



# *Histology & Embryology Periodical*

*Department of Histology and Embryology*

*Third Faculty of Medicine, Charles University in Prague*

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**April  
2015**

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## *What's up...*

A busy month ahead;

Course 5: **“Development of cells and tissues”**

Lecture: **Thalidomide**

When you listen to the lecture, consider it not merely a lesson on a history of one of medicinal drugs. The thalidomide case was the first and the most obvious example of adverse effects of the drugs and chemicals thrown to the market after the WWII. Some call it a “chemical revolution” giving the number of new synthetic chemicals that have been introduced into commerce. The story of thalidomide was like a bombshell in the excitement of the postwar years. All involved were shocked; medical professionals, scientists and public alike. In medicine, the thalidomide case shattered **the myth of the placental barrier**; that is a belief that the placenta acts as an impenetrable shield that protects developing organism from any harm. In science, the case enforced the principle **“timing is everything”**, not necessarily the dose. Limb development has a critical period between the fifth and eighth week of pregnancy. If a thalidomide pill was swallowed within the critical time a baby was born with various damage

on his/her limbs. If on the other hand, pills were used prior to or after the critical period, baby was normally healthy. The thalidomide case also brought different standards for testing of new chemicals... as you will hear at the lecture.

**Tue, March 31, 2015 at 11,30 am** in the Syllaba lecture hall.

Lecture: **Basic morphogenetic processes**

Don't miss for sure!

**Wed, April 1, 2015 at 11,30 am** in the Syllaba lecture hall

## **Week 7**

Lectures:

**Signaling during development**

**Blastogenesis, Implantation, Placenta**

**Notogenesis, Neurulation**

**Embryonal development**

## **Week 8**

Lectures:

**Histogenesis**

**Developmental toxicity & Pharmacotherapy during pregnancy**

**Aging of organisms**

**Seminar: Early development, chick embryo**

The chick embryo as the premier research model organism – here we are with the early development demonstration

## **Week 9**

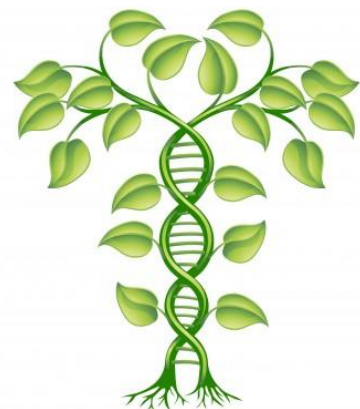
Seminar: **Embryology** – you, personally or in a team, will work on a topic from embryology and present it to your classmates!

Seminar: **Clinical detective story 6** – an evaluation of the fetal risks after intrauterine exposition to various agents.

## **Reminders**

Your workbook is your proof of your activity during practicals. The elementary sense of using your workbooks is using them during the classes, not completing them at the end of semester.

During the practicals in both remaining courses of the summer semester; “Development” and “Tissues”, your teachers and assistants will ensure that your **workbooks are updated.**



## First-ever World Birth Defect Day

The Center for Disease Control (CDC) introduced **March 3** as World Birth Defect Day (WBDD). Every year on March 3 the public attention should be turned towards the facts that birth defects (BD) are:

- **Common** - about 6% newborns worldwide annually, (about 7.9 million) are born with a serious BD (This number corresponds to the number of defects diagnosed at the end of 1 year of life. It includes such inborn defects which cannot be diagnosed just after the birth – glandular hypospadias, some heart defects, hip dysplasia. On the other hand, inborn developmental defects, diagnosed at birth, like cleft lip and/or palate, severe cyanotic heart defects, polydactyly etc. occur in 2,5-3 % newborns).
- **Critical** – one in every five infant deaths is caused by a birth defect
- often **Curable** – the WBDD should increase awareness of available treatment services
- **Preventable**: e.g. neural tube birth defects are preventable by daily intake of 400mg of folic acid yet birth defects such as spina bifida or anencephaly occur in 1 of 1000 birth. And some BD are totally preventable, for example the fetal alcoholic syndrome however, prenatal alcohol exposure still affects 1 in 100 Americans.

