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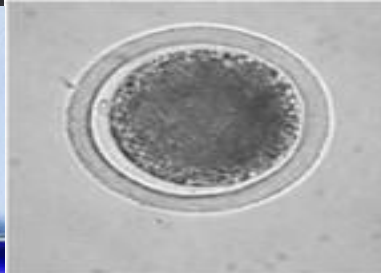
Egg harvesting for stem cell research

Medical risks and ethical problems

پاور پوینٹ و رائے: نیما جعفری رستگار

Abstract

- ▶ Since the birth of the world's first 'test-tube baby', Louise Brown, in 1978, egg-harvesting procedures have become increasingly widely used in IVF.
- ▶ Increasingly, researchers are seeking eggs from young women to be used for embryo cloning procedures.
- ▶ The harvesting of multiple eggs often involves the administration of drugs that have not been approved for this purpose.
- ▶ Also these drugs have not been adequately studied for their long-term effects on women despite research providing some evidence of significant harm to women in both the short and long term.
- ▶ In addition, egg harvesting is taking place in a research climate that may lead to the exploitation of young women.



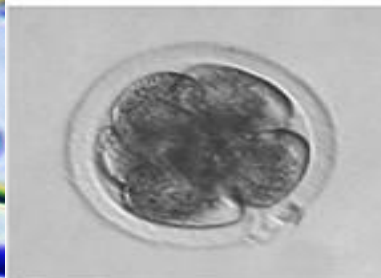
mature oocyte (0hpi)



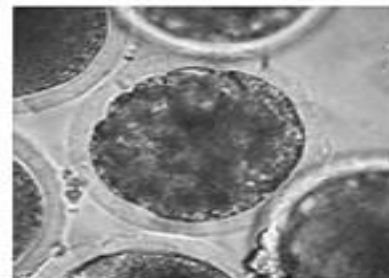
2-cell (24.1hpi)



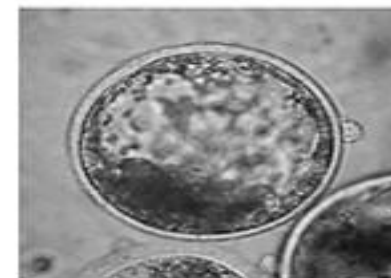
3-4-bl (34.9hpi)



8-16-bl (86.9hpi)



morula (107.3hpi)



blastocyst (142.9hpi)



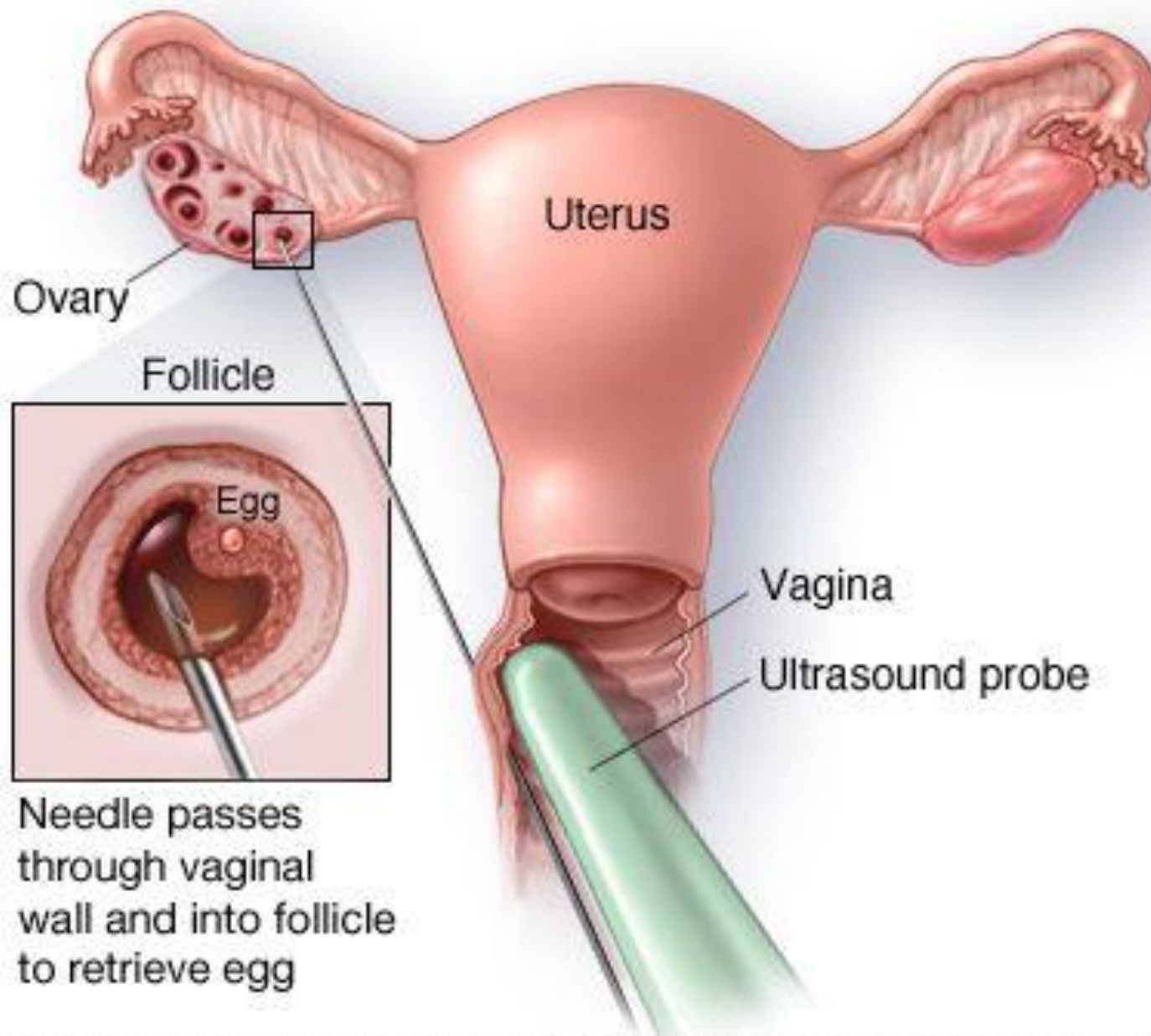
Women's health and human rights advocates are concerned

