Abstract purpose: The aim of the study was to assess the knowledge gap of school psychologists in epilepsy.

Abstract methods: Questionnaires were distributed to 30 school psychologists in Kaunas, Lithuania, containing 31 items about epilepsy which were divided into 4 main fields: medical aspects, prevention of social isolation, prevention of epilepsy consequences, and impact of epilepsy on personality. The respondents rated their knowledge, their wish to improve the knowledge, their ability to share the knowledge, and the importance of the specific topic.

Abstract results: The knowledge gap in medical aspects of epilepsy was 44.3%, in prevention of social isolation 44.4%, in prevention of epilepsy consequences 51.5%, and in impact of epilepsy on personality 26.6%. The importance of knowledge in each field was rated accordingly, as 35.7%, 57.0%, 62.7% and 60.7%. Some topics emerged where the knowledge was extremely poor and nevertheless the interest was very small: principles of pharmacological (23.3%) and surgical treatment (16.7%), drugs for epilepsy (16.7%), legislation (33.3%), search for financial help (36.7%). The most important topics that the psychologists would like update their knowledge concerned child's development and upbringing (83.3%), seizure first aid, search for psychological help, special needs (80.0% each) and the impact of epilepsy on the personality in adulthood (76.70%). There was not a single topic that the psychologists were sure they could share their knowledge with others, even concerning the psychosocial issues.

Conclusions: The basic knowledge of psychologists about epilepsy and its consequences is insufficient. This may result in poor self-confidence and their inability to use their professional experience in a creative way when counseling patients with epilepsy.

SHOULD ALL PATIENTS BE TREATED IN STROKE UNITS?

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Stroke care in Europe has developed considerably within recent years being legitimized by the proven effectiveness of stroke units compared to any other setting of hospital care. Compared to treatment in general medical hospital wards that do not specialize or exclusively treat strokes and do not have a dedicated and well-trained personel, stroke units are considered superior in all outcome parameters: 3% less mortality, 2% less institutionalization and 5% more return home independent. Such effectiveness has a similar magnitude (number-needed-to-treat [NNT]: 16) than the one shown for intravenous thrombolysis (NNT: 18) and 4 times more than aspirin (NNT: 83). Considering that the target population for stroke units is at least 4 times greater than the one considered appropriate for thrombolysis today, the clinical effectiveness outnumber the effectiveness of any other scientifically proven measure of stroke care today.

In some European countries the setting up of stroke units is a success story only comparable to the development of coronary care units in the 1970ties. Other countries still have a system that favours only tertiary treatment or academic centers. There, triage systems along some cut-off markers such as pre-stroke disability have been established. In spite of the available evidence there is considerable heterogeneity between various models of stroke care throughout Europe. More recent evidence on the effectiveness of continuous monitoring of vital function, the role of neurologists versus non-neurologists and the importance of seamless early rehabilitation will be reviewed and some quality markers for monitoring the efficiency of stroke units will be presented.

USE AND MISUSE OF LASER EVOKED POTENTIALS IN PAIN PATIENTS

Garcia-Larrea L.
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Laser evoked potentials (LEPs) are cortical responses to cutaneous stimulation by laser pulses, which selectively excite the free nerve endings (A-delta and C) in the superficial skin layers. Late LEPs (150–400 ms) reflect activation of peripheral A-delta fibres, and ultralate LEPs (800–1200 ms) that of the unmyelinated C-fibres. LEPs have proved reliable in assessing damage to the peripheral and central nociceptive system in peripheral neuropathies, idiopathic and symptomatic trigeminal neuralgia, syringomyelia, multiple sclerosis, Wallenberg syndrome, and brain infarction. LEPs are diagnostically useful in peripheral and central neuropathic pains, and are more sensitive than any other neurophysiological test. The finding of LEP attenuation or suppression to stimulation of a painful territory substantiates the diagnosis of neuropathic pain. In neuropathic pain LEP attenuation is observed even in case of hyperalgesia or allodynia; in these latter cases, ultra-late components (800–900 ms) may appear concomitantly with the attenuation or disappearance of late responses. Emerging data suggests that the pattern of LEP abnormality differs in patients with neuropathic provoked pain (hyperalgesia, allodynia) and in patients with spontaneous pain exclusively. In fibromyalgia and myofascial syndromes, chronic fatigue syndrome, chronic inflammatory pains, and psychogenic pain, LEPs have been found normal or even facilitated (increased amplitude). In selected patients, normal or enhanced LEPs to stimulation of a painful territory may reflect enhanced attention toward the laser stimulus, and increase the diagnostic probability of psychogenic pain. Laser evoked potentials are the easiest and most reliable neurophysiological method of assessing function of nociceptive pathways. Their main limitation in clinical practice is that they are available in too few centres.

