neurology and Neuroscience , Surgery , Women's and Children's Health

Mustafa Olguner; Feza M. Akgür; Tunç Özdemir; Tanju Aktuğ; Erdener Özer

Pediatr Neurosurg (2000) 33 (5): 252–256.

https://doi.org/10.1159/000055964 Article history

PubMed:11155062

Amniotic fluid toxicity

- Role of meconium

In Utero Meconium Exposure Increases Spinal Cord Necrosis in a Rat Model of Myelomeningocele

By Jorge Correia-Pinto, Joaquim L. Reis, Grover M. Hutchins, Maria J. Baptista, José Estevão-Costa, Alan W. Flake, and Adelino F. Leite-Moreira
Porto, Portugal; Baltimore, Maryland; and Philadelphia, Pennsylvania

JNS JOURNAL OF NEUROSURGERY
OFFICIAL JOURNALS OF THE AANS SINCE 1944

In utero meconium passage in fetuses and newborns with myelomeningocele

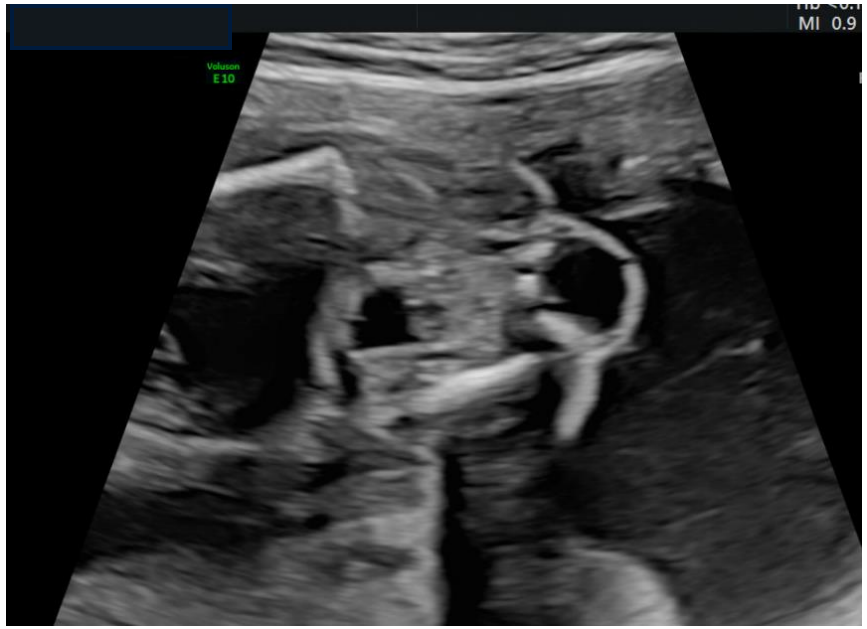
Clinical article

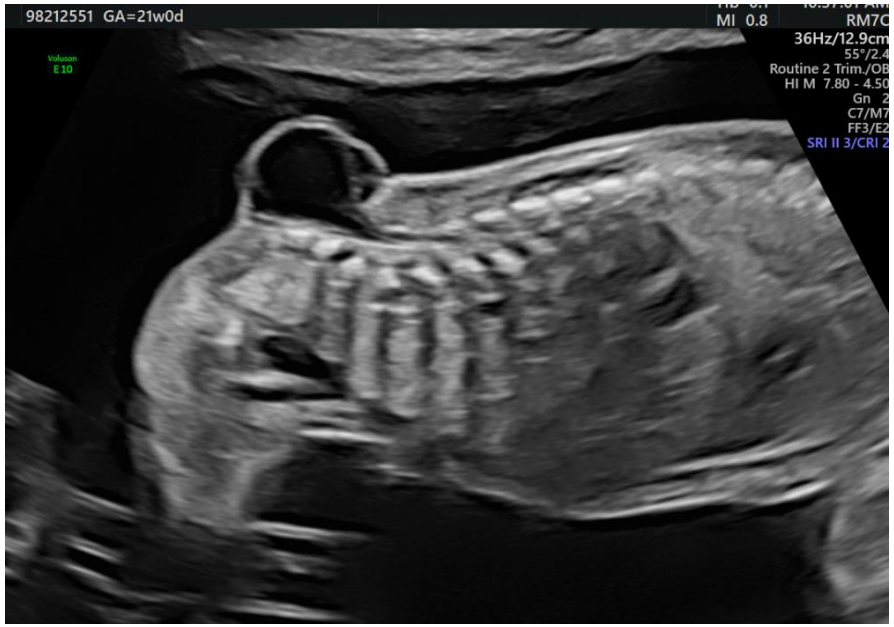
Enrico Danzer M.D., Linda M. Ernst M.D., Natalie E. Rintoul M.D., Mark P. J... View More