- ▶ young women are being asked to donate or sell their ova, not only for use in fertility clinics, but increasingly for non-clinical use in experimental cloning research.
- ▶ The harvesting of multiple eggs often involves the administration of hormonal drugs that have not been approved for this purpose and also their long-term effects haven't been investigated (despite many case reports)
- ▶ The collection of eggs for embryo cloning research is being conducted in the context of an international race for dominance the production of embryonic stem cells and related products that may result in substantial private financial gain while offering no therapeutic benefits that are accessible to the vast majority.

The harvesting of multiple eggs

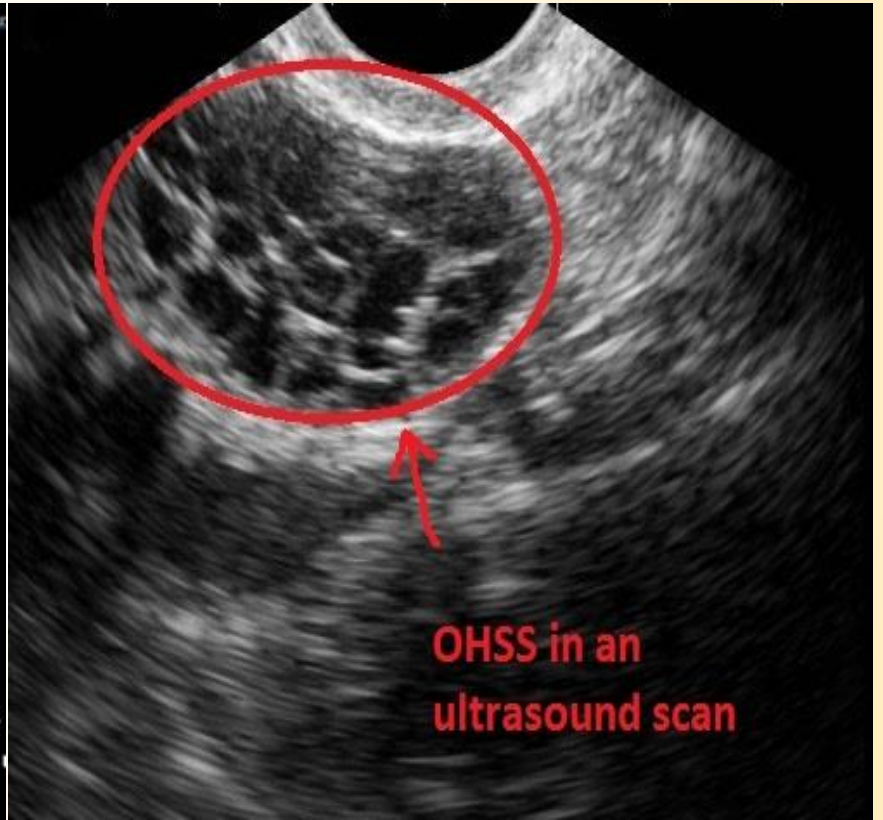
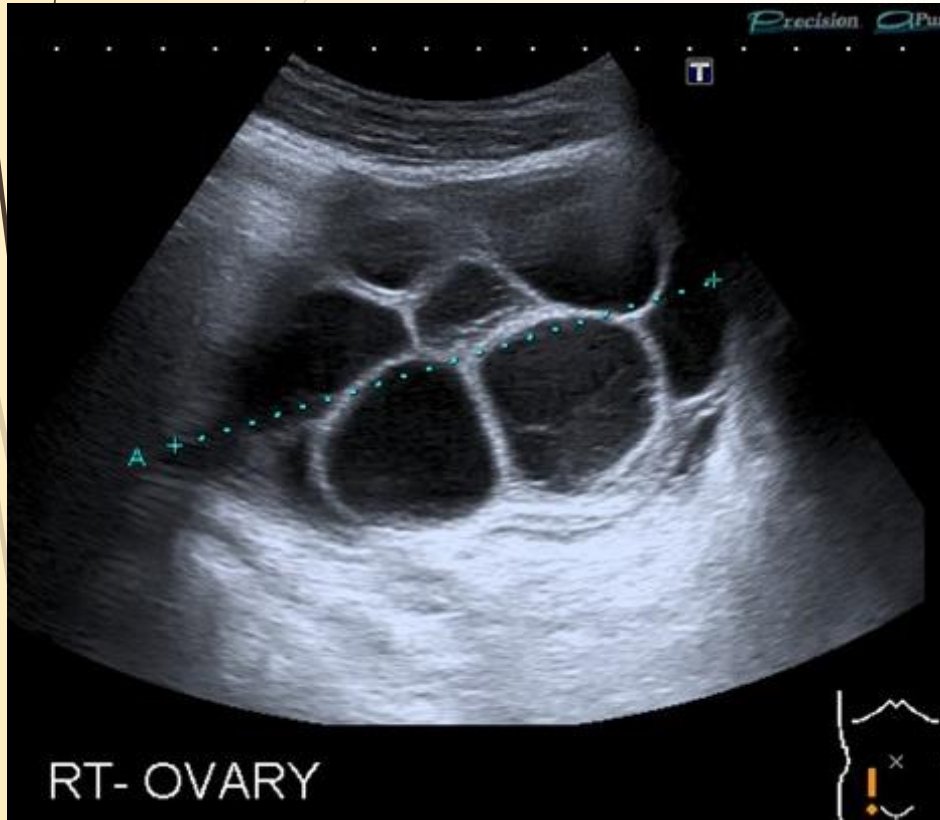
- ▶ The harvesting of multiple eggs is an invasive and uncomfortable two-stage process requiring many clinic visits, multiple injections of hormones, and one minor surgery at the least.
- ▶ Both stages, ovarian suppression and stimulation, require the use of powerful hormones and other drugs to manipulate a woman's body into producing many, often a dozen or more, eggs at a time rather than the normal one or two.
- ▶ The mature eggs are then collected surgically for use in IVF or in research.





Short and long term effects

- ▶ The most immediate serious risk is ovarian hyperstimulation syndrome (OHSS).
- ▶ mild forms occur in 10–20% of cycles .Symptoms of include nausea, vomiting, diarrhoea, and abdominal distention. which may persist or worsen over time to include rapid weight gain, accumulation of serous fluid in the abdominal cavities, respiratory Difficulty and...
