The background features several large, overlapping, colorful swirls in shades of green, purple, and blue. Scattered throughout are numerous small, yellow, triangular shapes, some pointing upwards and some downwards, creating a dynamic and abstract pattern.

# Current Practices and Ethical Issues of Reproductive Genetics

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Director, Clinical Genetics Service, HKSH



# Topics for Discussion

- Eugenics
  - Definition & Objectives
- Contemporary practices
  - Eugenics & Reproductive genetics
- Ethical & Regulatory Issues
- New advances
  - Genomic editing



# Definition of Eugenics

- Technique and policies
- that allow for the reproduction of people with the 'desired' attributes
- and reduce the reproduction of those with the 'undesired attributes'

Thomas GM and Rothman BK. AMA J of Ethics, 2016. vol.18,  
4:406-415



# Objective of Eugenics

- Coercion of people's reproductive choice
  - To 'improve' quality of the population
  - Prevention of suffering
  - Reduction of financial cost for whole society in caring for the disabled

King DS. Journ Medical Ethics. 1999:25:176-182.

# Francis Galton

- Founder of the 'Eugenics' movement, coined the term 1883
- Eugenics literally means good birth
- He opposed to coercion, believing that if people were properly informed they would naturally make the "right" reproductive decision





# Eugenics and Involuntary Sterilization: 1907-2015.

In England during the late nineteenth century, intellectuals, especially Francis Galton, called for a variety of **eugenic** policies aimed at ensuring the health of the human species.

Reilly PR. Annu Rev Genomics Hum Genet. 2015;16:351-68. doi:  
10.1146/annurev-genom-090314-024930

# Eugenics and Involuntary Sterilization: 1907-2015.

United States, Progressive movement embraced eugenic ideas, especially immigration restriction and sterilization.

Indiana enacted first eugenic **sterilization law** 1907

US Supreme Court upheld such laws in 1927.

State programs targeted **institutionalized, mentally disabled women**.



## Eugenics and Involuntary Sterilization: 1907-2015.

Beginning in the late 1930s, proponents rationalized involuntary sterilization as **protecting vulnerable** women from unwanted pregnancy.

By World War II, programs in the United States had sterilized approximately **60,000** persons.





# Eugenics and Involuntary Sterilization: 1907-2015.

After the horrific revelations concerning **Nazi** eugenics (German Hereditary Health Courts approved at least **400,000** sterilization operations in less than a decade), eugenic sterilization programs in the United States declined rapidly.



## Eugenics and Involuntary Sterilization: 1907-2015.

Simplistic eugenic thinking has faded, but **coerced sterilization** remains widespread, especially in China and India.

In many parts of the world, involuntary sterilization is still intermittently used against minority groups.



# Background of further Development of Eugenics

- Growth of genetics
- Introduction of prenatal diagnosis and termination of pregnancy
- Enactment of Abortion Laws
- Acceptability of Screening in Medicine
- Medicalization of pregnancy
- Public exclusion & discrimination of disability



# Development in Reproductive Genetics

- Prenatal testing
  - Non invasive prenatal testing
  - Prenatal diagnosis by
    - Chorionic villous sampling
    - Amniocentesis
- Preimplantation genetic diagnosis
- Future potentials
  - Genome editing
  - Mitochondrial transfer technology

