ABR – BVS 20-06-2008
Opleidingsdag: ALARA in de medische wereld
Journée de formation : ALARA dans le monde médical

The radiation protection principles in medicine: prerequisites and challenges

Dr Patrick Smeesters

MD, Radiation Protection Advisor, FANC
Lecturer (UCL, ULB)
Member of Art 31 GoE
Member of Belgian delegation to UNSCEAR

BSS: European competence and international elaboration
Main players and their roles

- **EU level**:
  - **Art 31 GoE**: **scientific evaluation and advice on EU BSS**
  - **EU Commission**: **proposes Directives/other**
- **Upstream**:
  - **UNSCEAR**, (com.1 et 2 ICRP, BEIR,…): **scientific evaluation**
  - **ICRP** (main commission): **recommendations RP**
- **In parallel**: Safety Standards **IAEA** (Fundamentals, Requirements, Guides): **« International BSS »** (**IAEA, FAO, ILO, NEA, WHO, PAHO**)

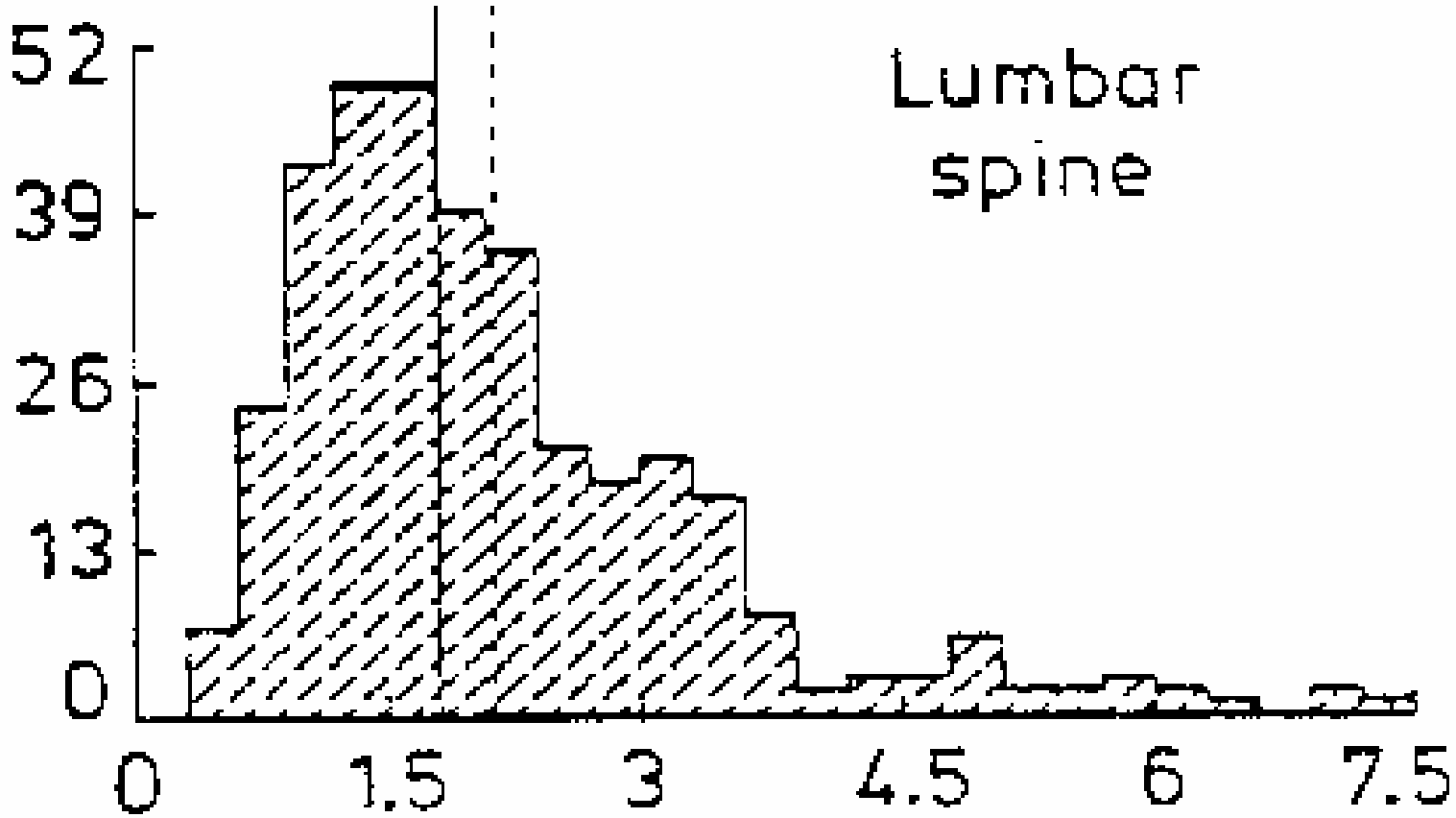
Council Directive of 3 September 1984

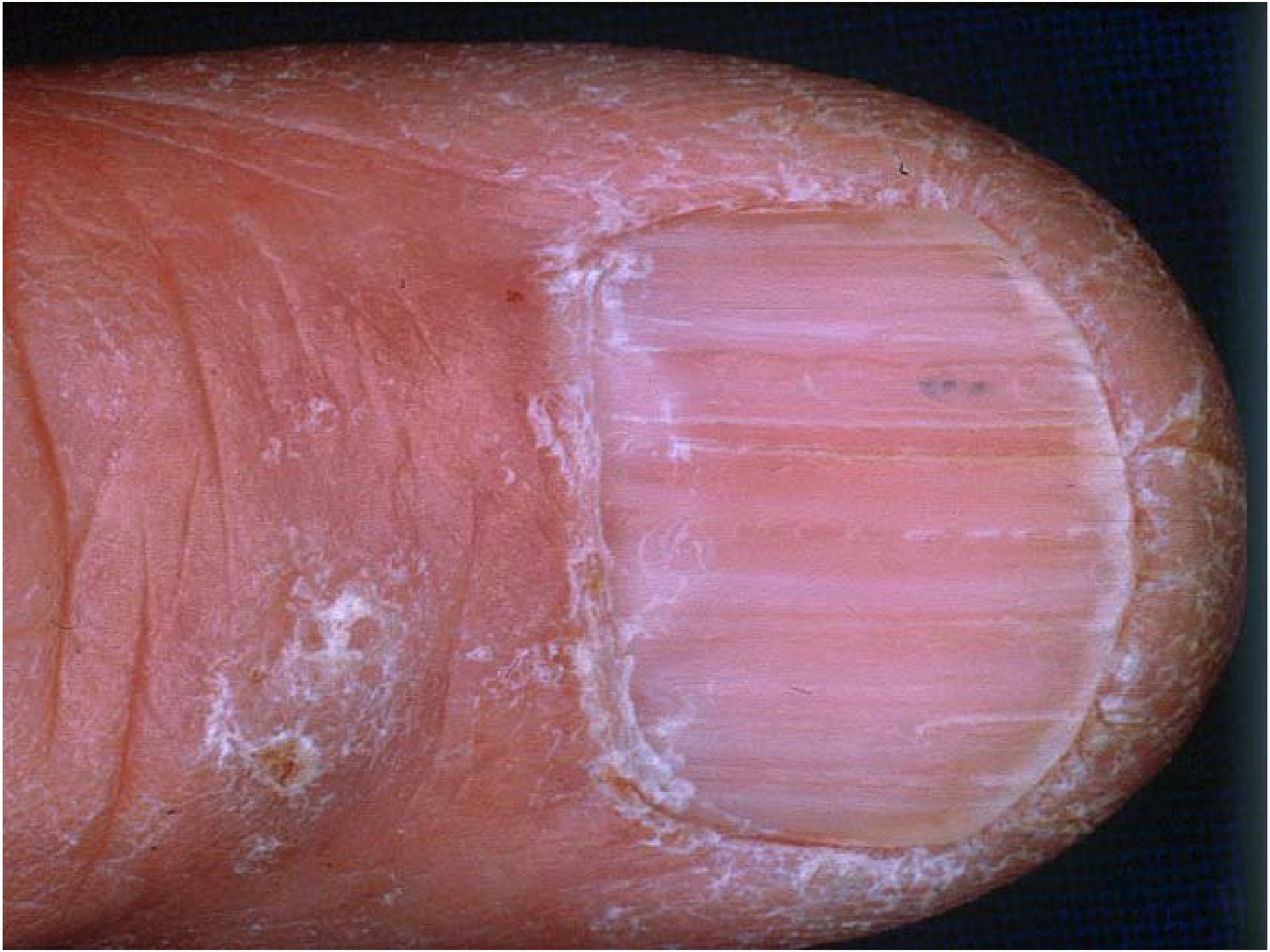
laying down basic measures for the radiation protection of persons undergoing medical examination or treatment