- ❖ severe forms: Thromboembolism, renal failure, adult respiratory distress, and haemorrhage from ovarian rupture and death.
- ▶ Long-term effects are poorly understood, Pharmaceutical firms have not been required by either the government or physicians to collect safety data for IVF drugs regarding risk of cancer or other health conditions despite the drugs having been available for several decades.



Drugs

- ▶ Lupron (leuprolide acetate): commonly used in the first phase of egg harvesting, has not been approved for this purpose, but rather is used 'off label.'
- ▶ Antagon: has been approved for such use, but there's no data available on its long-term safety.
- ▶ clomiphene, another stimulant the ovaries, was associated with a 2.3-fold increased risk of ovarian tumours (also uterine cancer).
- ▶ more recent reproductive treatments often involve much higher exposures to gonadotrophins.
- ▶ most IVF protocols include luteal phase support for several weeks with supplemental progestogens. This raises further concern, since these agents have been linked to increases in breast cancer risk.

TABLE 2. MEDICATIONS USED IN INFERTILITY

Generic Name	Brand Name
Clomiphene citrate	Clomid, Serophene
Metformin	Fortamet, Glucophage, Riomet, Glumetza
Follicle-stimulating hormone injection	Bravelle, Follistim AQ, Gonal-F
Luteinizing hormone injection	Luveris
Human chorionic gonadotropin	A.P.L., Pregnyl, Novarel, Ovidrel
Human menopausal gonadotropin injections	Repronex, Menopur
Dopamine agonists	Parlodel, Cycloset (bromocriptine) Dostinex (cabergoline)
Gonadotropin-releasing hormone injection	Factrel
Gonadotropin-releasing hormone agonist injection, nasal spray, or implant	Lupron depot (leuprolide acetate) Synarel (nafarelin acetate) Zoladex (goserelin acetate)



Adapted from reference 9.

