Surgical Mesh for Transvaginal Repair of Pelvic Organ Prolapse in the Anterior Vaginal Compartment

Obstetrics and Gynecology Devices Panel of the Medical Advisory Committee

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February 12, 2019

Ethicon Expert Meeting: Meshes for Pelvic Floor Repair

Friday, February 23rd , 2007; Location: Oststr. 1, Norderstedt, Meeting Room "Forum"

External Participants:

Prof. M. Cosson
Prof. B. Klosterhalfen
Prof. J. Deprest
Prof. B. Jaquetin
Dr. Arlt
Dr. D. Miller
Dr. K. Lobodasch

Ethicon:

Bob Roda
Cliff Volpe
Dave Robinson
Axel Arnaud
J. Flatow
O. Berthier
Ed Jacobs

P. Köhler
Alda Astani
K. Spychaj
P. Meier
J. Holste
J. Trzewik
B. Hellhammer

"Agenda-febr Mesh Meeting.doc"

Agenda:

PLAINTIFFS' TRIAL EXHIBIT P0785

Highlights from the presentations and related discussion (Please see CD as well):

Introduction and update of project "LIGHTning" (P. Meier)

PM gave a quick overview of the history of the project. Project is now in development phase. Team has achieved discovery work successfully. Ultrapro is the most promising available mesh for pelvic floor repair. Further animal and clinical data has to be collected prior launch of a product to substantiate this.

Plaintiff's EXHIBIT NO. 598 3/28/12 A. M. MITCHELL

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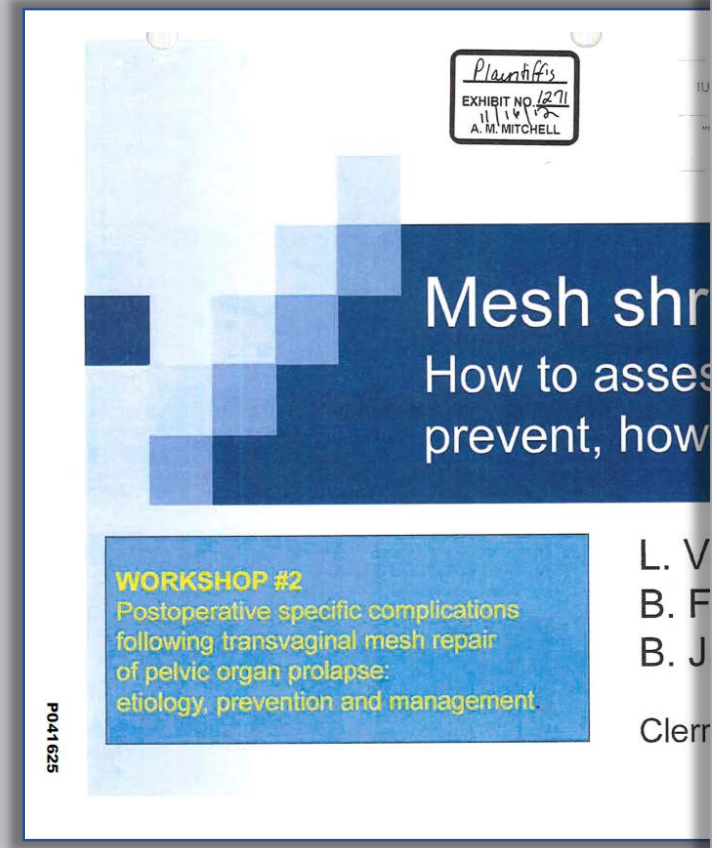
The following summary of unmet needs generated June 2nd 2006 was again confirmed without any adding:

Unmet clinical needs	**Priority (points)**
No shrinkage / no long-term contraction Fibrosis reduction Severe contraction → Dyspareunia → sexual function↓ *Tension response ↓* *→ ↓ Sexual pain?* *No folding of mesh* *No rigidity*	10
No vaginal distortion, normal vaginal wall, maintain sexual function, normal sexual function	8
Elasticity simulating physiology	5
No chronic pain Patient comfort *Less erosion* *Less vaginal mesh exposition*	4 2
BIO-active, " long term " - 90 days • growth factors • anti-bacterial • hormonal • angiogenesis	3
Better handling *Implantation process:* *→ Make it easier* *→ Correct placement* *Simple application* *Even simpler to apply*	3



What did we learn from abdominal wall repair studies?

