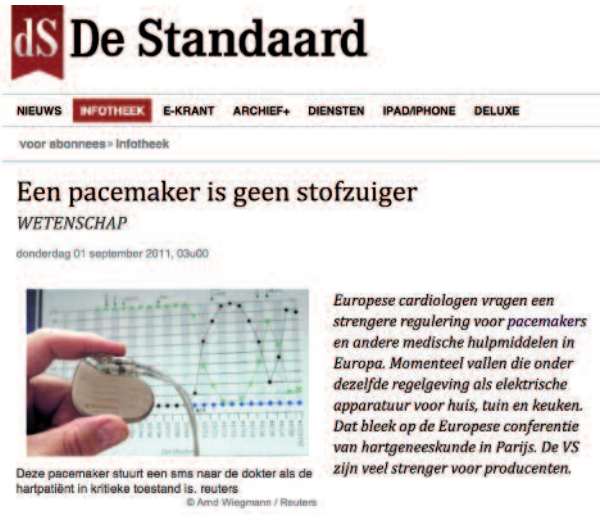
Editorial

Pacemakers are not vacuum cleaners*

Towards new guidelines for the introduction of novel medical devices in pelvic floor surgery

Our Belgian lay press recently became aware of the trend amongst medical professionals that the introduction of novel medical devices may need some more formal oversight. For making that point, they were quoting from a debate during a cardiologist's meeting, with a one liner that the "requirements for bringing a new pacemaker or stent onto the market is from a regulatory viewpoint as simple as marketing a new vacuum cleaner" (*Een pacemaker is geen stofzuiger. De Standaard, 1/9/2011, Figure 1*). Patients would get scared for less !


dS De Standaard

NIEUWS INFOTHEEK E-KRANT ARCHIEF+ DIENSTEN IPAD/IPHONE DELUXE

voor abonnees » infotheek

Een pacemaker is geen stofzuiger

WETENSCHAP

donderdag 01 september 2011, 03u00

Deze pacemaker stuurt een sms naar de dokter als de hartpatiënt in kritieke toestand is. reuters

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Europese cardiologen vragen een strengere regulering voor pacemakers en andere medische hulpmiddelen in Europa. Momenteel vallen die onder dezelfde regelgeving als elektrische apparatuur voor huis, tuin en keuken. Dat bleek op de Europese conferentie van hartgeneeskunde in Parijs. De VS zijn veel strenger voor producenten.

Apparently, the press missed July 13th, 2011 the updated *health notification* from the Food and Drug Administration (FDA) on the surgical placement of mesh via the vagina to repair pelvic organ prolapse (POP) (essentials summarized in Table 1) (*http://www.fda.gov/ MedicalDevices/Safety/AlertsandNotices/ucm262435.htm#.Th3ej3Bki9s.email*). It bluntly states that vaginal mesh placement "*may expose patients to greater risk than other surgical options*". Further it says that this greater risk "*comes without evidence of greater clinical benefit*". The FDA based the need to update its previous notification (*US Food and Drug Administration. FDA public health notification: serious complications associated with transvaginal placement of surgical mesh in repair of pelvic organ prolapsed and stress urinary incontinence. Ocotober 20, 2008. Available at: http://www.fda.gov/cdrh/safety/102008-surgicalmesh.html*) on a fivefold increase of the number of adverse events reported via the Manufacturers And User facility Device Experience (MAUDE) database, letting them to conclude that adverse events are *not rare (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/ cfMAUDE/search.CFM. Accessed Sept 5, 2011)*. Moreover, the FDA considers reclassifying these devices as class III, rather than class II products, i.e. devices that are potentially harmful to patients. Obviously statements of a U.S. based regulator FDA have no direct relevance to Europe, but it's explicit wording may not stay without consequence.

This editorial has no ambition to make the final judgment on the scientific basis or opportunity of mesh use in POP and incontinence surgery, nor does it review the opportunity of this health notification at all. This discussion will certainly be triggered in the months to come, probably in a not to serene atmosphere since the public debate will be kicked off this week in a public advisory committee meeting (http://www.fda.gov/AdvisoryCommittees/Calendar/ucm262495.htm. Accessed Sept 5th, 2011). Being our selves still partly confused on the actual place of mesh surgery, you will *not* find here any straight forward guidance on mesh use.

Our editorial will first focus on some juridical aspects to. In view of this we re-read a number of earlier published critical comments and opinion papers on this issue. We certainly are not medicolegal experts, but what we want to do is to remind you of a number of legal aspects, which one should bear in mind even more meticulously than ever, when using novel meshes and trocars, certainly *outside clinical trials*.

* This text represents the personal opinion of the authors.

Table 1. — Excerpt of FDA recommendations for health care providers.

- Inform the patient about the benefits and risks of non-surgical options, non-mesh surgery, surgical mesh placed abdominally and the likely success of these alternatives compared to transvaginal surgery with mesh.
- Obtain specialized training for each mesh placement technique, and be aware of the risks of surgical mesh.
- Inform patients that implantation … is permanent, and that some complications … may require additional surgery that may or may not correct the complication.
- Inform patients about the potential for serious complications and their effect on quality of life.
- Choose mesh surgery only after weighing the risks and benefits of surgery with mesh versus all surgical and non-surgical alternatives.
- Ensure that the patient understands the postoperative risks and complications of mesh surgery as well as limited long-term outcomes data.
- Provide the patient with product insert.

