Embryoscopy
Anatomy & Diagnostic Value

Presentation Objectives

Terminology

The development of embryoscopy

Technique failure rate

Early Embryo anatomy

Diagnostic value

Possibilities for embryo treatment

Review of the literature

ESHRE Campus

Dubrovnik, Croatia
24 -25 September 2010

The determinants of a successful pregnancy

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Terminology

- ☑ Embryoscopy – direct visualization of an embryo usually 5-10 weeks previous to fusion of the chorion and amnion
- ☑ Fetoscopy – usually 14-25 weeks. Phenotypic evaluation added to the karyotype analysis
- ☑ Should be restricted to families at high risk for recurrence of genetic conditions associated with external fetal anomalies not detectable by ultrasound

Entry and Inspection

Embryoscopy can be performed

- ☒ Trans abdominally
- ☒ Trans cervically
- ☒ Usually before 11 weeks the telescope reaches the extracoelomic space
- ☒ The amniotic cavity is formed after 11 weeks of gestation

The Development of Embryoscopy

- Dr Bjorn Westin in 1954, performed hystero-embryoscopy in 3 embryos before TOP during early 2nd trimester
- He used the McCarthy's 10 mm telescope
- Two cases were performed under GA and one with local anaesthesia
- He reported active embryo extremities movements and he counted over 30 swallowing movements per minute

The development of Embryoscopy

Scrimgeour JB and Valenti C, 1970's

- Direct endocopic examinations of embryos by laparotomy and a small opening of the myometrium

The development of Embryoscopy and the first direct fetal biopsies

- ☑ *Rodeck 1980 and Elias 1983*
- ☑ Perform the first "Fetoscopies"
- ☑ Transabdominal insertion of the endoscope under real-time US guidance for direct fetal observation, fetal blood sampling and fetal skin biopsies

The Development of Embryoscopy

- Embryoscopy was considered as an obsolete option during 1980 while the abortion rate was **4 - 8%**
- The US was then well developed and helped a lot in early fetal anomaly diagnosis
- Daffos F performs an US guided direct fetal blood sampling

Technological advances…

The recent optic and instrument technological advances offer better visualization with smaller diameter telescopes enabling better and more accurate diagnostic capabilities

Also enable minimal operative procedures to the fetus with less complications for the fetus and the mother

Embryoscopy and recent molecular achievements

- First trials presented minor benefits and limited diagnostic potentials due to poor technical facilities

- Recent molecular biology achievements and technical advances as well as social needs and demands will accelerate the clinical application of embryoscopy for early diagnosis and probably embryo treatment…

