39th International Danube Symposium
for Neurological Sciences and Continuing Education
in conjunction with the
1st International Congress on ADHS
from childhood to adult disease

History and current development of a field called Neuroethics

F. Gerstenbrand
Medical University of Innsbruck,
Department of Neurology

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What is medicine?

- A long hard grind
- A reliable way to get money and status
- Human biology — A science
- Using science to treat and prevent illness and injury — A branch of engineering

Stephen Pitts, MD, MPH
Emory University, 1998

Some differences between science and medicine

Stephen Pitts, 1998

- Science
  - General hypotheses about truth in the universe
  - Decisions optional
  - Focus on **experiments**, usually animals or tissues
  - Practiced by pleasant, principled hard-working people mostly on weekdays
- Medicine
  - Specific hypotheses about individual patients
  - Decisions required
  - Focus on **systematic reviews** of scientific evidence
  - Practiced day and night by complaining grouches with big mortgages

Definition of ethics

- **Ethics:** Part of philosophy dealing with morality
- **Moral** is search for an inner standard
- **Kant' s Categorical Imperativ:**
  The individual shall act in a way that this action can be regarded as general law

Ethics

- Altruism
- Sense of Honour
- Justness
- Respect for others
- Solidarity
- Ability to forgive

Occidental Ethics

Western ethical thinking, "Christian Ethics"

Founders:
- Socrates, Plato, Aristoteles
  Greek philosophy: moral virtue
  values are natural rather than conventional
  ethics as science
- Saint Augustinus, Thomas Aquinas
  Incorporation of Greek ethics
  Attainment of happiness
  God given natural order
- Immanuel Kant
  Categorical imperative: the individual shall act in a way that his action can be regarded as general law
- Modern ethics
  Different schools:
  Value ethics, existentialistic ethics, American bioethics, Marxian ethics, theological ethics

Non Western Ethics
partly religious fixed

- Ethical rules in Buddhism
  end of rebirth cicle, Nirvana
- Ethical rules in Confucianism
  appreciation of well being of the community above the well being of the individual
- Ethical rules in Mosaic religion
- Ethical rules in Islamic religion
- Ethical rules of natural religions
  Massai religion, African religious communities, Schamanism, etc.

Bioethical principles

Medical conduct, physicians obligations

(Belmont Criteria, 1979)

- Autonomy of the patient
- Beneficience
- Non-maleficiency
- Justice
- Trust

Patient-Doctor Relationship

- Expectation of personal attention
- Trust
- Individualized treatment
- Best available of best care
- Best benefit to risk/ratio

Hippocratic oath

Obligation to heal
Not do anything to harm the patient
No continuation of therapy in untreatable disease
No therapy in advanced physical and mental destruction
No continuation of life prolongation for hours or days
No prolongation of suffering during dying
Not to tell anyone the details of patients
No admitting of lethal poison, even as advice

Will to respect the teacher like own parents, sharing one's life support with teacher or successors of the teacher, treated as own brothers
Medical teaching to own sons and the sons of the teacher or to pupils bound on physicians rules and oath

World Medical Association, Helsinki Declaration, 1964
Medical Research Involving Human Subjects
Ethical Principles

- Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects
- In medical research on human subject, considerations related to the well-being of the human subject should take precedence over the interest of science and society
- International Code of Medical Ethics : A physician shall act only in patient interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient
- Ethical Principles to provide guidance for physicians and other participants in medical research involving human subjects
  Including identifiable material or identifiable data

UNESCO-Declaration on Bioethics and Human Rights

Universal Draft, Paris, 24.6.2005

UNESCO

- SHS: Social and Human Sciences
- BIOETHICS

UNESCO Bioethics Declaration on Human Rights

Paris, September 2005

Person's identity includes

- biological
- psychological
- social
- cultural and
- spiritual dimensions

Informed consent generally

... is necessary for each human being (patient and healthy volunteers involved in):

- any preventive, diagnostic and/or therapeutic medical intervention
- scientific research (basic research, clinical studies) according to
  - ICH-GCP (Good Clinical Practice)
  - GMP (Good manufacturing practice)
  - Clinical trial for new diagnostic and therapeutic methods

Informed consent

... is based on:

- Domestic and international law in accordance with human rights law
- Declaration of Helsinki, 1964 (with amendments)
- Declaration on Bioethics and Human Rights, Paris, 2005

Declaration of Paris, 2005

Article 6a - Consent

Any preventive, diagnostic and therapeutic medical intervention is only to be carried out with the prior, free and informed consent of the person concerned, based on adequate information.

The consent should, where appropriate, be expressed and may be withdrawn by the person concerned at any time and for any reason without disadvantage or prejudice.

Informed consent

patient able to consent

- Content of written information
  - Aims
  - Expected benefits for the subjects and/or others
  - References treatment/placebo
  - Risks and inconveniences
  - If applicable, an explanation of alternative standard medical therapy
- Consent must be documented by either the subject's dated signature or by the signature of an independent witness
- The signature confirms that the consent is based on information, that has been understood and that the subject has voluntary chosen to participate the treatment program

Declaration of Paris, 2005

Article 6b – Consent I

clinical trial

Scientific research should only be carried out with the prior, free, express and informed consent of the person concerned. The information should be adequate, provided in a comprehensible form and should include the modalities for withdrawal of consent.