- **Mesh repair**
  - **Reduce the rate of recurrence** compared with traditional suture repair
  - Works by both direct mechanical sealing (sublay) and induction of a scar plate formation
- **Several complications** associated with the use of mesh may be due to the **chronic inflammatory reaction** to the mesh or **a loss of compliance after degradation of the material**
- **Mesh shrinkage**, folding and migration, may result in some cases in a **recurrent hernia** and also **pain**

Amid PK, Hernia 1997
LeBlanc KA, Hernia 2001

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TRANSVAGINALMESH OR GRAFTS COMPARED WITH NATIVE TISSUE REPAIR FOR VAGINAL PROLAPSE (Review)

Maher C,

Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse (Review)

Authors' conclusions

While transvaginal permanent mesh is associated with lower rates of awareness of prolapse, repeat surgery for prolapse, and prolapse on examination than native tissue repair, it is also associated with higher rates of repeat surgery for prolapse or stress urinary incontinence or mesh exposure (as a composite outcome), and with higher rates of bladder injury at surgery and de novo stress urinary incontinence. The risk-benefit profile means that transvaginal mesh has limited utility in primary surgery. While it is possible that in women with higher risk of recurrence the benefits may outweigh the risks, there is currently no evidence to support this position.

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TRANSVAGINALMESH OR GRAFTS COMPARED WITH NATIVE TISSUE REPAIR FOR VAGINAL PROLAPSE (Review)

Maher C,

Low to moderate quality evidence suggests that there are advantages to using [illegible] compared to native tissue repair, including lower rates of awareness of prolapse, repeat surgery for prolapse, and recurrent prolapse on examination. The evidence suggests that if 19% of women are aware of prolapse after native tissue repair, between 10% and 15% will be aware of prolapse after permanent mesh repair. If the rate of recurrent prolapse on examination after a native tissue repair is assumed to be 38%, the risk would be between 11% and 20% after a repair with transvaginal permanent mesh. However, there are also problems associated with

Quality of the evidence

Overall, the quality of the evidence ranged from very low to moderate. The main limitations were poor reporting of study methods, inconsistency, and imprecision.

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INDUSTRY SPONSORSHIP AND RESEARCH OUTCOME (REVIEW)