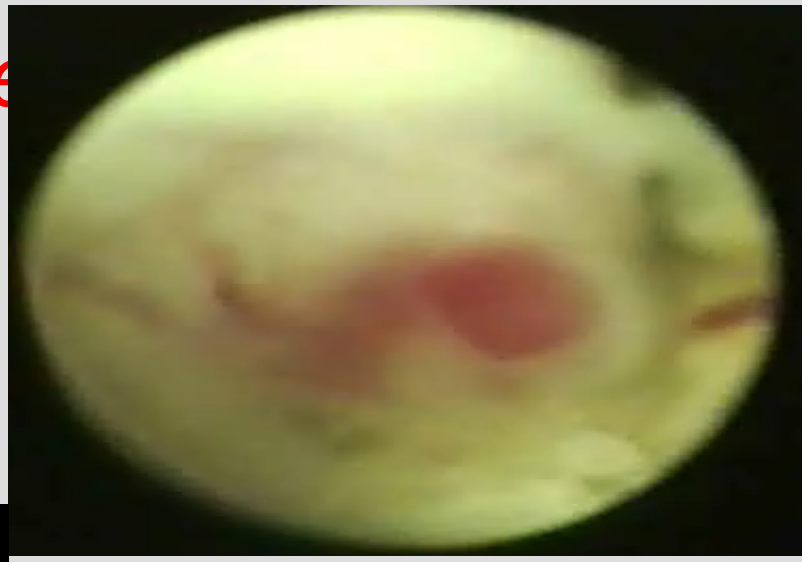
The value of Embryoscopy

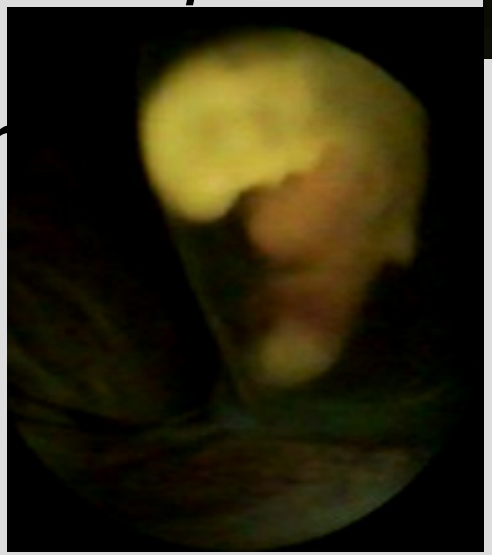
- Diagnostic
  - ✓ Etiology of missed and recurrent abortions
  - ✓ Reevaluate normal embryo status / anatomy, physiology
  - ✓ Phenotype of embryos with suspected US abnormalities
- Therapeutic
  - ✓ Cervical ectopic pregnancy
  - ✓ Stem cell therapy
  - ✓ Gene therapy

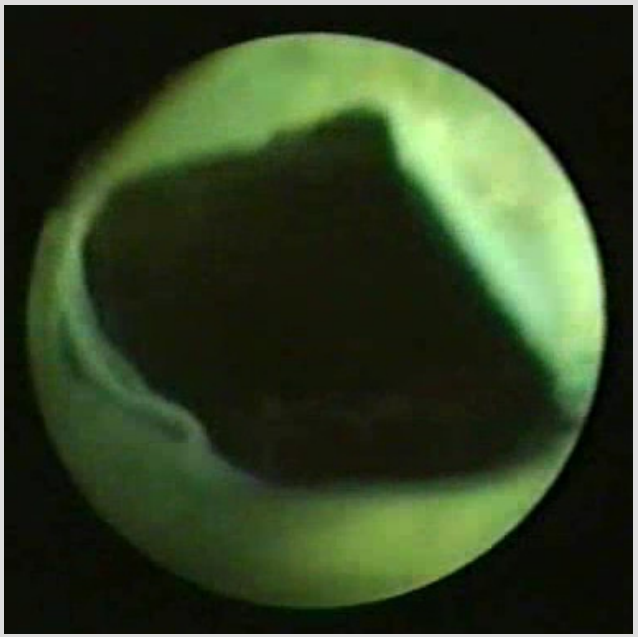
In Vivo Evaluation of early embryo development and its surrounding environment