The CDC collaborates with 11 other organizations to implement the WBDD, among others Organization of Teratology Information Specialists (OTIS), European Network of Teratology Information Services (ENTIS), and Teratology Society (TS).

For more information go to;

<https://www.mothersbaby.org/experts-spread-message-about-preventable-birth-defects-on-first-ever-world-birth-defects-day-p157523#157523>

## Epigenetic inheritance & ancestral exposure

**Environmental factors such as toxins or nutrition have been shown to promote the epigenetic transgenerational inheritance of adult onset disease and phenotypic variation.**

As is often the case in science, it take a brilliant failure to make a groundbreaking discovery. In 2005, biologist Michael Skinner at Washington State University led a team trying to test a hypothesis that a fungicide vinclozolin has the ability to disrupt the development of reproductive organs. The research was not going well and in the midst of all that Skinner's colleague came to tell him that by mistake she bred an unplanned 4<sup>th</sup> generation of the exposed rats, i.e. their great-grandchildren<sup>1</sup>. To their big surprise, the researchers identified low sperm count and a host of adult-onset diseases of organs such as prostate or kidney, testis abnormalities, odd immune responses, tumor development and a number of blood abnormalities such as hypercholesterolemia not only in the exposed animals (O generation) but also in the first, second and third generation.<sup>2</sup> What is it? How biological information are transmitted from one generation to the next besides written in genes?

*“Epigenetics refers to long-term modification of gene activity that can be inherited, either somatically or transgenerationally, but that are independent of*

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<sup>1</sup> Interlandi, J. *The toxins that affected your great-grandparents could be in your genes*. Smithsonian magazine, December 2013.

<sup>2</sup> Skinner, M., K., Anway, M., D. *Endocrine disruptor vinclozolin induced epigenetic transgenerational adult-onset disease*. Critical review of Oncogenesis, 2007. **13** (1), pp. 75-82.

alterations in the primary base sequence of the organism's DNA"<sup>3</sup>

The classic example of transgenerational effect of prenatal exposure is represented by the data from a "natural" experiment of Dutch Hunger Winter in 1944-45. Offspring from mothers exposed to undernutrition during gestation, and even their grandchildren, have been shown increased rates of cardiovascular disease, type-2 diabetes and breast cancer, and offspring of prenatally exposed fathers may lead to increased chronic disease rate in adulthood<sup>4</sup>. There is a growing body of evidence from animals and humans suggesting that dietary factors *in utero* such as protein, ethanol, vitamin E or folate intake can have effects on subsequent generations.<sup>5</sup>

*Epigenetic effects include primarily three different interacting mechanisms: 1) methylated groups attached to DNA described by Dr. Skinner like "burrs stuck to a knit sweater"<sup>1</sup>; 2) histone modification; and 3) non-coding micro RNAs which are responsible for gene expression during development and throughout life.*<sup>6</sup>

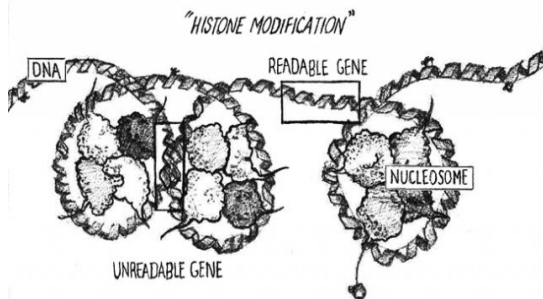


Fig1. A simplified drawing of DNA, histones and methylated groups.<sup>7</sup>

<sup>3</sup> Brown, C., J., Rupert, J., L. *Hypoxia and environmental epigenetics*. High Altitude Medicine & Biology, 2014. **15**(3), pp. 323-330.

<sup>4</sup> Veenendaal MV et al. *Transgenerational effects of prenatal exposure to the 1944-45 Dutch famine*. BJOG, 2013. **120**(5), pp. 548-53.

<sup>5</sup> McKay, J., A., Mathers, J., C. *Diet induced epigenetic changes and their implications for health*. Acta Physiologica, 2011. **202**(2), pp.103-18.