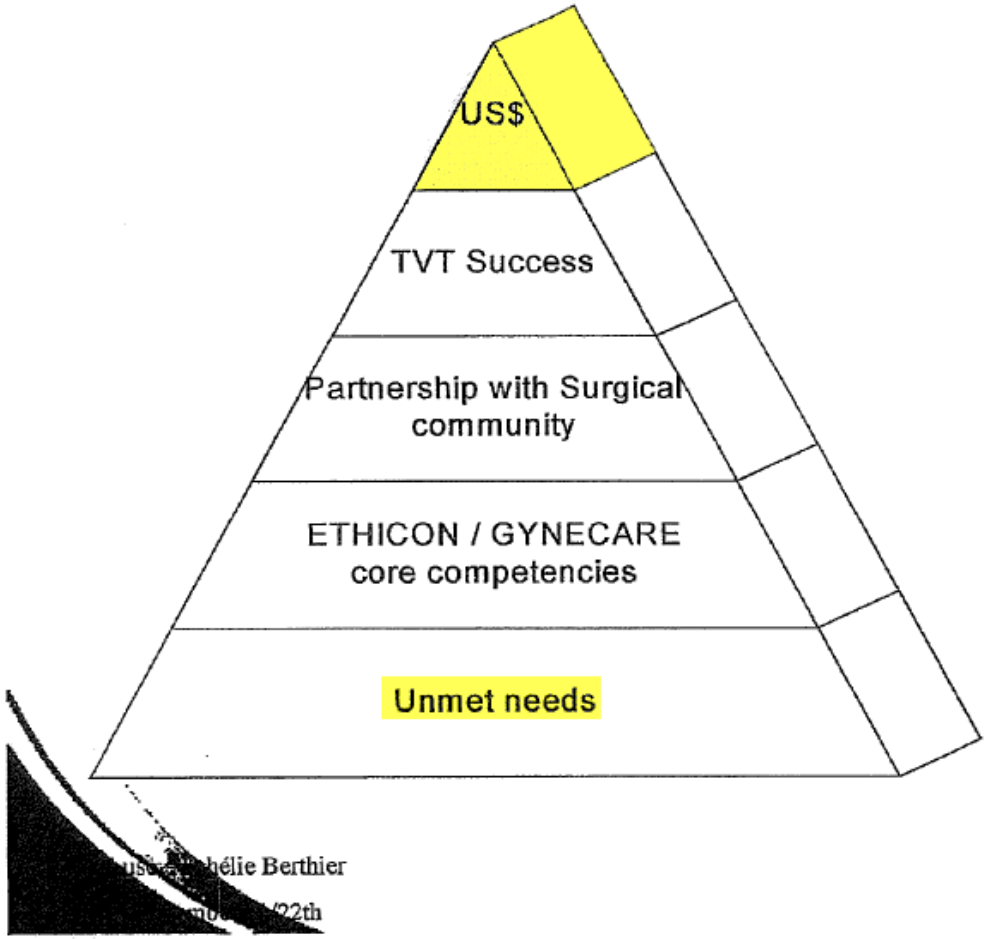
Lundh A

Lundh A, Lexchin J, Mintzes B, Schroll JB, Bero L

Authors' conclusions

Sponsorship of drug and device studies by the manufacturing company leads to more favorable efficacy results and conclusions than sponsorship by other sources.

Why focus on Pelvic Floor?



Key elements

Gynecare

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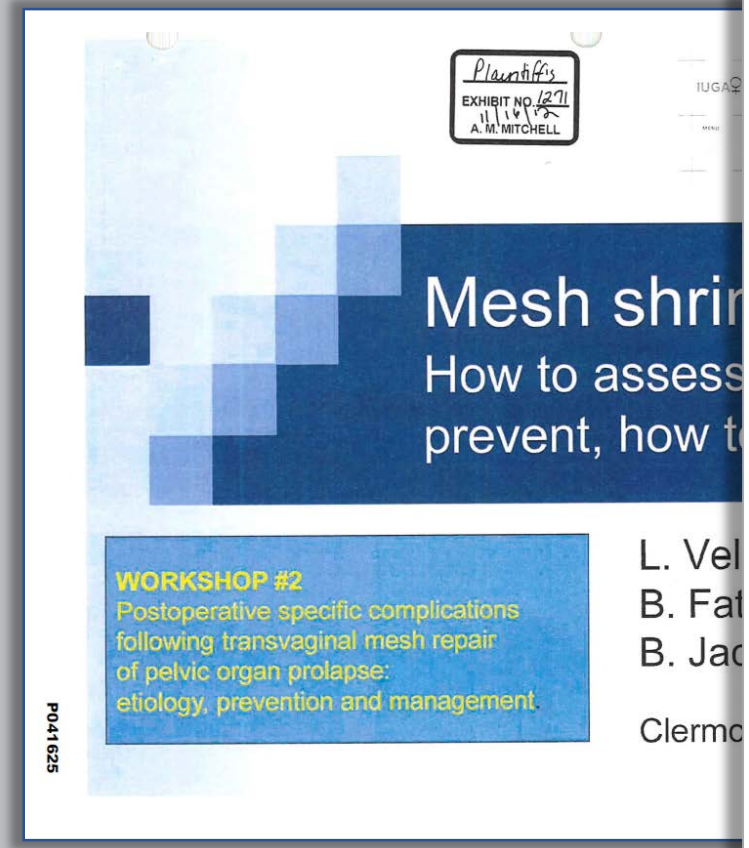

What is specific to vaginal surgery ?

- Much of what we know about grafts comes from research involving the abdominal wall hernias
- Poor knowledge of the vaginal in vivo response to the materials
- The vagina has an important vascularity and endogenous microflora that may have an impact on host tissue response and biomechanical properties of grafts used in pelvic reconstructive

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- no mesh is the best mesh
  - lightweight concept with a high pore to implant area ratio

1. adopt physiological demands

- no mesh is the best mesh

2007 unpublished data)

2. max elongation limit (< 40 % at 10 kPa (10 kN/m²= 1N/cm²) contact pressure (var. Moritsen. 2007; Janda 2006; O'Dell 2007)
   1. extreme 17 kN/m² (O'Dell 2007))
3. min. plastically softening under stretching: Eplast < Ultrapro
4. shrinkage/stiffening
   1. pore size > 3 mm
   2. pore size > 1 mm under stretch (mesh + stress shielding component only)
   - stress shielding of mesh implant (duration < 7d) (Abramov 2006)
5. anisotropic behavior 1:2 (long:vert) (Yamada 1971; Rubod 2007)
   1. 8:1 (lightning)< 1:1 (Gynemesh) < 1:2 (Thunder)< 1:8 (Ultrapro)
6. softness pattern (to be discussed)

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Preliminary requirements

- no mesh is the best mesh
  - lightweight concept with a high pore to implant area ratio

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no mesh is the best mesh

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6. softness pattern arms vs. body, Erosion prevention zone

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ETHICON

Improving lives by advancing the standard of care in tissue repair

P040380