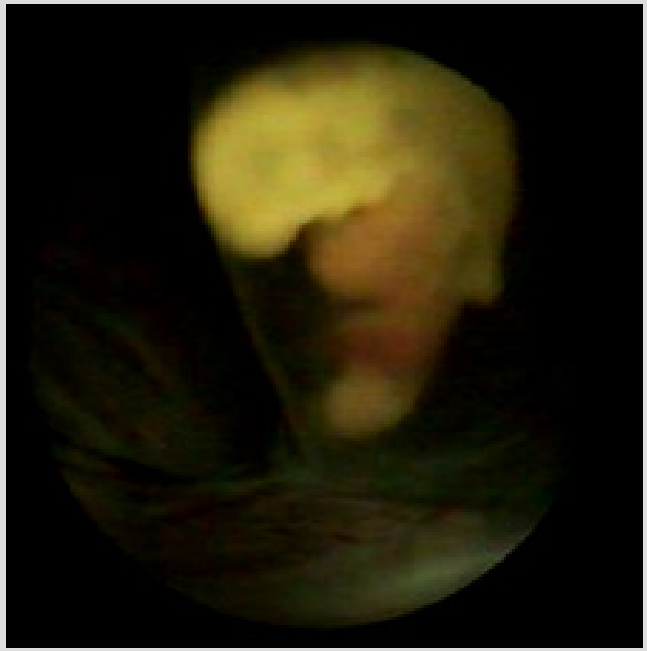
The following can be cle

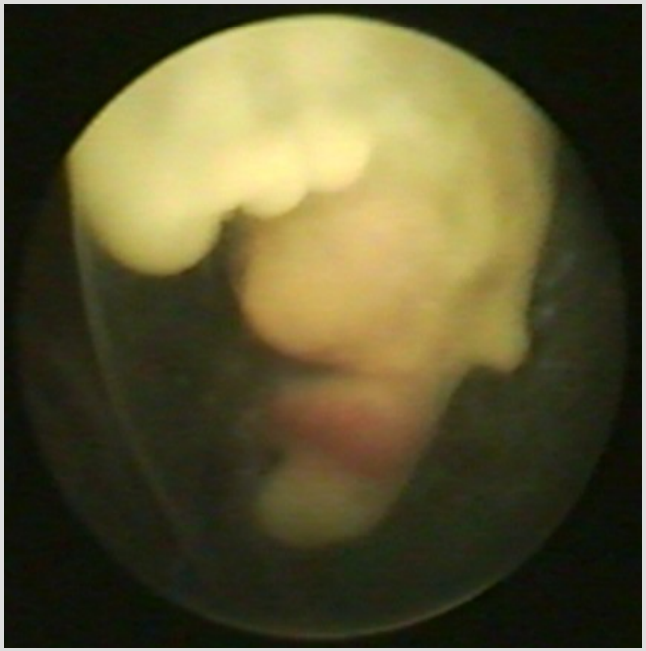
- *Cervical canal*
- *Intrauterine cavity*
- *Pregnancy sac*
- *Chorion and*
- *Umbilical cor*
- *Embryo*
- *Alantois*











Cervical Ectopic Pregnancy

- US evaluation at 5+4 weeks.
- Mild bleeding
- Pregnancy G4 after 3 TOPs

- Embryoscopy in order to inject methotrexate. Successful hysteroscopic clearance of the cervical ectopic pregnancy (video)

Embryoscopy: Searching for the Etiology of Recurrent Spontaneous Abortions

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Definition and Abortion Risk Rate

- ✓ Recurrent spontaneous abortions (RSA) refer to three or more consecutive spontaneous abortions *(Hannes 1992)*

- ✓ Risk for SA after 1st Abortion 20-25%
- ✓ Risk for SA after 2nd Abortion 40-50%
- ✓ Risk for SA after ≥ 3rd Abortion 60% and levels of

- ✓ Most couples have at least a 60% chance of delivering a live-borne infant with three or more spontaneous abortions *(Poland et al. 1977)*

The frequency of factors affecting RSA

(Dhont M. 2003, Kuttech WH 1999)

1. Genetic abnormalities 3-5%
2. Uterine anatom. abnor. (hereditary & acquired 15-20%)
3. Immunologic (Antiphosphol.& Anticardiolipin 15-25%)
4. Endocrine / metabolic disorders 5-8% (DM, PCOD etc)
5. Environmental factors 5-10% (occupation, smoking etc)
6. Unexplained 40% can not identify the etiology
   (Stephenson MD 1996)

Patients and Methods

- 38 patients with history of RSA
- All patients underwent history, general body and gynecological examinations and laboratory investigations and hysteroscopy during their last abortion

Patients

Our study - RSA patients with

- unexplained etiology 15
- uterine cavity abnormalities corrected 7
- anticardiolipin syndrome 2
- endocrinological factor 5
- suspected thrombophilia, treated w LMH 8
- treated with husband WBC 1

The technique of Embryoscopy

- Visualization of dead human embryos up to the age of 12 weeks

- TransCervical
- Instruments: Telescope 3.5mm, 5mm, 30^{o}, single flow
- Metal Halide light source 270 Watts
- Distention medium: Normal saline
- No use of anesthesia or sedation

Targets of the Study

- ✓ Standardization of the technique
- ✓ Evaluation of the potentials of the technique
- ✓ Evaluation of the characteristics of the pregnancy sac and its contents
- ✓ Correlation of the embryo external characteristics and its genetic analysis