<sup>6</sup> Harris, M. Reviewer's commentary on Veenendaal M., V. et al. *Transgenerational effects of prenatal exposure to the 1944-45 Dutch famine*. BJOG, 2013. **120**(5), pp. 548-53.

*"Unlike the information encoded in the DNA sequence, which is invariant between most cell types and over time, epigenetic information is **tissue specific** and can change in response to exogenous and endogenous perturbations."*<sup>3</sup>

Besides nutrition, embryo/fetal exposure to environmental factors, too promotes the epigenetic transgenerational inheritance of adult onset disease and phenotypic variations. For example, a DDT exposure in ancestors during a critical window of germline (sperms and oocytes) development can promote the transgenerational inheritance of obesity and a number of associated complex disease traits<sup>8</sup>, fungicide vinclozolin has been shown to cause transgenerational altered stress response<sup>9</sup>, the effect of exposure to phthalates on asthma was recently linked to DNA methylation<sup>10</sup>, a response to stress is suspect of epigenetic inheritance<sup>8</sup>, and the examples are many, many more. All in all, epigenetics is a hot field these days.

But, epigenetics was not born yesterday either. **Aristoteles** believed that the environment sculpted the phenotype of individuals and that these effects were represented in their descendants, **Jean-Baptiste Lamarck** (1744-1829) laid out his views on inheritance of acquired characteristics known as "soft inheritance", **Conrad Waddington**, the prominent 20<sup>th</sup> century

<sup>7</sup> Kloc, J. *An Illustrated guide to epigenetics*. Mother Jones [online]. Last updated Feb 8, 2011. [Cited 03.24. 2015]. Available at: <http://www.motherjones.com/environment/2011/02/illustrated-guide-epigenetics>

<sup>8</sup> Skinner, M., K. et al. *Ancestral Dichlorodiphenyltrichloroethane (DDT) exposure promotes epigenetic transgenerational inheritance of obesity*. BMC Medicine, 2013. **11**:228.

<sup>9</sup> Crews, D. et al. *Epigenetic transgenerational inheritance of altered stress responses*. PNAS, 2012. **109** (23), pp. 9143-9148.

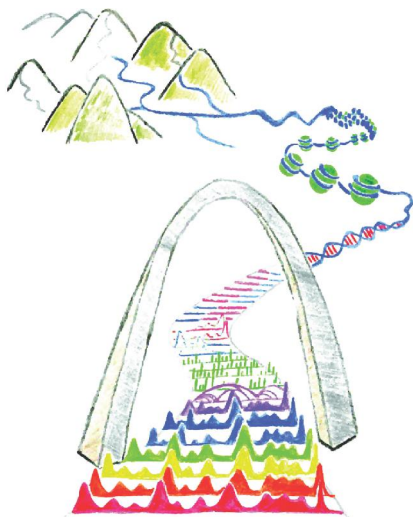
<sup>10</sup> Wang, I-J. et al. *Effects of phthalate exposure on asthma may be mediated through alterations in DNA methylation*. Clinical Epigenetics, 2015. 7:27.



developmental biologist, coined the term epigenetics in his classic paper “The epigenotype” in 1942, **Riggs and Holliday** and **Pugh** in 1975 proposed that DNA can be methylated in bacteria....<sup>11</sup>

*“Epigenetics plays a prominent role in understanding acclimation, adaptation, and evolution... it is an exciting yet still somewhat enigmatic and highly immature, field of biology”<sup>11</sup>*

Comparative biologists David Crews and Warren Burggren <sup>11</sup> observe the use of the word “epigenetics” in several meanings. The predominant use is in medicine and refers to the literal meaning of epigenetics – “above genetics”, and focuses on epigenetics as a pathological process, e.g. “epigenetics of cancer”. On the other hand, life science circles view epigenetic phenomena as an adaptive mechanism, with ecological and evolutionary implication. A third, and more holistic view, sees epigenetics as a “perspective”. And that is probably the way how to approach the greatly expanding field of epigenetic; as a new layer in a complexity of inheritance and individual phenotype.



<sup>11</sup> Burggren, W., W., Crews, D. *Epigenetics in Comparative Biology: Why we should pay attention*. Interactive and Comparative Biology, 2014. **54** (1), pp. 7-20.

