Contributions of Hormonal Cytology to Reproductive Health in Girls and Adolescents

An ancient technique for monitoring contemporary problems

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Introduction

Hormonal cytology developed during the 20th century.
It describes cyclic changes in vaginal cells in animals and humans during the menstrual cycle.

The pathology of reproductive health focuses frequently on sexually transmitted diseases and their prevention.

However, even in subpopulations with minimal risk, we deal with significant disorders having a potential impact on future fertility.
Material and methods

- 2006-2015: 6688 vaginal fornix cytologies
- 2350 patients investigated

A more detailed analysis:
- three-year period from 2013-2015
- 452 patients
  - many of them investigated several times, and
  - monitored for a period longer than the three years analysed.

- Most patients were children, while a small part were adult women.
Patients investigated with hormonal cytology in the years 2013-2015 (n = 452).

- Central disorders: hypopituitarism; inborn growth disorders, malformations
- Peripheral gonadal disorders, inborn metabolic disorders
- Ovarian cysts
- Hyperandrogenic syndrome
- Autoimmune disorders: DM I, m. Crohn, thyroiditis, celiakia
- Pubertas praecox: thelarche praecox, early menarche
- Late menarche
- Dysfunctional juvenile metrorrhagia
- Eating disorders: Anorexia mentalis, bulimia, psychiatric disorders
- Obesity
- Excessive sport activity
- Secondary oligomenorrhea
- Dysmenorrhea NOS
Illustrative cases

- Central disorders: hypopituitarism; inborn growth disorders, malformations
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27 years. **Hypopituitarism.** Born in Ukraine. Homozygot - PROP1-related combined pituitary hormone deficiency.

March 2013, first visit. Primary amenorrhea.

Habitus of a child (149cm, 42kg).
March 2014. Miniestrogenisation started. Humatrope inj.; Hydrocortisone, Euthyrox, Caltrate

Thoughtful multidisciplinary two-year substitution process resulted into normalization of stature, female habitus and menarche at 30 years of age.
March 2014. Miniestrogenisation started. Humatrope inj.; Hydrocortisone, Euthyrox, Caltrate

27 years

<table>
<thead>
<tr>
<th>March 2013: 149 cm, 42 kg</th>
<th>May 2014: 154 cm, 43.2 kg</th>
<th>August 2014: 156 cm, 45 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI 100-0-0; IE 0</td>
<td>MI 90-10-0; IE 0</td>
<td>MI 30-50-20; IE 20</td>
</tr>
<tr>
<td>Resting phase</td>
<td>Initial maturation</td>
<td>Partial maturation</td>
</tr>
<tr>
<td>MI 80-20-0; IE 0</td>
<td>MI 20-80-0; IE 20</td>
<td>MI 0-40-60; IE 40</td>
</tr>
<tr>
<td>Resting phase with minimal maturation</td>
<td>Continued maturation</td>
<td>Cytogram of reproduction period</td>
</tr>
</tbody>
</table>

Miniestrogenisation only as not to block the GH effect

October 2014. 158 cm, 46 kg. April 2015. 160 cm, 50 kg. May 2015. 162 cm, 51.2 kg.

Thoughtful multidisciplinary two-year substitution process resulted into normalization of stature, female habitus and menarche at 30 years of age.

(Altogether 13 HC investigations.)
16 years. 158 cm. 47 kg. Crohn’s disease.

16 years.


February 2013. Duphaston stopped end 2013

13th day of cycle.
The oestrogen effect less expressed

22nd day of cycle.
Insufficient gestagen opposition

April 2014.

June 2014.

22nd day of cycle.
Persistent insufficient gestagen opposition.

18th day of cycle.
Improved gestagen opposition

October 2014.


Duphaston administration continued. HCs: persistent partial lack of gestagen opposition. 2016. Continues to be followed up.
16 years.


February 2013. 13th day of cycle. The oestrogen effect less expressed. Duphaston stopped end 2013.

June 2014. 22nd day of cycle. Persistent insufficient gestagen opposition.


April 2014. 22nd day of cycle. Insufficient gestagen opposition.

October 2014. 18th day of cycle. Improved gestagen opposition.
December 2012. First visit. Thelarche since birth.
Fastened bone age – 3.5 years.
December 2012. First visit. Thelarche since birth.

April 2013. Persistent thelarche. Fastened bone age.

By using hormonal cytology minimal signs of maturation were detected. With conservative approach, dietary measures and observation they regressed to cytogram of child resting phase.

1 year 7 months

1 year 11 months. Bone age 3,5 years.

2 years 11 months. Bone age 4 years.

February 2016. 4 years 9 months. 106 cm. 18.4 kg. Thelarche fully regressed.
1 year 7 months  December 2012. First visit. Thelarche since birth.

