Sir,

With great interest have we read the publication by Wright et al. (2011b) in which they describe ovarian surface epithelium (OSE) replacement after epithelietectomy (OSEx) in primates. Our special attention was caught by their observations at the fimbria/ovary surface junction, a compartment that has recently been recognized as a likely site of origin for epithelial ovarian carcinomas. Based on genetic and pathological evidence, at least a substantial part of serous ovarian cancers is now thought to arise from the fimbrial epithelium (FE) rather than from the OSE (Bowtell, 2010; Kurman and Shih le, 2011).

When ovaries from female rhesus macaques were ridded of epithelial cells, a surface epithelium of the denuded ovaries was partially restored with cell densities comparable with normal surface epithelium being achieved only around the fimbria/ovarian surface junction. Further regions of the ovarian surface were sparsely populated, even as long as 6–12 months after epithelietectomy. Wright et al. (2011b) suggest the possibility that the partial replacement of the OSE is accomplished by migration of FE cells towards the ovarian surface. As fimbria and ovarian surface are immediately adjacent, this appears highly plausible, all the more as gene expression profiles from restored OSE and FE cells turned out to be remarkably similar. Moreover, transitional cell types were described at the fimbria/ovarian surface junction. Physiologically, this interconversion between FE and OSE could be a natural event associated with destruction of the ovarian surface during follicular rupture with each ovulation, and could involve the transfer of OSE cells to the fimbria, and fimbrial cells to the ovary.

At the apex of unruptured pre-ovulatory follicles, ovarian surface epithelial cells become sparse and are shed to an extent that is individually specific and species-dependent (Bjersing and Cajander, 1975; Dietl et al., 1987, Wright et al., 2011a). During follicular rupture, damage to the ovarian surface and thereby a loss of OSE are inevitable at the site of rupture. During ovulation, close contact between the ovulation point and the fimbriated end of the fallopian tube is a natural requirement to enable the uptake of the egg cell via the fimbria. At this instant, FE cells can simply be transferred to the ovarian surface. The required mechanical forces appear to be quite low—in the laboratory, FE cells can be eluted from the fallopian tube by mere flushing (Piek et al., 2001). Consequently, FE cells may not only repopulate the ovarian surface but also be incorporated into the ovaries via formation of inclusion cysts (Kurman and Shih le, 2011). Accumulating evidence now shows that high-grade serous ovarian carcinomas (the most frequent subtype of ovarian cancer) mostly originate from the fallopian tube but may also arise via a secondary pathway right in the ovary. Considering that tumours often take decades until they manifest (Beerenwinkel et al., 2011), FE cells that have repopulated ruptured ovarian surface epithelia might thus be the culprits for later tumour development in some cases. Ovulation itself which, at least in primates, does not require the OSE (Wright et al., 2010), may further contribute to ovarian carcinogenesis via free radicals in the follicular fluid and via inflammatory mediators released in response to follicular rupture and during tissue repair (Murdoch and Martinchick, 2004). This is in complete agreement with epidemiological data showing that women who have used ovulation-inhibiting oral contraceptives over a number of years bear a reduced risk of developing ovarian cancer (Ory, 1987; Beral et al., 2007).

Thus, by demonstrating that FE cells from the fallopian tube may replace OSE in primates, Wright et al. (2011b) further fuel the current hypothesis that high-grade serous ovarian cancer may originate in the ovary as well as the fallopian tube. Moreover, they provide a plausible link between the known protective effect of oral contraceptives and a mechanism which possibly contributes to ovarian carcinogenesis. With regard to cancer prevention, this suggests that salpingectomy performed during hysterectomy or sterilization should confer a considerable degree of protection against ovarian cancer (Dietl and Wischhusen, 2011). Consequently, preventive salpingectomy (possibly combined with OSEx) might become a suitable alternative to salpingo-oophorectomy which—while still being the safest option—comes at the price of serious side effects.

References


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**Reply: The fimbria/ovarian surface junction**

Sir,

A body of data has accumulated in recent years that indicates that high-grade serous carcinomas have multiple origins, and this concept is still evolving. A broader consideration of these origins may require assessment of whether ovarian surface epithelium (OSE) and fimbrial epithelium (FE) are interconvertible. If they are, it may not be practical to distinguish between them. They may be defined primarily by location and distinctions may be quite labile and environment specific. The Letter by Dietl et al. comments on our observations (Wright et al., 2011a) that FE may replace OSE after removal of the surface epithelium by epitheliotomy (OSEX), and we would like to add observations from a companion manuscript (Wright et al., 2011b) that may be complementary to FE transfer to the ovary: OSE cells may be displaced by ovulation and transferred to the fimbria.

Critical experiments are needed to determine whether, and to what extent, the transfer of cells from each population occurs, and how important the ovarian compartment is to the transformation of FE/OSE. Transfer of FE to the ovarian environment may enhance risk by subjecting these cells to ovulatory damage and/or incorporating them into inclusion cysts. Alternatively, transfer of OSE cells to the fimbria may promote tumorigenesis by releasing displaced cells from unidentified ovarian cues that account for the relatively low levels of proliferation and enhanced DNA repair seen in OSE versus FE. Yet a third possibility is that the primate OSE does not undergo cyclic proliferative repair after ovulation, but instead is naturally replaced by migrating FE. Resolving each of these possibilities will have clinical significance in determining whether salpingectomy or OSEX alone, or in combination, will protect against high-grade serous carcinomas without sacrificing ovarian function and fertility.

### References


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**The effect of needle diameter on duration of oocyte collection procedure**

Sir,

I read the article by Wikland et al. (2011) with great interest. I am intrigued with the authors’ finding of similar collection times with the new reduced diameter needle. Poiseuille’s law states that at a constant driving pressure the flow rate of liquid through a capillary tube is directly proportional to the fourth power of the radius of the tube and inversely proportional to the length and viscosity of the tube (Steiner, 2011). Accordingly, I would expect the collection time to be different between two needles with inner diameters differing by 40%.

### References


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**Reply: The effect of needle diameter on duration of oocyte collection procedure**

Sir,

We thank Dr. Steiner for his interest in our study (Wikland et al., 2011) and the comment. The question about collection time with reference to Poiseuille’s law is relevant. According to this law one would expect a longer collection time for the thinner needle.