Risks to offspring

- ▶ human data are sorely lacking.
- ▶ However, a recent report that ovarian stimulation treatment in mice results in several significant abnormalities in their offspring does provide reason for concern.
- ▶ These effects include growth retardation, a delay in ossification (bone development) and an eight-fold increase in a significant rib deformity.

Historical pattern of hormonal modifications

- widespread prescription of DES (Diethylstilbestrol)to pregnant women in the 50's to prevent miscarriage or premature birth. Even though DES was shown not to prevent miscarriage in early years it was still used until 1971 when a study documented the alarming occurrence of an often fatal form of vaginal cancer in the young daughters born to women who had been given DES. Also caused infertility in female offspring. Five to ten million women worldwide were exposed to DES.
- hormone replacement therapy (HRT), after being vigorously marketed to menopausal women for decades, often advertised as a way of preventing future disease, was found to increase risks for a variety of serious health issues.
- Policy makers have a particular obligation to protect non-patient 'donors' from the possible threat of irreversible harm by insisting that prevention takes precedence over everything else.

ESTROGENS	Formulations	Starting Dose	Maximum Dose	
Bioidentical	Spironolactone	50 - 100 mg OD	200 mg BID	
	17-beta estradiol (E2)	Cyproterone	12.5 - 25 mg OD	50 mg OD
	Conjugated Estrogen*	0.625 mg OD	1.25 mg OD	
	Estradiol (oral)*	1 - 2mg OD	4 mg OD	
	Estradiol Patch (transdermal) *g	0.1 mg OD / apply path 2x/week	0.2 mg OD / apply path 2x/week	
	Estrone sulfate (E1)	Estradiol valerate** injectable (IM) ^l	10mg q 2/52	10mg q 1/52



	Medication	Post-Menopausal Replacement Dose	Gender Reassignment Dose	
Estropipate (E1)	Conjugated Equine Estrogens (<i>Premarin</i>)	0.625 mg PO qd	Starting: 1.25-2.5 mg PO qd Average: 5 mg PO qd Maximum: 10 mg PO qd	
Estriol (E3)	Ethinyl Estradiol (<i>Estinyf</i>)	0.05 mg PO qd	Starting: 0.1-0.2 mg PO qd Average: 0.4 mg PO qd Maximum: 0.5 mg PO qd	
Non-Bioidentical	Ethinyl estradiol	Estradiol (<i>Estrace, Gynodiol</i>)	0.5 mg PO qd Starting: 1-2 mg PO qd Average: 4 mg PO qd Maximum: 5 mg PO qd	
	Esterified estrogens	Estradiol Valerate injection (<i>Delestrogen</i>)	10 mg IM q2wks Starting: 20-40 mg IM q2wks Average: 40 mg IM q 2wks Maximum: 40-60 mg IM q2wks	
	Conjugated equine estrogens (CEE)	Estradiol patch (<i>Alora, Climera, Esclim, Estraderm, Vivelle, Vivelle-Dot</i>)	0.05 mg/d dermal (change 0.5-1.0 mg patches once-twice/week)	Starting: 0.1-0.2mg/d Average: 0.2-0.3mg/d Maximum: 0.3mg/d
	Dienestrol			

Food for thought!

- ▶ Human embryo cloning has been described as 'a wildly inefficient process', often requiring hundreds of eggs to produce a single viable clone. Strictly for research alone, then, eggs will need to be harvested from many thousands of women.
- ▶ And, if embryonic stem cells were to prove useful in medical treatments, something not yet accomplished even with proof-of-principle laboratory research, countless more eggs would be needed for the many millions of people with conditions that the treatments will supposedly cure.
- ▶ While some other jurisdictions reject all payment for eggs (e.g. Canada) it is not the case in the US where the fees that women are paid for eggs for IVF has been rising. Depending on the location and on features of the potential 'donor,' compensation may range from a low of US\$3000 in some parts of the US to many times that. Advertisements employ the euphemism of 'donation', provide altruistic rationales, and usually define payment as reimbursement for time and expenses to make the exchange more palatable to all parties. As a result, young women who face large education-related debts can, and often do, undergo repeated rounds of ovarian stimulation to finance their schooling or other needs without giving adequate consideration to the health consequences.
- ▶ When the doctor becomes the agent of a third party, in this case a researcher, and relates to the patient with the researcher's interests in mind, the doctor is violating the basic assumptions of the doctor-patient relationship.
- ▶ Also the use of misleading language and terms as to how the eggs will be used is a major concern.

reference

- ▶ Article

Egg harvesting for stem cell research: medical risks and ethical problems

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