# Special Sessions

The influence of Jean Martin Charcot upon contemporary art

#### SS1-1

Art in Charcot's career

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Abstract not received

#### SS1-2

Charcot - Artiste? Was Charcot really a connoisseur?

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Because of his talented drawings and the many references to the great museums of Europe found in his publications, Charcot is often considered as 'Charcot-artiste', an artist and a connoisseur of art. His biographers describe with relish the splendor of his somptuous residence. His furniture and various artefacts (actually part of the artshop of Madame Charcot) were accumulated in a somber setting in neorenaissance style. The biographers talk about the Master's taste for XVIIth century Dutch paintings, its realism and rabelais-like witty eloquence. This presentation will show that the decoration and artefacts found in Charcot's residences actually reflect the fashion of his youth, a fashion which ignored or despised the immense artistic movement of his own century, from Corot and Delacroix to the Impressionists. And yet this was a time when real connaisseurs gathered collections of such universal value that their homes are now authentic museums. To find 'Charcot-artiste', one needs to look elsewhere. The talent of his masterly clinical presentations recreated in the concision, sobriety and elegance of his scientific writing make us understand why his lessons attracted the elite of his time, scientists and laypersons alike.

#### SS1-3

#### Charcot as an artist?

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Abstract not received

Evidence-based neurology and clinical pharmacology

#### SS2-1

The biochemical and molecular basic aspects of neuropharmacological research

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Abstract not received

#### SS2-2

#### Actual issues in evidence based neurology

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Abstract not received

#### SS2-3

# The role of neuroimaging in clinical neuropharmacological research

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Abstract not received

#### SS2-4

#### Ethics in evidence-based medicine

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Evidence-based Medicine can be of great value for actual medical decisions by offering new diagnostic procedures and new treatment programs supported by evidence. Evidence-based Medicine improves clinical decisions by providing reliable and unbiased scientific data. Evidence Based Medicine can also help by elaborating rules for withdrawing and withholding (futile or inappropriate) therapies. The Declaration of

Helsinki of 1964 with its different amendments was created by the World Medical Association to regulate medial research involving human subjects. As of May 1st, 2004, the clinical trial directive 2001/20/EC makes compliance with the ICH-GCP guidelines (International Conference for Harmonization - Good Clinical Practice) obligatory for EU-member states. The advice of independent Ethics Committees (IEC) helps in balancing the benefit /risk assessment for the patient. Western ethical rules demand strict observation of the basic principles of human rights and dignity when applying modern technology for medical purposes. Randomized control clinical trials producing the highest quality of evidence are increasingly influencing medical practice. The quality of evidence depends on properly designed, executed, interpreted and published trials. Studies can suffer from various forms of bias undermining internal validity. The results of trials comparing patient groups in order to identify and quantify causal associations are valid for the patient population investigated thus determining external validity. Review articles, editorials, meta-analyses, consensus statements and guidelines can be helpful for interpreting trial data, however all are vulnerable to publication bias. Underreporting of negative results, nonpublication of unwanted results and unprofessional citation practices have all been recognized as factors distorting evidence. An obligatory register for all clinical trials has been advocated repeatedly in order to counteract publication bias. An EU register for clinical trials is in preparation but will only be accessible to regulatory authorities. Public perception can introduce another source of bias; emergency research, research in children and research in patient not able to consent is still widely afflicted by these negative attitudes. Conflicts of interest have surfaced as another disturbing influence. Financial conflicts of interest have recently prompted regulatory and political action. And last but not least, a less recognized conflict of interest is medical research conducted in poor countries for the primary benefit of wealthier regions thereby violating basic ethical and scientific principles. Cases of scientific fraud and misconduct have been addressed by several leading medical journals. It is up to the medical community to face the challenges of bias, conflicts of interest and fraud. Ethics committees and professional societies have to contribute to the process of promoting scientific integrity and true professionalism. Recognizing and rejecting biased evidence will dry up its sources and pave the way for unbiased and soundly based evidence in medicine. Evidence-based Medicine in its last consequence can only achieve its true aim, i.e. the best available treatment for individual patients, through judicious application of evidence based knowledge together with experience based medicine by experienced physicians. This will preserve the value of experience-based medicine rooting in thousands of years of caring for the health needs of human beings.

Hyperbaric oxygenation therapy. An effective approach to special neurologic disorders

SS3-1

Introduction

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Dr Henshaw, a British physician, performed in 1664 the first therapeutic attempts with a pressure chamber. His pressure chamber was operated by a pair of bellows. Only two centuries after the first attempt, the pressure chamber therapy was taken up in France and later in the USA it reached its climax in the early twenties of the last century, with the largest pressure chamber constructed by Cunningham. This giant project consisted of a six storied-building, where each level held 12 beds, but it never came in function. Priestly discovered oxygen in 1775. In 1789 Lavoiser and Seguin distributed the idea of toxic properties of oxygen, which refrained the therapeutic purposes. The Draeger manufactory developed 1917 a system of hyperbaric oxygenation for treating diving accident victims, but the apparatus was never built. Behnke and Shaw used the system of hyperbaric oxyenation for treatment of decompression disease in 1937. The Dutch physician Dr Boerema is considered as the father of modern hyperbaric medicine. In the 1950s he was the first to perform cardiac surgery under hypothermia and HBO with elongated asytolic periods. In animal experiments he could show that with the help of HBO organ functions of pigs could be sustained without blood supply. In 1965 Ingvar and Larsen were the first using the HBO method for treatment of ischemic stroke. In the last 8 years hyperbaric oxygenation from the field of neurology has drawn varying degrees of attention. An explanation could be the non-selected indication for treatment of neurological diseases, the absence of neurologists in the HBO-centers and the occurrence of some accidents within the pressure chamber system in the past. But in the last few years neurology has rediscovered hyperbaric oxygenation. Undoubtedly the standard indication for HBO is decompression therapy of diving accident victims with commonly neurological complications. In various HBO-centers first experiences with HBO as basic therapy for acute and chronic neurological conditions, as well as part of multi component treatment were gained. First therapeutic results are presented for traumatic brain injury of moderate severity and for acute stroke. In chronic neurological conditions like in state after anoxic accidents and in cerebral palsy positive therapeutic results are published. It is progress, that neurology is considering HBO in therapy in acute as well as in chronic neurological conditions. The explanations of HBO in acute states of brain damage is the interaction in the metabolism of partly damaged brain cells under the principle that oxygen under pressure is supporting the functions even without blood supply, in chronic neurological conditions with HBO the dendrite system seems to be