# Development in Reproductive Genetics

- Prenatal testing

- Non invasive prenatal testing

- Prenatal testing

- Chorionic villus sampling

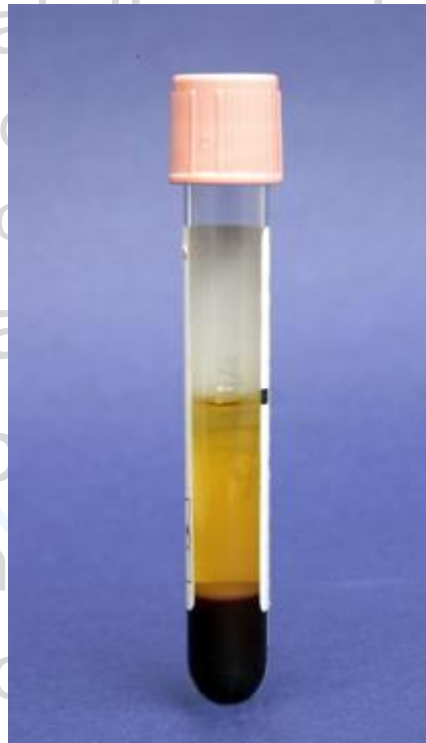
- Amniocentesis

- Preimplantation genetic testing

- Future possibilities

- Genomic imprinting

- Mitochondrial DNA



# Development in Reproductive Genetics

- Prenatal testing

- Non invasive prenatal testing

- Prenatal diagnosis by

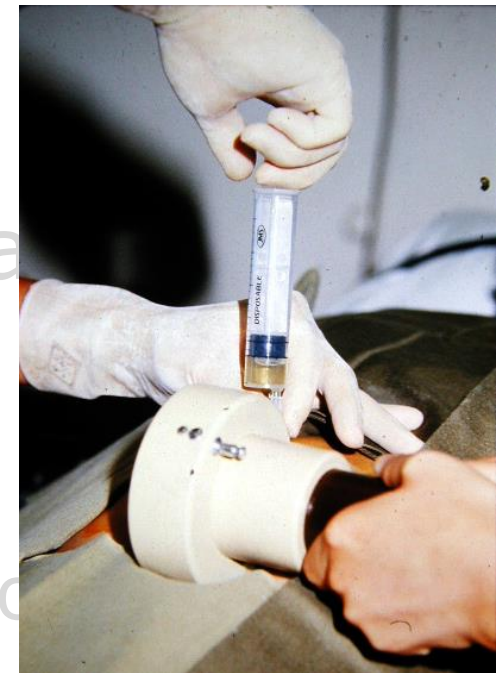
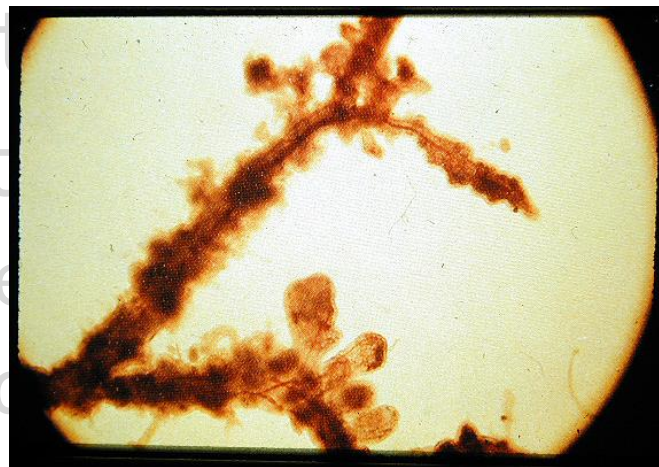
- Chorionic villous sampling
    - Amniocentesis

- Preimplantation

- Future potential

- Genome editing

- Mitochondrial





# Contemporary eugenics

- **Historical eugenics** refer to the atrocities operated on populations in history
- **Contemporary eugenics** operated on individuals at present

Ref. Thomas GM and Rothman BK. AMA J of Ethics, 2016. vol.18, 4:406-415



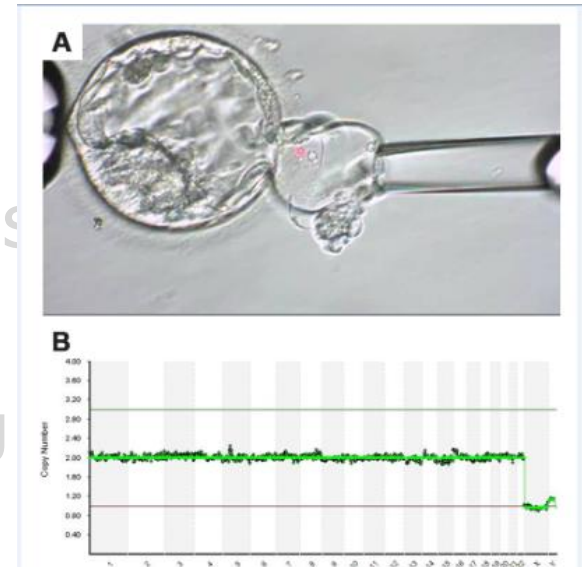
# Contemporary Eugenics (Cont'd)

- Criticisms on prenatal screening and testing
  - Parental decisions has **little choice**
  - Autonomy compromised through **routinization** of reproductive technology
  - **negative** portrayal of disabilities, with decrease in social support



# Development in Reproductive Genetics

- Prenatal testing
  - Non invasive prenatal test
  - Prenatal diagnosis by
    - Chorionic villous sampling
    - Amniocentesis
- **Preimplantation genetic diagnosis**
- Future potentials
  - Genome editing
  - Mitochondrial transfer technology



# Preimplantation Genetic Diagnosis (PGD) and Eugenics

- Characteristics of PGD
  - poses less emotional pressure on the female
  - Increases the culture of 'prevention'
  - The females' right to choose is less
  - IVF clinic and doctors' decision power increased instead of parental choice offered at genetic counselling clinics

Ref. King DS. Journ Medical Ethics. 1999:25:176-182.