NEUROETHICS IN DAILY NEUROLOGICAL PRACTICE AND IN CLINICAL RESEARCH

Gerstenbrand F., Struhal W., Müller Ch.
Vienna

Ethics is a part of philosophy dealing with morality, moral is search for an inner standard. The 6 demands of ethics are: altruism, sense of honour, justice, respect for others, solitarity and the ability to forgive. Imanuel Kant crystallized the ethical demands in the categorical imperative, the individual shall act in a way, that this action can be regarded as general law. This sentence has to be accepted as an independent basical rule for every human beiing.

Bioethical principle, for medical contact and for physicians obligations are created in the Belmont Criteria (1979) with the demand for autonomy of the patients beneficience, nonmalefficience, justice and trust. In the Hippocratic Oath the obligation of a physician is clear defined in the main demands as are to heal, not do to anything to harm a patient and not to continue therapy in untreatable disease as well as not to admit a lethal poison even as advanced. In addition the Hippocratic Oath obliged the physician to respect his teacher like own parents.

The so called Western Ethics or the Occidental Ethics were founded by Socrates, Plato and Aristoteles based on moral virtue with natural values. Saint Augustinus and Thomas d'Aquina incorporated in the Greek ethics the Christian philosophy with a God given natural order. The western ethical thinking have to be differentiated from ethical rules based on different religious as well as various ideologies. Ethical rules in Buddhism and in Konfuzianism, partly in Islam and in the Mosaic religion are not comparable in details.

The modern physician in his daily practice as well as to be involved in clinical research all his activities have to be based on ethical rules. The Hippocratic demands, the Helsinki Convention of the World Medical Association (1964) and the Unesco-

Declaration of Paris (September 2005) are guiding the medical duties. Every patient is believing, that his doctor is on the highest level of education calculating of the best benefit for the diagnostic measures and for best treatment programme, which is individualized for him and with fully informed consent. The patients right is to accept or to refuse all the recommendation, but he can interrupt a running treatment. In such a situation the physician has to warn about the danger. For patients without the capacity to consent, the Paris Declaration has detailed advises (in Art. 7).

The Helsinki Declaration clearly expresses, that every medical progress is based on research, involving experiments with human beings. The rules and obligations are defined in detaileds. One of the main points is the obligation to follow the basical principles of ICH-GCP, which include an exact monitoring, audits and inspections, strict anonymity and carefully achieving the results. An exact protocol has to be approved by an Ethical Committee.

Every medical doctor, neurologist and psychiatrist has to integrate individual clinical expertise, best external evidence using trustful evidence based medicine and deep application to rise the best for the patient.

DIAGNOSIS CHALENGES IN LOW GRADE ASTROCITOMA CASE REPORT

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Clinic of Neurology

Backgraund: Brain tumor may simulate pseudotumoral form of Multiple Sclerosis (MS) at its initial presentation (1). On the other hand MS may have a quite variable clinical presentation, and for that reason may simulate or hide other central nervous system (CNS) (2). Interobserver variability in the diagnosis of diffuse astrocitomas has been high owing to subjective diagnostic criteria, overlapping morphologic features, and variations in training and practice among pathologists. The most difficult distinction, especially on frozen section is between gliosis and low grade astrocytoma (3).