Results

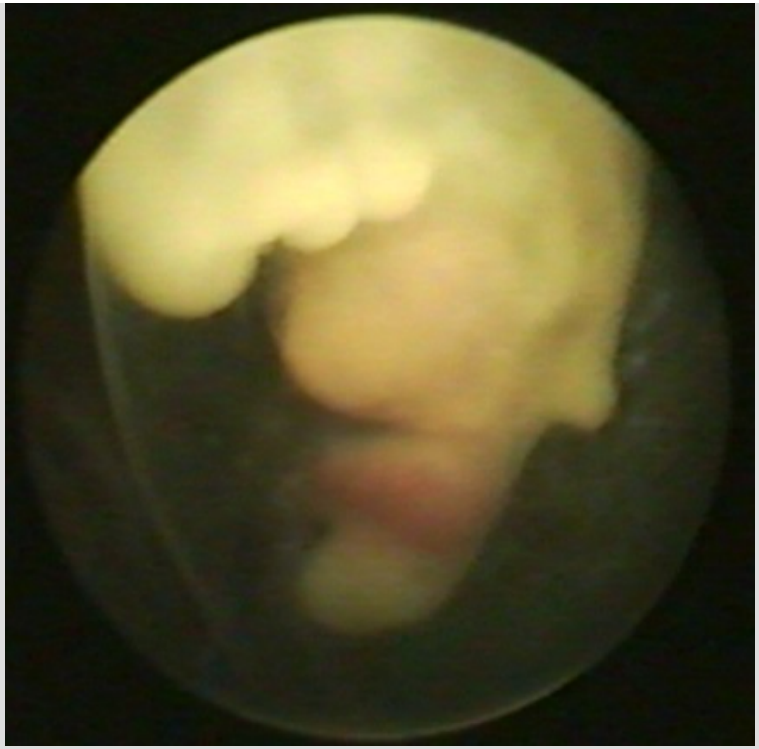
- ✪ The total of 35 embryos were evaluated
- ✪ In 35/38 cases embryoscopy was successful and complete evaluation of the embryo and pregnancy sac was performed
- ✪ The beta-hCG serum level was zero in three weeks after the D&C

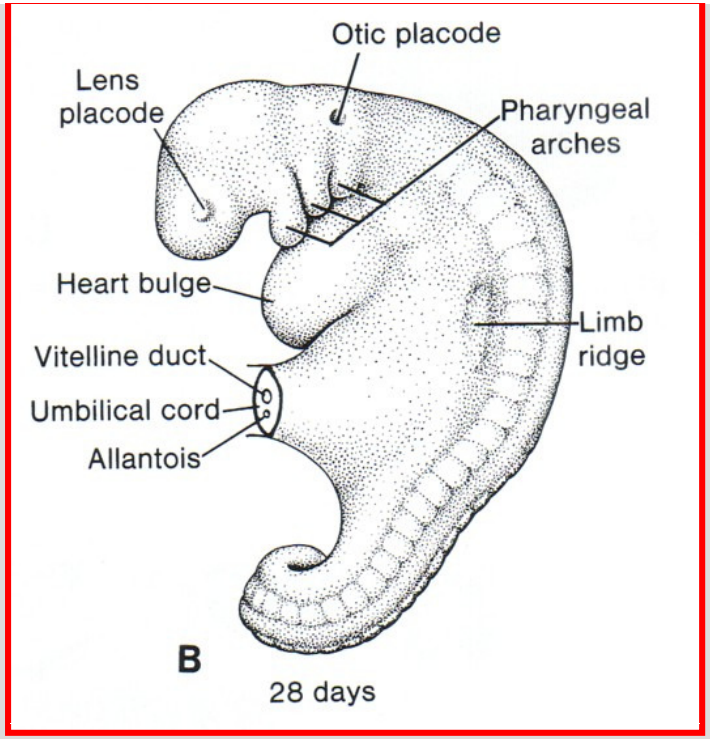
Correlation of the embryo morphology and embryo karyotype