## **Messenger RNA & horizontal gene transfer**

In a research article published in *Genome Biology* in March 2015, the scientists from the University of Cambridge used genes corresponding to certain type of mRNA – transcriptomes – of humans and other primates, flies and nematode worms to identify a gene transfer from one species to another.

**Horizontal transgenics** is well-known in single cell organisms such as bacteria, however its existence in high organisms is much less established, and is controversial in humans (based on our anthropocentric tradition many still tend to think that humans are a unique branch on the tree of life).

The results of this study suggest that humans have at least 145 genes picked up from other species by their forebears (e.g. genes for synthesis of the “cellular glue” – hyaluronic acid from fungi, or obesity associated gene from marine algae), and provide at least 33 new examples of horizontally acquired genes. The researchers conclude that although horizontal gene transfer is generally lower in eukaryotes that in prokaryotes, it’s far from rare, and that it has contributed and continues to contribute, to the evolution of many, perhaps all, animals.

The research article is accessible online at:  
<http://genomebiology.com/2015/16/1/50>

## Endocrine disruptors III

### Theo Colborn (1927-2014)



For the past two or three decades, scientists around the world have been contributing to the growing body of research on endocrine disruptors. The scientist who sparked the research as well as public and governmental attention is the “founding

mother” of endocrine disruptors, Theo Colborn.

In her early life she was a pharmacist, she and her husband ran drugstores first in New Jersey, and then in Carbondale, Colorado where they moved along with their four children. In her life as a scientist, she completed a Master’s degree in Science – her specialty was freshwater ecology, then she pursued a course of study towards a Ph.D. She was awarded the title with minors in epidemiology, toxicology, and water chemistry in 1985, at age 58.

She moved to Washington, D.C., winning a fellowship, worked for the government on the renewed Clean Air Act. Then she was offered a job for

World Wildlife and The Conservation Foundation. This was a ground-breaking moment because the findings in the report “Great Lakes, Great Legacy?” turned out to become a kickoff for the whole new field soon after named “endocrine disruption”. The paper described an underlying problem in the seemingly cleaned Lakes; persistent, bioactive, toxic substances pollute the Great Lakes, accumulate in sediment and make their **way up the food chain**, causing adverse impact on metabolism and development. The most troubling aspect was the fact that “in most cases, the adult animals show **no visible sign of ill health, except abnormal behavior.**”<sup>12</sup>

Theo Colborn was the first to realize that something

was disturbingly wrong in and around the Lakes, something other than the obvious outcomes of the then heavily polluted waters, on humans and wildlife alike, such as cancer or allergies. At that time, late 1980s, the words “toxic chemical” have become almost **synonymous with cancer** “not only in the public mind but in the minds of scientists and regulators as well.”<sup>13</sup> When she put the many papers she collected for the study and her wits together she realized that terns in

*Until one is committed there is hesitancy, the chance to draw back, always ineffectiveness.*

*Concerning acts of initiative (and creation) there is one elementary truth the ignorance of which kills countless ideas and splendid plans; that the moment one definitely commits oneself then Providence moves too.*

*All sorts of things occur to help one that would never otherwise have occurred. A whole stream of events issues from the decision, raising in one’s favor all manner of unforeseen incidents and meetings and material assistance which no man could have dreamt would come his way.*

*Whatever you can do, or dream you can, begin it. Boldness has genius, power, and magic in it.*

*Begin it now.*

– J. W. Goethe –

(Theo Colborn’s favorite quote which she kept taped to the wall at TEDX)

<sup>12</sup> Grossman, E., *A brief biography of Theo Colborn* [online]. [Cited 03.25.2015]. Available from: <http://endocrinedisruption.org/assets/media/documents/Colborn%20bio%20short%20version.pdf>

<sup>13</sup> Colborn, T., Dumanovski, D., Myers, J., P. Our stolen future: are we threatening our fertility, intelligence, and survival?: a scientific detective story. 1<sup>st</sup> ed. Plume, 1996. ISBN: 0-452-27414-1

polluted areas neglecting their nests, indifference in usually vigilant nesting Japanese quails about their incubating eggs, missing eyes and clubbed feet in cormorants, diminishing size of the fish testicles in the Baltic, abnormal mating behavior in bald eagles preceded with the appearance of the eggshell thinning and the collapse of the entire eagle population, vanished mink populations, female herring gulls nesting together and feminization of their male counterparts' reproductive tracts, young birds suffering a mysterious wasting syndrome when they appeared healthy and normal for days only to begin to languish, waste away and die soon after, children and mothers living near the Lakes who's diet consisted of lots of fish that were scoring poorly on tests assessing their neurological development lagging behind in measures that tend to predict later IQ; Colborn realized that all the symptoms have one in common; their early development has been compromised.