History: We report the case of a 21 years old woman with an abrupt onset of symptoms (right ataxic hemiparesis) with 20 days before hospitalisation and who was diagnosticated as "possible Multiple Sclerosis".Cerebral MRI showed a big lesion (3,3/2 cm) with faint smaller areas contrast enhancement, in left periventricular white matter,without distort the lateral ventricle and several smaller white matter unenhanced lesions. CSF analysis showed a limfocitar pleiocitosis. Visual Evocated Potentials was normal. Serological anlaysis showed an Elisa test for Borellia IgM positive, positive ANA and Anti Sm anticorpes. Quantitative EEG showed a perilesional hiperactivity. Stereotactic biopsy confirmed the diagnostic of: Grade II Astrocytoma – fibrillary subtipe.

Discussion: Authors analysed the differential diagnosis between diffuse astrocytoma, pseudotumoral multiple sclerosis, parasitosis and vasculitis, with a revew of the literature.By reporting this atypical case of low grade astrocytoma (by his debut, localissation, MRI characteristics) the authors emphazise the necessity to evocate this etiological hypothesis in the diagnosis algoritm of any motor weakness in young people.

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EFFECTS OF GAP JUNCTIONS BLOCKERS ON INHIBITORY NEURONAL NETWORKS SYNCHRONICITY IN EPILEPTIC CORTEX

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Communication through gap junctions (GJs) is increasingly recognized as an important mechanism for synchronizing neuronal networks under physiological and pathological conditions such as epileptic seizures (3, 4). We have previously shown that GABA receptor-mediated synchronous events are recorded in 4-amino-pyridine (4AP) – treated neocortical slices obtained from patients undergoing surgery for epileptic disorders such as temporal lobe epilepsy (TLE) (1, 7) or focal cortical dysplasia (FCD) (2, 5). These events, which continue to occur during application of ionotropic glutamatergic receptor antagonists, represent the post-synaptic response of principal neurons to GABA released following the synchronous firing of interneurons (7). Here, we sought evidence for a role played by GJs in the human neocortex during the generation of these synchronous GABA receptor-mediated potentials in brain slices (6).

Field potentials and intracellular recordings were obtained in neocortical slices from TLE patients during application of 4AP (50 µM) and glutamatergic receptors antagonists. Spontaneous synchronous events (duration = 0.2–1.1 s; intervals of occurrence = 3–27 s) were recorded in the slices. The synchronicity of the potentials recorded at two locations distant up to 5 mm was decreased by GJ blockers (carbenoxolone, octanol, quinine and quinidine) within 20 min of application. Longer times of application could lead to the disappearance of the spontaneous events. Spontaneous synchronous events (duration 0.4–8 s; intervals of occurrence 0.5–90 s) occur in some FCD neocortical slices in the absence of any pharmacological manipulation. These types of events were slowed down and their synchronicity was decreased by the GJ blocker carbenoxolone. In addition, we found that decoupling GJs could block the ictal discharges generated by FCD slices during 4AP treatment.

Our data indicate that GJs: (i) contribute to the spread and phase locking of synchronous events in neocortical slices from TLE patients during blockade of glutamatergic transmission; (ii) play a role in the generation of synchronous activity in FCD slices superfused with normal medium; and (iii) participate to ictal-like discharges in this type of tissue during 4AP application.