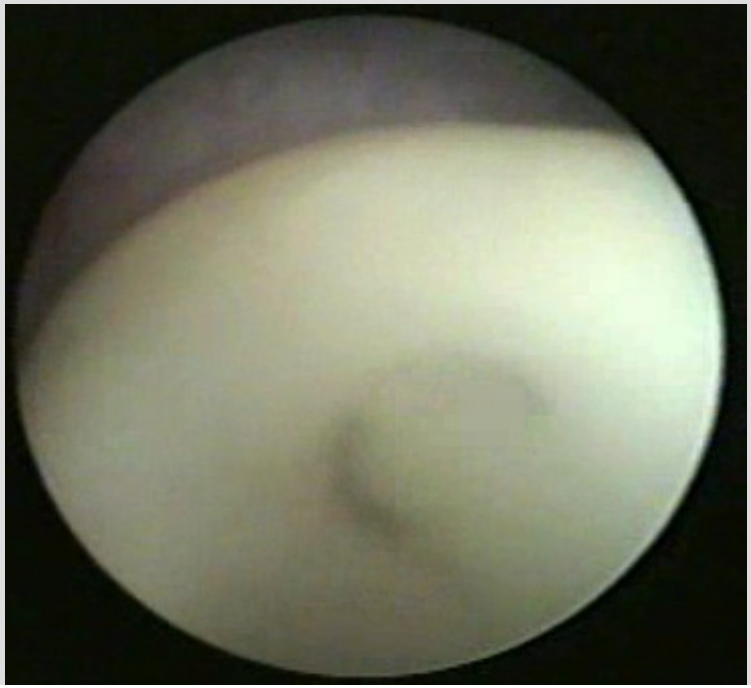
	Variety of possibilities	**Cases**	**%**
A	Normal phenotype and normal karyotype	5/35	14
B	Normal phenotype and abnormal karyotype	2/35	6
C	Abnormal phenotype and normal karyotype	5/35	14
D	Abnormal phenotype and abnormal karyotype	23/35	66

ZT

- 29 y old, M+1
- G1-G3 Recurrent Abortions
- Complete Workup for RA – normal results
- G4 – Crystal Heparine (CH) and LMH – term pregnancy healthy baby
- G5 – CH + LMH at 6 weeks missed abortion – Embryoscopy revealed anencephaly and abdominal malformations