The recognition of endocrine disruptors has been revolutionary to toxicology for several reasons. In the traditional toxicology the effect of a drug increases with an increasing dose. On the other hand, endocrine disruptors don't respect such a linear fashion rather, very low level of expose can produce serious and lasting health effects. Timing of an exposure is second, no less important factor. They say, "timing is everything", especially in development. In developmental biology, "critical period" refers to an interval in which a tissue or organ is susceptible to an agent. Prior to or after such a period there might be very small or no effect of such an agent while an exposure during the critical period may have a grim

outcome. The last important difference between endocrine disruptors vs. traditional toxins is the multigenerational effect. In that regard, endocrine disruption is a piece in the grand mosaic that teaches us about development and inheritance.

Theo Colborn saw that big picture, the whole mosaic. She recognized the widespread disruption of the endocrine system as an international public health issue.<sup>14</sup> She kept up on statistics that would show a steady rise of neurodevelopmental, cognitive and behavioral issues among children worldwide that leading scientists and pediatricians call a pandemic. Theo Colborn was particularly concerned about the neurological problem that are disrupting "nurturing relationships between parents and children"<sup>12</sup>. She saw endocrine disruption not just a matter of an individual physical fitness rather, that the entire humane kind is at risk of destroying their future.

In 2003, at age 76, Theo Colborn founded The Endocrine Disruption Exchange (TEDX) ([www.endocrinedisruption.org](http://www.endocrinedisruption.org)), a non-profit research organization committed to endocrine disruptor research. She believed in cross-disciplinary environmental health research and supported and mentored students sometimes six decades younger than she, and held a special encouragement for young women in science. Theo Colborn passed away in December last year at age of 87 years.

*"Fewer and fewer people will be healthy and intelligent enough to provide the leadership society needs to work toward world peace. Fossil-fuel derived chemicals are depriving humanity of its integrity and the fate of the human race should no longer be put at risk because current toxicological testing has failed to detect damage from chemical exposure that does not fall under the current antiquated regulatory rubric."*

*Theo Colborn<sup>14</sup>*

<sup>14</sup> Colborne, T. *Endocrine disruption, Public Health, and National and International Security* [online]. PSR, 11.4.2010. [Cited 03. 12-2015]. Available from: <http://www.psr.org/environment-and-health/environmental-health-policy-institute/responses/endocrine-disruption-public-health-and-national-and-international-security.html>



## ***Repetitio mater studiorum....***

### **... Q & A**

#### **Female Reproductive System**

Q1: Ovulation is triggered by a dramatic increase in a hormone called...?

Q2: What is the acidophilic glycoprotein coat that surrounds oocyte?

Q3: What wakes up the primordial follicle from its quiescent state?

Q4: The antral follicle is also called....?

Q5: What is ovulated?

Q6: What is the external layer of uterus called?

Q7: What is another name for the greater vestibular gland? And the name for the lesser vestibular glands?

Q8: What is the connective tissue layer around the primary follicle?

Q9: What is called the layer of cells between zona pellucida and basal lamina of the primary follicle?

Q10: During the first 7-10 days of the cycle, what is the main stimulating hormone?

Q11: What are the mature gametes called?

Q12: What is the connective tissue that surrounds ovary?

Q13: Which hormone maintains the corpus luteum during pregnancy?

Q14: What gland in the male is the homologous to the greater vestibular gland in the female?

Q15: What are follicular cells?