Declaration of Paris, 2005

Article 6b – Consent II
clinical trial

The consent may be withdrawn by the person concerned at any time and for any reason without any disadvantage or prejudice.

Exceptions to this principle should be made only in accordance with ethical and legal standards, adopted by states, consistent with the principles and provisions set out in this Declaration, in particular in Article 27, and international human rights law.

Declaration of Paris, 2005

Article 7
Persons **without** the capacity to consent
part I

In accordance with domestic law, special protections is to be given to persons who do not have the capacity to consent:

a) authorization for **research and medical practice** should be obtained in accordance with the best interest of the person concerned and in accordance with domestic law. However, the person concerned should be involved to the greatest extent possible in the decision-making process of consent, as well as that of withdrawing consent.

Declaration of Paris, 2005

Article 7
Persons **without** the capacity to consent
part II

b) **Research** should only be carried out for his or her direct health benefit, subject to the authorization and the protective conditions prescribed by law, and if there is no research alternative of comparable effectiveness with research participants able to consent.

Declaration of Paris 2005

Article 7
Persons **without** the capacity to consent
part III

b) **Research** which does not have potential to direct health benefit should only be undertaken by way of exception, with the utmost restraint, exposing the person only to a minimal risk and minimal burden and, if the research is expected to contribute to the health benefit of other persons in the same category, subject to the conditions prescribed by law and compatible with the protection of the individual's human rights. Refusal of such persons to take part in research should be respected.

Patients unable to consent

Decision making on behalf of patients

- Presumed consent in emergency situations
- Proxy consent by an authorised person (legal representative)
- Living will
  - Advanced directives
  - Previously expressed wishes

Patients unable to consent

(temporary – permanently)

Neurology-Psychiatry

Basic legal prerequisite for every medical intervention:
Informed consent – better „valid consent"

Protection of vulnerable persons

Inability to consent in routine medical practice
(Reduced capacity)
Specific laws, rules and regulations

- Children (parents and guardians as proxy depending on maturity of minors
- Patients with cognitive impairments
- Apallic Syndrome/Vegetative State
- Patients with severe progressive or terminal disease
- Patients in intensive care units

Patients unable to consent

Different responsibilities

- In clinical practice
  the treating and responsible physician
  - he is often the true protector of the incapacitated patient
- In research
  Conflicting interest of responsible physician in the clinical trial with the treatment obligation
  - Protecting the research subject
  - Advancing medical knowledge

Informed consent

patient incapable included in a clinical trial
according to Declaration of Paris, 2005

- If the subject is incapable of giving personal consent (e.g. unconsciousness), the inclusion of such patients may be acceptable if
  - The Independent Ethics Committee (IEC) is in principle in agreement
  - Participation will promote the welfare and interest of the subject
  - If possible, written consent of a legally valid representative
- Consent in a non-therapeutic study the legal representative always has to be informed
- Any information becoming available during the trial which might be of relevance for the subject must be made known to the legal representative

Rights and responsibilities

Physician and patient

- The treating physician has the individual responsibility for his patient. Highest level of his education and training is essential and necessary.
- The treating physician is guided by ethical principles, medical guidelines, declaration, domestic and international law and human rights law.
- The personal responsibility of the physician to his patient can't be replaced.
- Patient's right is to accept or to refuse the recommendation of a treatment program.
- Patient's right is to interrupt a running treatment program
- The physician's obligation is to inform the patient about the danger for his health to refuse or to interrupt a treatment program.

Quality of medical care

Three factors will determine the quality of medical care:

- individual clinical expertise
- Individual clinical experience
- scientific evidence

Best available medical care & quality of scientific evidence - 1

Providing the best possible medical care of an individual patient depends on

- ability and willingness of the respective physician to
  - integrate individual clinical expertise
  - and the best external evidence
  - (true evidence-based medicine)

Best available medical care & quality of scientific evidence – 2

Sound scientific evidence is the basis for modern medicine

- **prevention**
- **diagnosis**
- **treatment**
- **rehabilitation**
- **but also for <u>regulatory approval</u>**

Best available medical care & quality of scientific evidence – 3

- The practice of contemporary medicine **crucially** depends on the quality of scientific evidence
- Experimental based medicine has to be taken into consideration even without EDM (Electronic Data Methods) background

Best available medical care & quality of scientific evidence – 4

<u>Scientific evidence</u>

- is never static
- is subject to constant change and adjustment (new facts)
- can be flawed in many different ways
- can never be perfect

Evidenced Based Medicine

- a cultural and methodological ethically based position to clinical practice helping to make decisions based on clinical expertise and an intimate knowledge of the individual patient's situations, beliefs, and priorities
- considered to be the scientifically grounded art of medicine
- de-emphasizes intuition and unsystematic clinical experience as grounds for medical decision-making

Evidence Based Medicine Definition I

- Evidence based medicine involves integrating clinical expertise with the best available clinical evidence derived from systematic research.
- Individual clinical expertise is the proficiency and judgment that each clinician acquires through clinical experience and practice.