# Preimplantation Genetic Diagnosis (PGD) and Eugenics (cont'd)

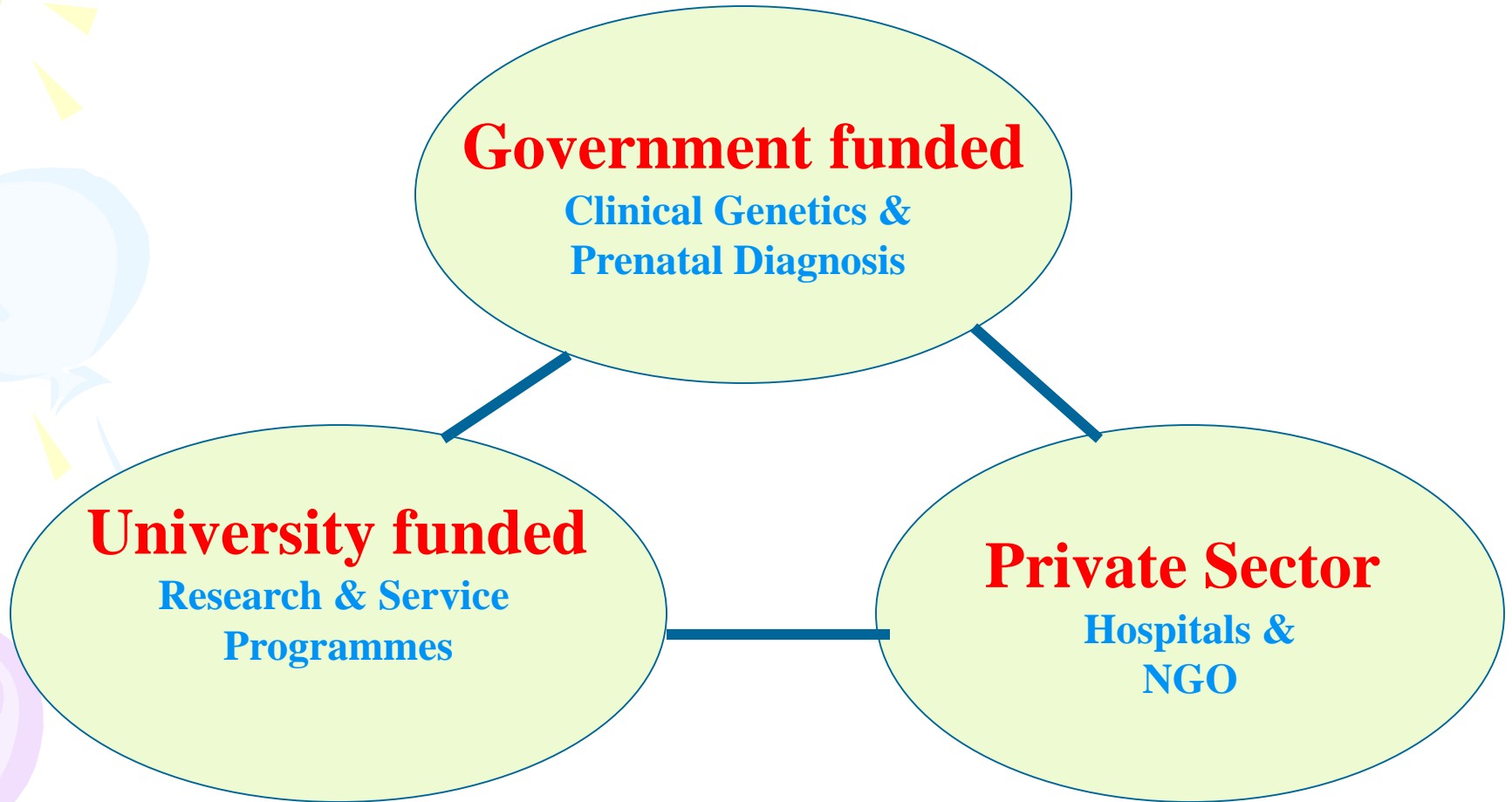
- Potential outcome of PGD
  - Increased choosiness for the 'Best' genetic profile
  - **Elimination** of
    - 'Minor' undesirable traits
    - 'curable' conditions
    - 'late onset conditions
    - Even autosomal recessive carriers