SS3-2

HBO in cerebral hypoxic lesions caused by cerebrovascular obstruction: Experimental and clinical investigations

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Background: A cerebral energy crisis resulting from thromboembolic events and/or obstructive vessel disease needs therapeutic intervention to reduce secondary damage of brain tissue, especially so called 'penumbra'-regions. Increased

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#### Ethics in Evidence-Based Medicine

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## **Bioethical principles**

Medical conduct, physicians obligations (Belmont Criteria, 1979)

- · Autonomy of the patient
- · Beneficence for the patient
- · Non mal efficiency to the patient
- · Justice
- Trust

#### Clinical Trials in Medicine **Basic Principles** Good clinical practice (GCP)

- 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

#### Clinical Trials in Medicine **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
  - Dangerous or disturbing invasive procedures
  - Distress by contact of study
  - Dangerous treatment (inadequate safety information,
  - withdrawal of the proven substance) Insufficient confidentiality
  - Low insurance coverage

#### Clinical Trials in Medicine **Bad Clinical Practice (2)**

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

# Basic ideology of EBM

- · To keep up with the rapidly growing medical literature
- To improve clinicians skills in asking answerable questions and finding the best answer to open questions
- · Can provide a framework for critically appraising evidence
- · Integrating each patients unique features with evidence of clinical expertise to apply the gained evidence for the treatment of a patients group

SE Straus, DL Sackett, 1998

#### Definition EBM 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

## **Definition EBM II**

- 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

## **Definition EBM III**

 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

# Instructions for practicing EBM

- Converting the need for information into clinically relevant, answerable questions
- Finding the best evidence to answer the running questions
- EBM can provide a framework for critically appraising evidence
- Integrating the appraisal with clinical expertise and applying the results to clinical practice
- Evaluating the performance

SE Straus, DL Sackett, 1998

# 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

# Contents of Cochrane Library

Seven separate databases

- The Cochrane Database of Systematic Reviews (CDSR)
- · The Database of Abstracts of Reviews of Effects (DARE)
- The Cochrane Central Register of Controlled Trials (CENTRAL)
- The Cochrane Database of Methodology Reviews (CDMR)
- The Cochrane Methology Register (CMR)
- The Health Technology Assessment Database (HTA)
- The NHS Economic Evaluation Database (NHS EED)
  - Five of this provide coverage of EBM
  - Two provide information on research methodology

Cochrane Website, 2004

# EBM of clinical diagnoses I

usefulness of diagnostic tests

- · Single publication should answer following questions:
  - Do test results in affected patients differ from those in normal individuals?
  - Are patients with certain test results more likely to have the target disorder?
  - Do test results distinguish patients with and without the target disorder?
  - Do patients undergoing the diagnostic test fare better than those untested?

DL Sackett, RB Haynes 2002

# EBM of clinical diagnoses II

usefulness of diagnostic tests

- · Keys to validity in diagnostic test studies:
  - Independent, blind comparison of test results with a reference standard among a consecutive series of patients suspected (but not known) to have the target disorder
  - Inclusion of missing and indeterminate results
  - Replication of studies in other settings

DL Sackett, RB Haynes 2002

# EBM in the rapeutical methods I

- · Key questions are:
  - Are the results of the EBM publications valid and useful for the individual patient?
  - Does employing the technique of the EBM publication improve quality of life and quality of care for the individual patient?
  - Are the prognostic markers suitable for the individual patient?
  - CAT makers (critically appraised topic): one page summary that includes information on the patient, the evidence and the clinical bottom line

SE Straus, DL Sackett, 1998

# EBM in therapeutical methods II

- Integrating the evidence with clinical expertise and knowledge of the unique features of patients and their situations, rights and expectations
- Incorporate the evidence into the care of a particular patient
- Evaluate the performance, 5 steps
  - 1. Was the question answerable

  - Was good evidence found quickly Was evidence effectively appraised
  - Was the integration of the appraisal with clinical expertise
  - the patients unique features left them with a rational acceptable management strategy

SE Straus, DL Sackett, 1998

#### Critics EBM I

- · Cultural and methodological approach
- Converts the abstract exercise of reading and appraising the literature into a pragmatic process
- Internal hias
  - 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

#### Critics EBM II

- "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 usatisfactory)
- For many rarer conditions there is no "high level" evidence (pediatrics, subspeciality surger, etc.)

DS Celermajer, 2001