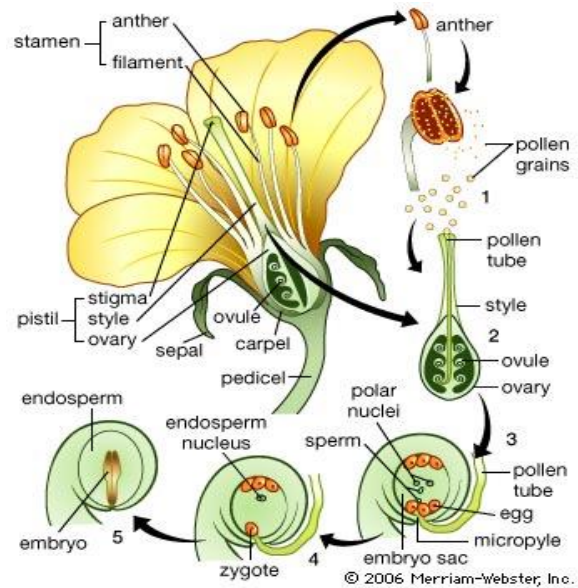


Fig: Life cycle flowering plant<sup>15</sup>

A1: LH, luteinizing hormone

A2: *Zona Pellucida*

A3: Counterbalance of various stimulatory and inhibitory hormones and locally produced GF<sup>16</sup>

A4: Secondary follicle

A5 a Graafian follicle

A6: Perimetrium

A7: Bartholin's gland, and Skene's glands

A8: *Theca folliculi*

A9: *Stratum granulosum*

A10: FSH, follicle-stimulating hormone

A11: Ova

A12: *Tunica albuginea*

A13: hCG, human chorionic gonadotropine

A14: Cowper's gland (*glandula bulbourethralis*)

A15: Granulosa cells

<sup>15</sup> Nicole. Life cycle of flowering plants. Flower every[online] Last updated 05.16.2012. [Retrieved 3.27.2015]. Available at: <http://www.flowerevery.com/life-cycle-flowering-plant/>

<sup>16</sup> Fortune J. et al. *The primordial to primary follicle transition*. Molecular Cell Endocrinology, 2000. **163** (1-2).pp. 53-60.



## **Membra Jesu nostri patientis sanctissima**

"The most holy limbs of our suffering Jesus" is a seven songs oratory composed by **Dietrich Buxtehude** in the 17<sup>th</sup> century. The gorgeous lyrics, he wrote on Passion medieval texts, provide a medical student with a splendid opportunity to practice her/his Latin. Individual *cantatas* address seven different parts of Christ's crucified body; feet, knees, hands, side, breast, heart, and head.

The gorgeous, meditative music is available e.g. at:  
<https://www.youtube.com/watch?v=bWbBK2poJLE>

### **I. Ad pedes**

1. Sonata
2. Concerto

**Ecce super montes  
pedes evangelizantis  
et annunciantis pacem**

*(Behold, upon the mountains  
the feet of one bringing good news  
and proclaiming peace)*

3. Aria

**Salve mundi salutare,  
salve Jesu chare!**

**Cruci tuae me aptare  
vellem vere, tu scis quare,  
da mihi tui copiam**

4. Aria

**Clavos pedum, plagas duras,  
et tam graves impressuras  
circumplector cum affectu,  
tuo pavens in aspectu,  
tuorum memor vulnerum**

5. Aria

**Dulcis Jesu, pie deus,  
Ad te clamor licet reus,  
praebe mihi te benignum,  
ne repellas me indignum**

**de tuis sanctis pedibus**

6. Concerto

### **II. Ad genua**

1. Sonata
2. Concerto

**Ad ubera portabimini,  
et super genua blandicentur vobis**

3. Aria

**Salve Jesu, rex sanctorum,  
spes votiva peccatorum,  
crucis ligno tanquam reus,  
pendens homo verus deus,  
caducis nutans genibus**

4. Aria

**Quid sum tibi responsurus,  
actu vilis corde durus?**

**Quid rependam amatori,  
qui eligit pro memori,  
ne dupla morte morerer**

5. Aria

**Ut te quaeram mente pura,  
sit haec mea prima cura,  
non est labor et gravabor,  
sed sanabor et mundabor,  
cum te complexus fuero**