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MYASTHENIA GRAVIS TREATMENT BASED ON DISEASE PATHOGENESIS

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Myasthenia gravis (MG) is a well-defined autoimmune disease. Autoantibodies to acetylcholine receptors (AChR) in the postsynaptic membrane of the neuromuscular junction are directly pathogenic. 10–15% of MG patients does not have AChR antibodies. Thy-

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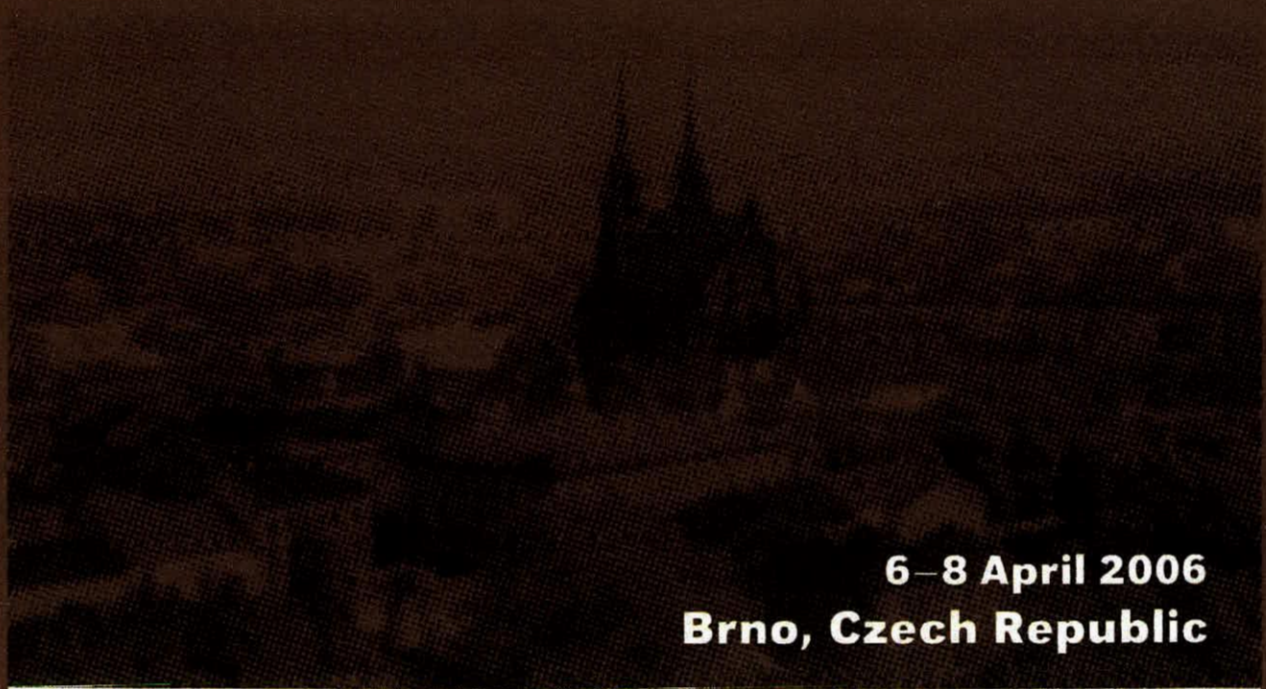

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Neuroethics in daily neurological practice and in clinical research

F Gerstenbrand, W.Struhal, Vienna

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Neuroethics in Daily Neurological Practice And Clinical Research

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The 38th International Danube Symposium for Neurological Sciences and Continuing Education

Brno, April 6-8, 2006

Different issues of neurosciences

Clinical Neurology – lesions in CNS & PNS

- Acute neurology, diagnosis and acute treatment topical based neurology
- Neuro-rehabilitation: → re-socialization
- Neurological care in „End-of-treatment"-states, Amelioration of Quality of Life

Basic research in neurology

Definition of Ethics

- **Ethics:** Part of philosophy dealing with morality
- **Moral** is search for an inner standard
- **Kant' s Categorical Imperative**:
  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 Christian thinking in Greek ethical laws
  Attainment of happiness
  God given natural order
- Immanuel Kant
  Categorical Imperative:
  the individual shall act in a way, that this action can be regarded as general law

Non Western Ethics

partly religious fixed

- Ethical rules in Buddhism
  end of being rebirth, 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 and 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 letal poison, even as advice

Will to respect the teacher like own parents, sharing one life support of 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 Bioethics Declaration on Human Rights

Paris, September 2005

Person's identity includes

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

Informed consent

(Declaration of Paris, 2005 - Article 6a)

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

Informed consent in daily practice

patient able to consent

- Content of written information (diagnostic, therapeutic measures)
  - 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 diagnostic and treatment program

Informed consent in clinical trials I patient able to consent

(Declaration of Paris, 2005 - Article 6b)

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.