Page Range: 141–146
Volume/Issue: Volume 3: Issue 2
DOI link: https://doi.org/10.3171/2008.10.PEDS08199

Risk stratification

- Ultrasound findings as predictors of motor function
- Amniotic fluid brain-specific proteins as biomarkers of injury





Ultrasound Obstet Gynecol 2016; **47**: 162–167
Published online 13 January 2016 in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.15732

Prenatal ultrasound evaluation of segmental level of neurological lesion in fetuses with myelomeningocele: development of a new technique

E. CARRERAS*, A. MAROTO*, T. ILLESCAS*, M. MELÉNDEZ†, S. ARÉVALO*, J. L. PEIRÓ‡, C. G. GARCÍA-FONTECHA§, M. BELFORT¶ and A. CUXART†

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Contents lists available at ScienceDirect

Journal of Proteomics

journal homepage: www.elsevier.com/locate/jprot

Molecular insights into myelomeningocele via proteomic analysis of amniotic fluid

Lucie Guilbaud [a,b,c,*,1], Kévin Roger [d,1], Andree Schmidt [e,f], Cerina Chhuon [d], Stephan Breimann [e,f], Joanna Lipecka [d], Sophie Dreux [g], Stephan A. Müller [e,f], Michel Zérah [h], Jérôme Larghero [c], Jean-Marie Jouannic [a,c], Stefan F. Lichtenthaler [e,f,i], Ida C. Guerrera [d]

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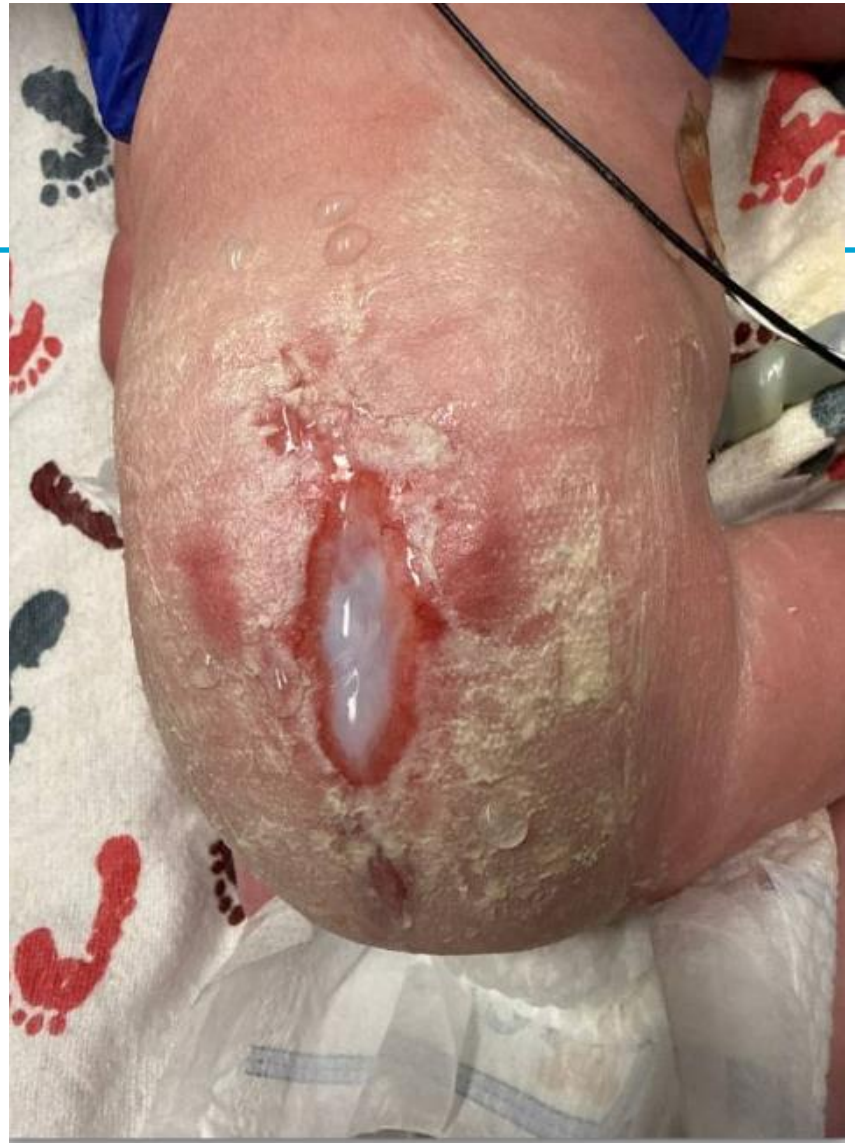
[i] Munich Cluster for Systems Neurology (SyNergy), Munich, Germany