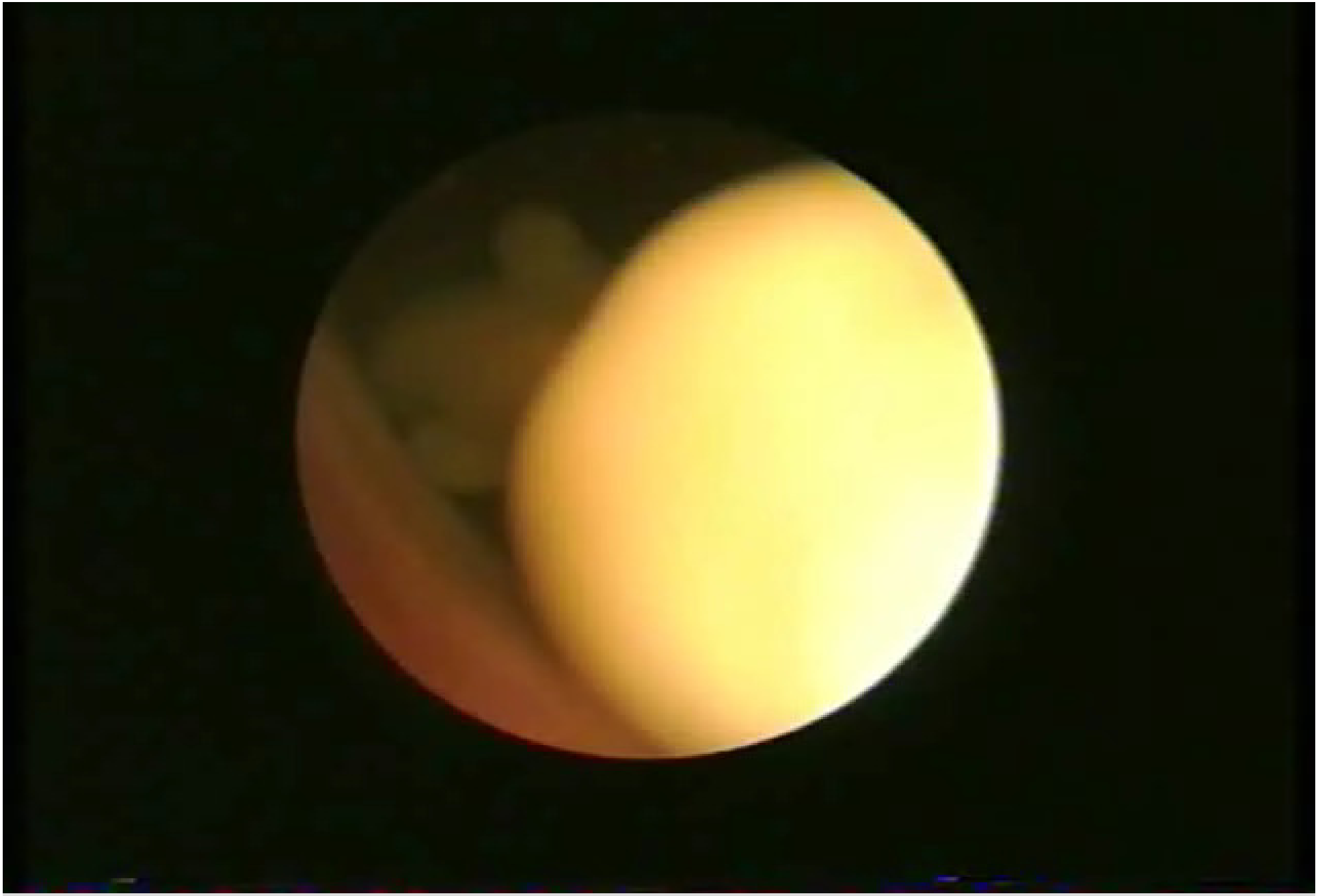

Otic placode
Lens placode
Pharyngeal arches
Heart bulge
Limb ridge
Vitelline duct
Umbilical cord
Allantois
B
28 days



HAA

- 40y old, 2yM+0,
- Subserous & Intramural fibroids
- Uterus enlarged 17w,
- G5, Ab(2)3
- Recurent Abortions