Mucowski et al last year elegantly pointed to some medicolegal controversies from an American perspective, which to me also apply to our practice (Mucowski *et al*., 2010). Though it might seem at first glance that when patients file a complaint because of perceived harm caused by the use of mesh, the liability would be with the manufacturer. This is however incorrect: liability can definitely be shifted away from the manufacturer to the physician. This concept is referred to as *learned intermediary doctrine*. It means that if a physician has been adequately warned about potential complications, it is the physician's duty to transfer these warnings to the patient. If not, she or he can be held responsible. The health notification dated July 13th, 2011 is very clear on the latter. It should be seen as an adequate and not deniable warning in this respect.

The second interesting point is that FDA clearance (or CE labeling!) for a novel mesh, whilst allowing introduction into the market, *may actually protect the manufacturer.* In other words, that clearance may actually render shifting liability to the physician more likely. In a way, clearance for the device may *bar claims* challenging the safety or performance of the device. In that case patients have to turn against their physicians (Riegel v Medtronic Inc, 552 US, 312, (2008). For both above reasons, it seems wise to include in the medical record formal documentation that one has clarified the potential risks of using the device to the patient. That documentation should also describe that the patient in return has consented to the use of the device, in a format imposed locally. Moreover, FDA recommends that patients are also given the product insert after the operation, like for any other permanent implant.

Consent does not prevent issues. The relationship between the patient and the surgeon is one of *fiduciary responsibility*, which means the patient trusts the physician has the level of knowledge to appropriately inform and assist the patient in decision. To protect the patient, the physician must have sufficient data, for instance, to support the performance of the mesh procedure involved, or in its absence, disclose the lack of (conclusive) data. The FDA judges that at present the evidence supporting the use of mesh is insufficient. The health notification recommends the surgeon to recognize that in most cases, POP can be treated successfully without mesh or not surgically. This unbalanced view as if there was an absolute absence of any evidence is to my opinion at least debatable. There is meta-analytic data on the anatomical benefit in the anterior compartment – though subjective or long term prevention of recurrence remains to be demonstrated (Jia *et al*., 2010). For apical prolapse repair with vaginal kits a systematic review has shown short term efficacy (Feiner *et al*., 2009). Again long term results are indeed missing, and abdominal sacrocolpopexy is associated with lesser device (mesh and trocars) complications (Feiner *et al*., 2009). For posterior repair the situation is different indeed, with one trial showing benefit, but others did not (Carey *et al*., 2009, Iglesia *et al*., 2010, Withagen *et al*., 2011). What is absolutely true is that mesh repairs keep on being associated with a higher than desirable number of graft related complications (Abed *et al*., 2011).

Some of you may find it harsh that I insist first on how this revised health notification may have consequences to the physician, rather than focusing on the patient. Nothing more untrue than that. Like all of us I am seriously concerned about their interest. It is just that we do at present not have all the answers. This pertains to the use of mesh as well as to the best procedure for introducing novel medical devices onto the market. This is logically the subject of ongoing and emotional debates (Morreim *et al*., 2006) (Wall *et al*., 2010). A balance between affordable and accessible innovation and efficient regulation is to be sought. Actually, the undersigned is part of a working group at the International Urogynaecological Association (IUGA), which recently drafted a proposed novel guideline for introduction of novel devices (Slack *et* al, in review). We actually agree that

these *cannot be introduced to the market without experimental research and clinical data or research*. We propose a pragmatic minimum clearance track for new products consisting (1) of an accurate and standardized description of the physical properties, (2) data on the biological properties gathered in animal experiments, (4) anatomical cadaveric studies, and (5) upfront clinical studies followed by a (6) compulsory registry on the first 1,000 patients implanted. Ideally manufacturers should support well-designed prospective (randomized) clinical trials that can support the claimed benefits of the new product. The latter is confirmed by the story of the sling procedure for stress incontinence. These became widely accepted after their evaluation in a randomized clinical trial, and certainly returned investment to the manufacturer (Ward *et al*., 2002). Such (or an amended) regulatory process for introduction of novel devices, will remove the burden from the patient and physician to become involved (without realizing it) in what is actually the first evaluation of the device.

Actually it creates a transparent, explicated and well regulated and overseen partnership between patients and surgeons, and the industry with the aim of improving outcomes of POP surgery. This may come at a price, both in terms of product development, a slight slow-down in the product innovation cycle, as well as the price to the end user. But at least it will prevent the marketing of "me too kits" by industrial partners who might not be committed to engage in comprehensive and long term care of the patient with POP, or the needlessly increasingly faster cycle of product innovations with marginal added value. Therefore the debate should not be seen as a threat, but rather a challenge for clarifying and improving partnership between patients, surgeons and the medical industry.

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