Informed consent in clinical trials II
patient able to consent
(Declaration of Paris, 2005 - Article 6b)

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, States adopted by, consistent with the principles and provisions set out in this Declaration.

Patients unable to consent

Neurology, Psychiatry
(temporary or permanently)

Basic legal prerequisite for every medical intervention

Inability to consent in routine medical practice
Protection of vulnerable persons

Specific laws, rules and regulations

- Children (parents and guardians as proxy depending on maturity of minors
- Patients with cognitive impairments (aphasia, frontal syndrome, etc.)
- Apallic Syndrome/Vegetative State
- Patients with severe progressive disease (terminal state)
- Patients in intensive care units

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 (recent date)

Persons **without** the capacity to consent I

(Declaration of Paris, 2005 - Article 7)

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.

Persons **without** the capacity to consent II

(Declaration of Paris, 2005 - Article 7)

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.

Persons **without** the capacity to consent III

(Declaration of Paris, 2005 - Article 7)

b) **Research** which does not have potential 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.

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, etc.), the inclusion of such patients may be acceptable if
  - The Independent Ethics Committee (IEC) is principally agreeing
  - Participation will promote the welfare and interest of the subject
  - written consent of a legally valid representative, if possible.
- 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

Patients unable to consent

Different responsibilities

- In clinical practice
  the responsible physician for treatment and diagnostic program
  - often the true protector of the incapacitated patient
- In research
  Conflicting interest of the responsible physician in clinical trial with his treatment obligation
  - Protecting the research subject
  - Advancing medical knowledge

Informed consent

generally

... is necessary for each human being (patient and healthy volunteer):

- 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)
  - GLP (Good Laboratory Practice)

  Clinical trial for each new diagnostic and therapeutic methods.

Informed consent in daily practice

... is based on:

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

Basic principles in daily practice 1

- Every human being has the right to live.
- Every human being has the right to most modern medical treatment and best nursing care.
- Every patient has to be cared according the basic human rights and medical principles.

Basic principles in daily practice 2

- Economic consideration are not acceptable following the Hippocratic principles and Universal Declaration on Human Rights (December 10th, 1948).
- According to Hippocratic principles every patient has to be treated in dignity but not to be "over-treated" by all modern possibilities.
- Maximal therapy can be renunciated in states of severe complication occurring in patients without hope of remission (hopeless prognosis).

Basic principles in daily practice 3

- The renunciation of maximal therapy is a directive following the Hippocratic principles.
- According to medical rules even a decision for end of life by legal institutions, Supreme court, etc. is not acceptable.
- Such decision can not to be realized by a physician (→ accusation for active euthanasia).

Human research and subject protection (NIH, FDA)

basic rules

- Informed consent to the patient
- Education and training of investigator
- Appropriate training for investigator in bioethics and other issues related to research involving human subject
- Improved monitoring
- Conflicts of interests
- Civil monetary penalty for violation of research (investigator, research institute)

Principles of ICH-GCP for Clinical Trials

- In accordance with ethical principles
- Only if benefits justify the risks
- Rights, safety and well-being of trial subjects are most important
- Supported by adequate non-clinical and clinical information
- Scientifically sound with clear detailed protocol
- Compliance with study protocol and after approval by Independent Ethics Committee (IEC)
- Physician responsible for medical care of subjects and medical decisions

Good clinical practice (GCP) for trials on medical products

International Conference of Harmonization (ICH-GCP)