SE Straus, DL Sackett, 1998

Evidence Based Medicine Definition II

The practice of EBM is a process of lifelong self directed learning in which caring for patients, creates a need for clinically important information about diagnoses, prognoses, treatment and other healthcare issues.

SE Straus, DL Sackett, 1998

Evidence Based Medicine
Definition III

- Best available clinical evidence is clinically relevant research which may be from the basic sciences of medicine, but especially that derived from clinical research
- patient centered
- evaluates the accuracy and precision of diagnostic tests and prognostic markers
- efficacy and safety of therapeutic, rehabilitative, and preventive regimens

SE Straus, DL Sackett, 1998

Evidence Based Medicine
Critics I

- Among internal biases, economic-based interest may influence the development and diffusion of research and its results.
- difficulty to convert EBM into clinical practice recommendations - it is nearly impossible to make recommendations that are appropriate in every situation.
- EBM cannot be evaluated as the scientific "totem" of the third millennium, neither as the clinical digest of medical literature.

Evidence Based Medicine
Critics II

- Cultural and methodological approach
- Converts the abstract exercise of reading and appraising the literature into a pragmatic process
- Internal biases
  - Economic-based interest
  - Inappropriately applied filters of literature
  - Only based on the positive results of evidence
- Epistemological approach identifies external bias
  - EBM can be changed or removed every time by relevant new or emerging evidence
  - Cannot be evaluated as the scientific "totem" of the third millennium

M Timio et al, 2000

Evidence Based Medicine
Critics III

- "Evidence" in EBM must be of high quality in order to be useful but is not always the case
- "Real world" trials often do not give the same results as these highly artificial controlled clinical studies.
- EBM may be unreliable, sometimes giving different results to subsequent large randomized trials
- Bias in the hypotheses tested in large trials usually covered by commercially interested companies
- Process of journal review and publication is capricious, slow, may have a selection bias towards positive studies (communication channels for evidence are often unsatisfactory)
- For many rarer conditions there is no "high level" evidence (pediatrics, sub-specialization surgeon, etc.)

DS Celermajer, 2001

- Usually no trials of old people who are on many pills

S Butterworth, 2004

Evidence Based Medicine

- Clinicians are looking for new strategies to apply to diagnostic and therapeutic pathways and for the steps where EBM could be addressed when showing the full validity.

M. Timnio, D. Antiseri, 2000

Cochrane Library

- Reviews are more systemic and less biased than systematic reviews published in paper journals
- Cochrane Collaboration has taken steps to improve quality of reviews
- Readers of Cochrane reviews remain cautious, especially regarding conclusions that favour new interventions

Critics:

- Neurological diagnoses are based on meta analysis of in homogenous publications (phenomenologically and topically based)
- Experience based medicine gets more and more unessential

What is the Cochrane library

- Unique source of reliable and up-to-date information on the effects of interventions in health care.
- Health care relies not only on individual medical skills but also on best information
- Best information is compiled using the technique of evidence-based medicine
- The aim of the Cochrane library is to provide EBM information

Cochrane Website, 2004

Factors influencing European medicine

- Progress in research of biology and genetics
- Progress in basic research
- Progress in clinical medicine
- Increasing influence of ethical rules in clinical research
- Forced use of ICH-GCP in clinical trials
- Scarcity of resources
- Demographic developments
- Political changes in Europe
- Process of globalisation

- Trend to a predominance of Evidence Based Medicine
- Trend to the use of Cochrane library
- Loss of Experienced Based Medicine
- Loss of Traditional Medicine

Summarizing I

- Every human being has the right to live (Paris Declaration, 2005).
- Every human being has the right to most modern medical treatment and best nursing care (Paris Declaration, 2005).
- A patient with stroke has to be cared for according to the base right, basic human rights and the medical principles.

Summarizing II

- Economic consideration are not acceptable in treatment and life decision (Hippocratic principles and Universal Declaration on Human Rights (December 10th, 1948).
- According to Hippocratic principles patients with stroke have to be treated in dignity but not to be "over-treated" by all modern possibilities.
- In severe defect states of stroke-patients without hope of any improvement in upcoming severe complications maximal therapy can be renunciated.

Summarizing III

- The renunciation of maximal therapy is acceptable according the Hippocratic principles.
- According to medical rules a decision for end of life also by legal institutions (Supreme court, etc.) is not acceptable in Austria.
- Such decision can not to be realized by a physician, even though legal (danger to be accused for active euthanasia).

When medical uncertainty leads to moral uncertainty, it seems preferable, albeit harder, to confront the dual ambiguities than to bury them under either statistical criteria or unrelenting moral certitude.

Rhoden NK, 1994

Wenn medizinische Unsicherheit zu moralischer Unsicherheit führt, ist es vorzuziehen, obgleich schwerer, die Widersprüche gegenüberzustellen als sie entweder unter statistischen Kriterien oder einer unverminderten moralischen Gewissheit zu verbergen.

Rhoden NK, 1994

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FINAL PROGRAM

2007

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