April 2013. Persistent thelarche. Fastened bone age.


By using hormonal cytology minimal signs of maturation were detected. With conservative approach, dietary measures and observation they regressed to cytogram of child resting phase.

1 year 11 months. Bone age 3,5 years.

2 years 11 months. Bone age 4 years.

February 2016. 4 years 9 months. 106 cm. 18.4 kg. Thelarche fully regressed.
11 years, 6 months. 156 cm, 50 kg.  
Early menarche. Polymenorrhea.

May 2013. First visit.  
Menarche 2012.  
Frequent irregular cycle 14-20 days.
May 2013. 24th day of cycle.
Hormonal ablation of endometrium (Estrofem and Provera).

April 2014.
Polymenorrhea corrected – 28 day cycle restored.

13th day of cycle.
Oestrogen stimulation lower than usual.

24th day of cycle.

October 2015. 21st day of cycle.
Corresponding to the day of cycle.

Estrofem lowered and subsequently stopped.
Minimal gestagen administration continued.

January 2015 normalized menstrual cycle on combined therapy (Estrofem plus Provera).
May 2013. 24th day of cycle. Hormonal ablation of endometrium (Estrofem and Provera).


January 2015 normalized menstrual cycle on combined therapy (Estrofem plus Provera).

October 2015. 21st day of cycle. Corresponding to the day of cycle.

Estrofem lowered and subsequently stopped. Minimal gestagen administration continued.
Polymenorrhea sanata on combined hormonal therapy monitored with altogether 11 hormonal cytologies.

Menstrual calendar provides an overview of the therapy and intensity of bleeding recorded by the patient herself.
April 2014. First visit. 
Menarche 2009 at the age of 13 (body weight 51 kg). 
August 2013 stay in USA, loss of weight to 40 kg. 
Since November 2013 secondary amenorrhea.
18 years

April 2014: 166 cm; 43 kg
May 2014: 166 cm; 47,8 kg
June 2014: 166 cm; 51,1 kg
August 2014: 166 cm; 53 kg

Deep maturation arrest continues

Inhibition of maturation

Adult cytogram without gestagen effect

Deep maturation arrest continues

Partial features of gestagen opposition

22nd day of cycle

14th day of cycle

26th day of cycle

August 2014: 166 cm; 53 kg; Agolutin i.m.; Duphaston
March 2015: 166 cm; 53 kg; Duphaston
Sept. 2015: 166 cm; 56 kg; Duphaston th. stopped
March 2016: 166 cm; 57 kg; no hormonal therapy

December 2014. Weight 53, 8 kg. Menstruation started after 13 months. 9 more months of hormonal support

11 kg weight loss and subsequent secondary amenorrhea.
Treated with psychotherapy, combined hormonal therapy and monitored with hormonal cytologies.
Lost weight regained and a spontaneous menstrual cycle returned.
At the one-year follow-up point her favourable status continues.
April 2014. Secondary amenorrhea since November 2013

18 years

<table>
<thead>
<tr>
<th>Month</th>
<th>Height</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>April 2014</td>
<td>166 cm</td>
<td>43 kg</td>
</tr>
<tr>
<td>May 2014</td>
<td>166 cm</td>
<td>47.8 kg</td>
</tr>
<tr>
<td>June 2014</td>
<td>166 cm</td>
<td>51.1 kg</td>
</tr>
<tr>
<td>August 2014</td>
<td>166 cm</td>
<td>53 kg</td>
</tr>
</tbody>
</table>

- **Deep maturation arrest continues**
- **Inhibition of maturation**
- **Adult cytogram without gestagen effect**

- **Partial features**
- **22nd day of cycle**
- **14th day of cycle**
- **26th day of cycle**

- **Agolutin i.m.; Duphaston**
- **Sept. 2015: 166 cm; 56 kg; Duphaston th. stopped**
- **Dec. 2015: 166 cm; 57 kg; no hormonal therapy**

December 2014. Weight 53, 8 kg. Menstruation started after 13 months. 9 more months of hormonal support

11 kg weight loss and subsequent secondary amenorrhea. Treated with psychotherapy, combined hormonal therapy and monitored with hormonal cytologies. Lost weight regained and a spontaneous menstrual cycle returned. At the one-year follow-up point her favourable menstrual status continues.
Caring for reproductive health of women begins immediately after birth.

It covers a broad spectrum of risk conditions only recently detected thanks to advanced diagnostics (autoimmune and genetic diseases).

A large part relates to new socio-economic conditions (eating disorders, excessive training, and stress).

Hormonal cytology represents a non-invasive and economical method illustrating the direct steroid effect on targeted cells.

In a well-tuned setting of close clinical-pathological co-operation it contributes to reproductive health support by:

- Indicating the possible need and type of steroid therapy
- Monitoring the normalization of cycle disturbances
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