- Embryo missing right Eye



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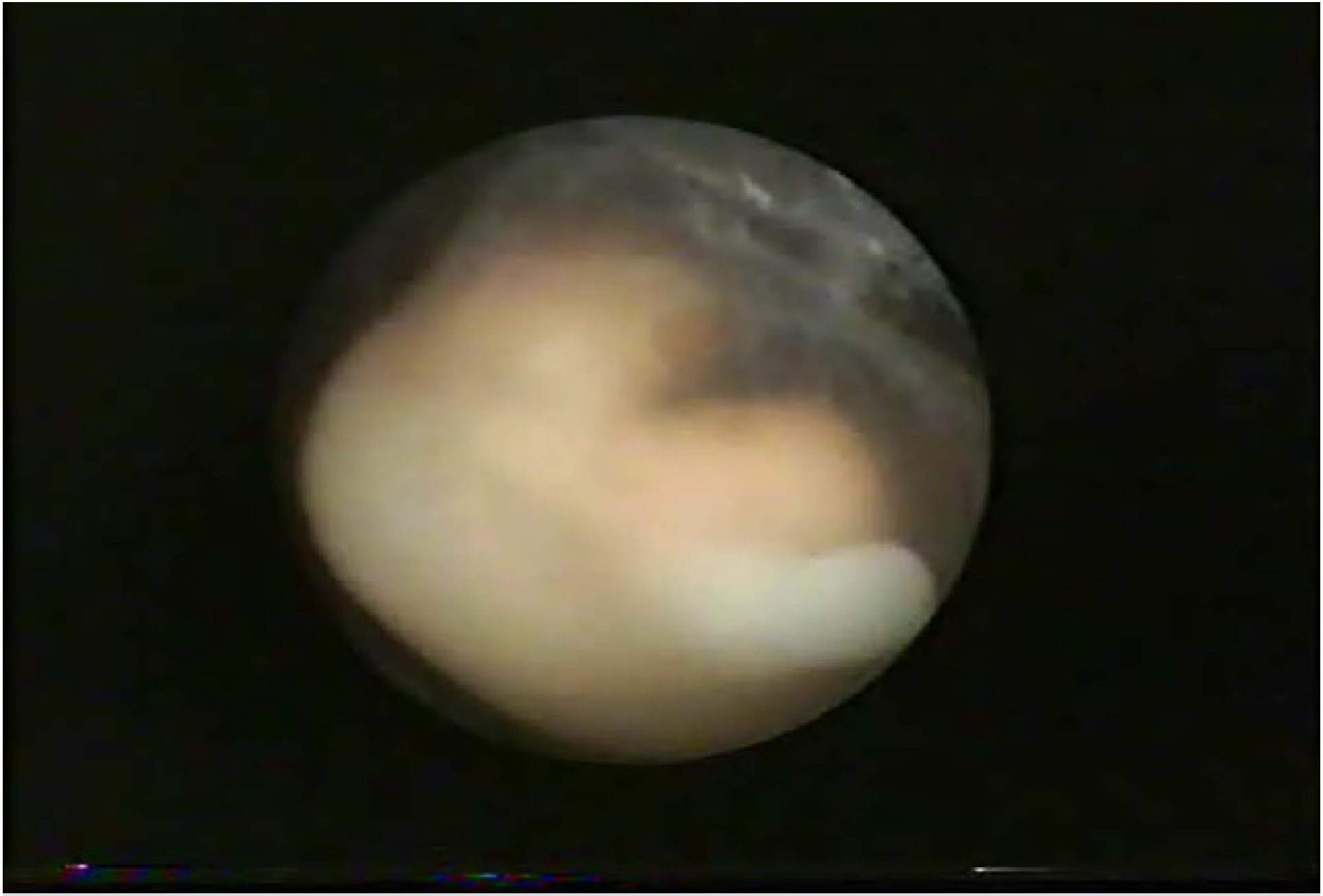
ZT

- Embryoscopy revealed
- Anencephany
- Abdominal malformation



Embryoscopy of Missed Abortion

- 233 cases by Philipp T et al in 2003 found
- 75% with abnormal karyotype,
- 18% - abnormal phenotype and normal karyotype ccompared to [14% our results SRA]
- 7% - normal phenotype and karyotype compared to [14% our results SRA]

Investigation of RSA etiology

- Rubio Carmen et al. 2004 (MSRM)
- RSA couples undergoing PGD compared to those cases that did not have RSA
- Numerical chromosomal abnormalities in human preimplantation embryos of women with RSA was 66% as compared to 33% found in non RSA patients.

Embryo Karyotype Accuracy after hysteroemryoscopy sampling

- Study of 71 gestational sacs from missed abortions 4-10w. Comparison between the cytogenetic results from hysteroembryoscopic biospies and those of the curettage material ***(Ferro J et al Fertil Steril 2003)***

- Embryo sampling success was 97.2%
- Enabled the diagnosis of a true palcental mosaicism and of each gestational sac in bizygotic twin missed abortions
- Karyotype missdiagnosis due to maternal contaminating tissue after D&C was 22%
- The finding of a 46,XX karyotype in the curettage material was not a reliable result

Conclusions

- ☒ Embryoscopy seems to be a valuable method for accurate diagnosis of the cause of spontaneous recurrent and missed abortions. This can be especially useful for future treatment purposes.
- ☒ The embryo external characteristics differ in cases of the same genetic abnormalities.
- ☒ Both Alantois and Chorion seem to be also affected from the genetic abnormality expressed in the embryo
- ☒ Cervical ectopic pregnancy can be treated by embryoscopy