Future practice

- Further refinement of in-utero surgery
- Therapeutic approaches with
  - Amniotic fluid exchange
  - Stem cell therapy
  - Targeted tx of neurotoxins



STEM CELLS TRANSLATIONAL MEDICINE

TISSUE ENGINEERING AND REGENERATIVE MEDICINE

Placental Mesenchymal Stromal Cells Rescue Ambulation in Ovine Myelomeningocele

AIJUN WANG,[a] ERIN G. BROWN,[a,*] LEE LANKFORD,[a,*] BENJAMIN A. KELLER,[a] CHRISTOPHER D. PIVETTI,[a] NICOLE A. SITKIN,[a] MICHAEL S. BEATTIE,[b] JACQUELINE C. BRESNAHAN,[b] DIANA L. FARMER[a]

Key Words. Stem cell • Placenta • Mesenchymal stem cells • Fetal stem cells • Cellular therapy

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ABSTRACT

Myelomeningocele (MMC)—commonly known as spina bifida—is a congenital birth defect that causes lifelong paralysis, incontinence, musculoskeletal deformities, and severe cognitive disabilities. The recent landmark Management of Myelomeningocele Study (MOMS) demonstrated for the first time in humans that in utero surgical repair of the MMC defect improves lower limb motor function, suggesting a capacity for improved neurologic outcomes in this disorder. However, functional recovery was incomplete, and 58% of the treated children were unable to walk independently at 30 months of age. In the present study, we demonstrate that using early gestation human placenta-derived mesenchymal stromal cells (PMSCs) to augment in utero repair of MMC results in significant and consistent improvement in neurologic function at birth in the rigorous fetal ovine model of MMC. In vitro, human PMSCs express characteristic MSC markers and trilineage differentiation potential. Protein array assays and enzyme-linked immunosorbent assay show that PMSCs secrete a variety of immunomodulatory and angiogenic cytokines. Compared with adult bone marrow MSCs, PMSCs secrete significantly higher levels of brain-derived neurotrophic factor and hepatocyte growth factor, both of which have known neuroprotective capabilities. In vivo, functional and histopathologic analysis demonstrated that human PMSCs mediate a significant, clinically relevant improvement in motor function in MMC lambs and increase the preservation of large neurons within the spinal cord. These preclinical results in the well-established fetal ovine model of MMC provide promising early support for translating in utero stem cell therapy for MMC into clinical application for patients. STEM CELLS TRANSLATIONAL MEDICINE *2015;4:659–669*

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Thank you for your time!

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