- Protection of trial subject
  - Ethics Committee
  - Informed consent (voluntary, detailed information)
  - Insurance
- Responsibility of the
  - Sponsor
  - Investigator
  - Monitor
- Data handling
  - Investigator
  - Sponsor/monitor
    Safety reporting of serious adverse events (SAE)
  - Archive of data
- Statistics (experimental design, randominisation, statistical analyse)
- Quality assurance

Bad Clinical Practice (1)

- Malevolence
  Sabotage of research, theft of data
- Fraud
  „Improvement" of data/results
  „Arbitrary", correction to meet inclusion criteria
  Totally or partially fabricated cases
- Violation of ethical principles
  Inadequate consequence
  Selection of subjects (inadequate exclusion of „high risk group")
  Dangerous or disturbing invasive procedures
  Distress by contact of study
  Dangerous treatment (inadequate safety information, withdrawal of the proved substance)
  Insufficient confidentiality
  Low insurance coverage

Bad Clinical Practice (2)

- Protocol violations
  - Insufficient knowledge/understanding
  - Omissions (tests left out)
  - Errors involving
    - patient selection
    - evaluation
    - dates
    - treatment (dose, concomitant medication, allocation)
    - blindness
- Erroneous Values
  - Work overload
  - negligence
  - incompetence

Clinical Trials in Medicine
Basic Principles and Problems

- Patient changes to an examination object
- Physician changes to investigator

- Protocol of the trial, prepared in an exact form
- Protocol submission to the Independent Ethics Committee (IEC)
- Sponsor: industry, academic
- Investigator with exact training

- Procedure according to the principles of ICH – GCP
- Exact monitoring during the trial
- Audits and inspections procedure
- Strict anonymity of the trial results
- Careful archive of the results
- Registration of each clinical trial (WHO, in discussion)

Future outlook for clinical trials

- ICH-GCP provides widely accepted and scientific standard for clinical trials
  ICH-GCP guidelines facilitates acceptance of foreign data
- Sponsors will increase their research activities outside of high-industrialized countries (USA, EU, etc.)
- Compliance with GCP, protocol and regulatory requirements
  Assurance that the results are credible and accurate
  Rights and integrity of trial subjects are protected
  More efficient clinical development
  Reduced number of necessary trials
  Facilitates use of global dossier for regulatory submissions in EU, USA, Japan, etc.
- Registration of each clinical trial (WHO, in discussion)

Best available medical care & quality of scientific evidence - 1

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 - 2

Providing the best possible medical care of an individual patient depends on the doctor´s ability and willingness to

- integrate individual clinical expertise
- the best external evidence
- true evidence based medicine (critical resonance including different libraries)

Best available medical care & quality of scientific evidence – 3

Sound scientific evidence is the basis for modern medicine

- **prevention**
- **diagnosis**
- **treatment**
- **rehabilitation**
- **but also for regulatory approval**

Best available medical care & quality of scientific evidence – 4

Scientific evidence

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

Best available medical care & quality of scientific evidence – 5

Conclusion:

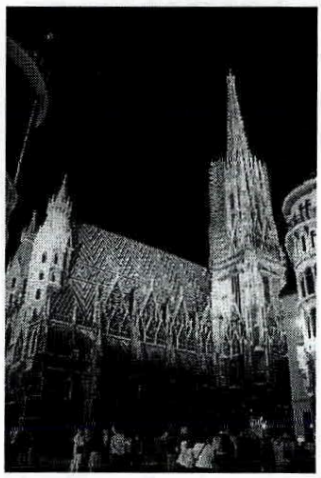
the practice of contemporary medicine depends crucially on the quality of scientific evidence

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.

"New ethical law in medical treatment" has to be created.

Greetings from Vienna!



Stephansdom by night

Wolfgang Amadeus Mozart
1756 – 1791
„Eine kleine Nachtmusik"

Decision to withhold „maximal therapy“

- Decision is made by treating physician considering certain facts:
  - Objective criterias: diagnosis and prognosis
  - Living will of the patient
  - How the patient himself would decide in this situation
  - Solicitor and family