6. Concerto

### **III. Ad manus**

1. Sonata
2. Concerto

**Quid sunt plagae istae  
in medio manuum tuarum?**

3. Aria

**Salve Jesu, pastor bone,  
fatigatus in agone,  
qui per lignum es distractus  
et ad lignum es compactus  
expansis sanctis manibus**

4. Aria

**Manus sanctae, vos amplector,**

**et gemendo condelector,  
grates ago plagis tantis,  
clavis duris guttis sanctis  
dans lachrymas cum osculis**

5. Aria

**In cruore tuo lotum  
me commendo tibi totum,  
tuae sanctae manus istae  
me defendant, Jesu  
Christe,  
extremis in periculis**

6. Concerto

#### IV. Ad latus

1. Sonata

2. Concerto

**Surge, amica mea,  
speciosa mea, et veni,  
columba mea  
inforaminibus petrae,  
in caverna maceriae**

3. Aria

**Salve latus salvatoris,  
in quo latet mel dulcoris,  
in quo patet vis amoris,  
ex quo scatet fons cruoris,  
qui corda lavat sordida**

4. Aria

**Ecce tibi apropinquo,  
parce, Jesu, si delinquo,  
verecunda quidem fronte,  
ad te tamen veni sponte  
scrutari tua vulnera**

5. Aria

**Hora mortis meus flatu  
intret Jesu, tuum latus,  
hinc exspirans in te vadat,  
ne hunc leo trux invadat,  
sed apud te permaneat**

6. Concerto

#### V. Ad pectus

1. Sonata

2. Concerto

**Sicut modo geniti infantes  
rationabiles,**

**et sine dolo concupiscite,**

**ut in eo crescatis in salutem.**

**Si tamen gustatis, quoniam  
dulcis est Dominus.**

3. Aria

**Salve, salus mea, deus,  
Jesu dulcis, amor meus,  
salve, pectus reverendum,  
cum tremore contingendum,  
amoris domicilium**

4. Aria

**Pectus mihi confer mundum,  
ardens, pium, gemebundum,  
voluntatem abnegatam,  
tibi semper conformatam,  
juncta virtutum copia**

5. Aria

**Ave, verum templum dei,  
precor miserere mei,  
tu totius arca boni,  
fac electis me apponi,  
vas dives deus omnium**

6. Concerto



#### VI. Ad cor

1. Sonata

2. Concerto

**Vulnerasti cor meum,  
soror mea, sponsa,  
vulnerasti cor meum.**

3. Aria

**Summi regis cor, aveto,  
te saluto corde laeto,  
te complecti me delectat  
et hoc meum cor affectat,  
ut ad te loquar, animes**

4. Aria

**Per medullam cordis mei,  
peccatoris atque rei,  
tuus amor transferatur,  
quo cor tuum rapiatur  
languens amoris vulnere**

5. Aria

**Viva cordis voce clamo,  
dulce cor, te namque amo,  
ad cor meum inclinare,  
ut se possit applicare  
devoto tibi pectore**

6. Concerto

**Vulnerasti corneum,  
soror mea, sponsa,  
vulnerasti corneum.**

## VII. Ad faciem

1. Sonata

2. Concerto

**Illustra faciem tuam super servum  
tuum,  
salvum me fac in misericordia tua**

3. Aria

**Salve, caput cruentatum,  
totum spinis coronatum,  
conquassatum, vulneratum,  
arundine verberatum  
facie sputis illita**

4. Aria

**Dum me mori est necesse,  
noli mihi tunc deesse,  
intremenda mortis hora  
veni, Jesu, absque mora,  
tuere me et libera me**

5. Aria

**Cum me jubes emigrare,  
Jesu chare, tunc appare,  
o amator amplectende,  
temet ipsum tunc ostende  
in cruce salutifera.**

6. Concerto

**Amen**

\*

Fig 3: Crucifixion by Giotto yr. 1320-1325,  
Musée des Beaux-Arts, Strasbourg, Alsace, France

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Wish you enjoy, meditatively,  
the remaining days of Lent  
and ...

**Happy Easter!**



The Internal Newsletter, Third Faculty of Medicine, Charles University in Prague.

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