# Preimplantation Genetic Diagnosis (PGD) and Eugenics (cont'd)

- Labelled as Consumer Eugenics
- Characteristics
  - Disrupting the parent child relation as we know now
  - Parental choice is greatly increased
  - Further decrease in tolerance to disabilities
  - Possibility that elites in the society will become more genetically privileged

# Genetic Services in Hong Kong

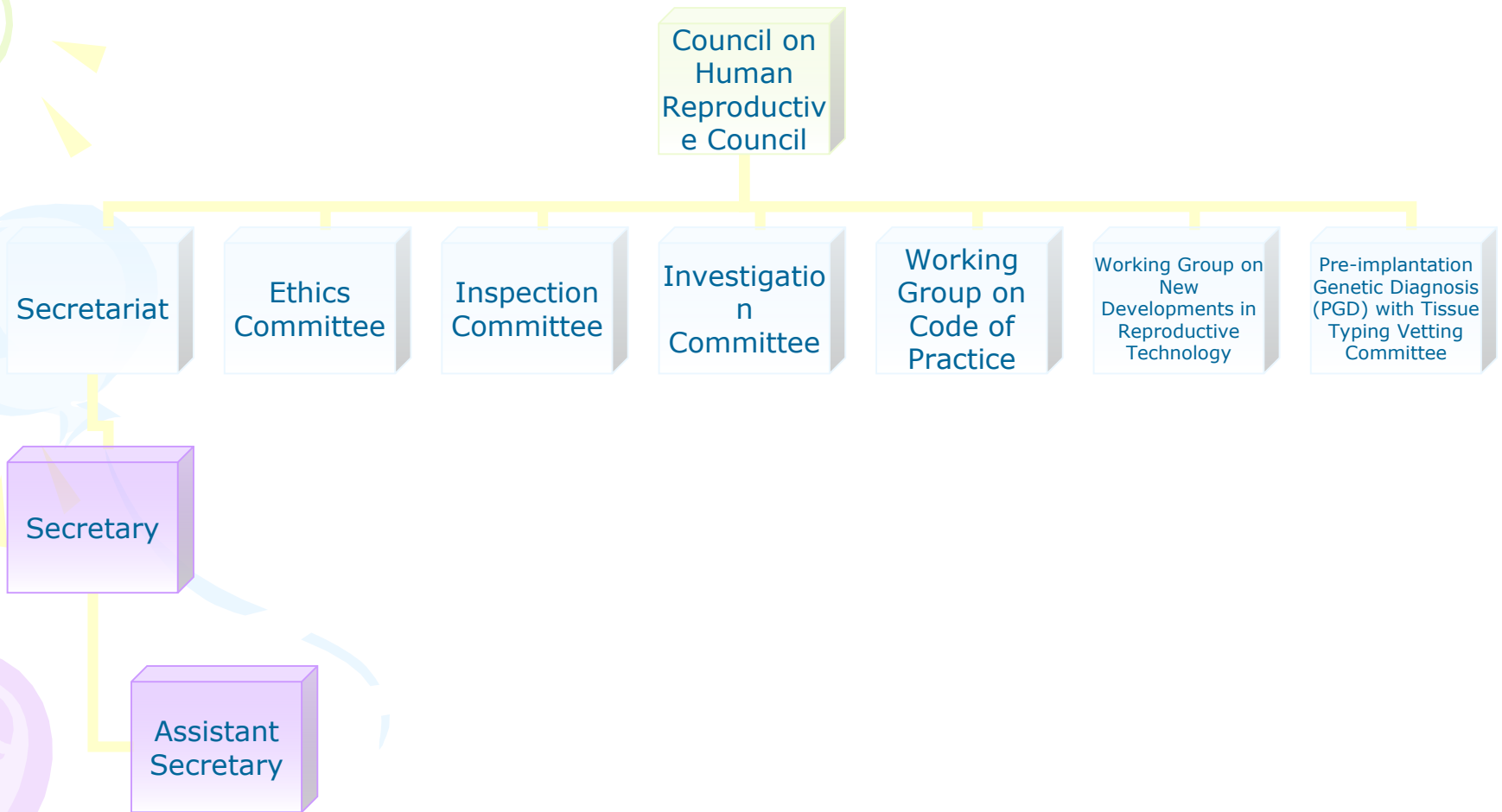




# Regulatory Development

- 2000 Human Reproductive Technology Ordinance (Cap. 561, Laws of Hong Kong)
- 2001 Council on HRT established
- 2002 Code of Practice

# Organization Chart of the Council on Human Reproductive Technology



# Ethics Committee Guiding Principles

- Human life in all forms warrants respect and moral considerations
- Welfare of child of paramount importance
- Personal autonomy, individual liberty and human integrity be safeguarded



# Ethics Committee Guiding Principles (cont'd)

- Recognition to basic community values (responsible parenthood, parental love, and the family)
- Use of resources based on principles of care, equality, justice and accountability, and a reasonable balance must be sought between individual and collective interests to protect vulnerable parties from harm or exploitation



# Development in Reproductive Genetics

- Prenatal testing
  - Non invasive prenatal testing
  - Prenatal diagnosis by
    - Chorionic villous sampling
    - Amniocentesis
- Preimplantation genetic diagnosis
- **Future potentials**
  - **Genome editing**
  - Mitochondrial transfer technology

# Genomic Editing

- DNA double stranded break (DSB) repair mechanics via
  - Non-homologous end joining
  - Homology directed repair
- Nuclease-based genome editing
  - Meganuclease
  - Zinc finger nuclease
  - TALEN (transcription activator-like effector nuclease)
  - CRISPR-Cas

Hybrid Meganuclease



ZFN



Zinc finger domains

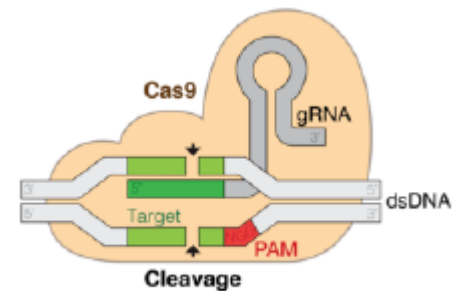
TALEN



TALE subunits

active FokI catalytic subunit heterodimer

Groups of engineered nucleases used for GEEN. Matching colors signify DNA recognition patterns



CRISPR/Cas9

# Debate on CRISPR/Cas9-targeted Genome Editing

- **Chinese** scientists Huang et al 2015 worked on tripronuclear zygote
- **US** scientists called for 'prudent pathway', 2015 NIH not fund editing on human embryos
- **UK** scientists disagree
  - 'research .... Is moral obligation'
  - Fertilisation & Embryology Authority approved research CRISPR on embryo




# Position Statement ASHG

- Statement approved by American Society of Human Genetics Board March 2017



- **Workgroup** from

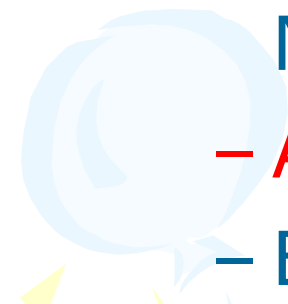

- UK Association of Genetic Nurses and Counsellors,
- Canadian Association of Genetic Counsellors,
- International Genetic Epidemiology Society, and
- US National Society of Genetic Counselors.



Ormond KE et al. Am J Hum Genet. 2017 Aug 3;101(2):167-176. doi: 10.1016/j.ajhg.2017.06.012.



# Position Statement ASHG

- Final statement also endorsed by
    - American Society for Reproductive Medicine,
    - **Asia Pacific Society of Human Genetics,**
    - British Society for Genetic Medicine,
    - Human Genetics Society of Australasia,
    - Professional Society of Genetic Counselors in Asia, and
    - Southern African Society for Human Genetics
- 
- 



# Position Statement ASHG

- (1) At this time, given the nature and number of unanswered scientific, ethical, and policy questions, it is **inappropriate** to perform germline gene editing that **culminates in human pregnancy**.
- (2) Currently, there is **no reason to prohibit in vitro** germline genome editing on human embryos and gametes, with appropriate oversight and consent from donors, to **facilitate research** on the possible future clinical applications of gene editing. There should be no prohibition on making public funds available to support this research.

# Position Statement ASHG

- (3) Future **clinical application** of human germline genome editing should not proceed unless, at a minimum, there is
  - (a) a compelling **medical** rationale,
  - (b) an evidence base that supports its **clinical** use,
  - (c) an **ethical** justification, and
  - (d) a **transparent** public process to solicit and incorporate stakeholder input.





# Conclusions

- Eugenics defined and utilized in different ways
- Lessons to be learnt from historical development of eugenics
- Contemporary eugenics is in practice
- Ethical & Regulatory issues of current practices discussed
- Advancing technologies



*Thank you!*