- followed patient-dose surveys
  - for similar examinations, **differences in doses by up to 2 orders of magnitude**

- Art.2.2
  - **Complementary training** for persons who are already in practice where competence in R.P. not approved by comp. Auth.

Distribution de doses typique





Evolutions since C.D. 1984

- research :
  - criteria and methods for quality assurance
  - optimisation of image quality and patient exposure
  - concept of Quality criteria for diagnostic radiographic images
  - methodology and instrumentation for assessing doses

- **Need for dissemination of knowledge and simplification**

- **Accidents in patients**

5 months after third angioplasty

Several months after 3rd angioplasty

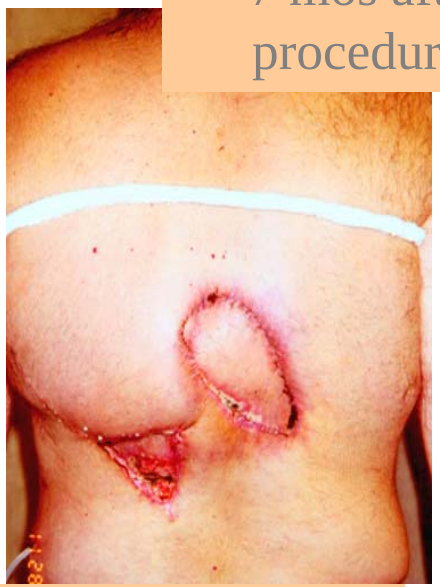
22 months after third angioplasty

4 mos after procedures

7 mos after procedures

9 mos after procedures

22 mos after procedures

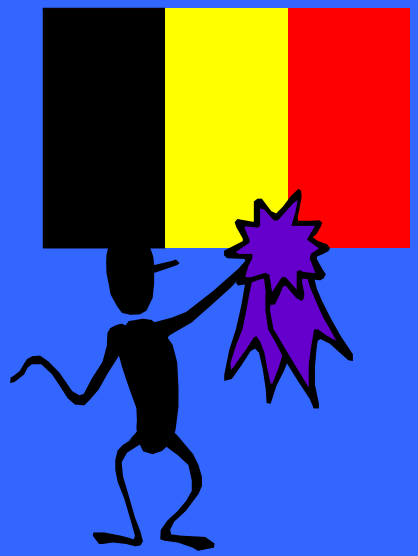


23 mos after procedures

Three TIPS procedures in 1 week in type II diabetic. Total procedure time 13 - 16 hours. Three weeks later noticed 13-cm x 17-cm mottled oval discoloration on back. Initially diagnosed as strep infection, then as herpes I, then as allergic reaction to oral diabetic medications. Diagnosis of radiodermitis obtained months later!

“Mycturition cystourethrography in selected children’s hospitals in Europe” (K. Schneider et all., 1999)

ospital	Scr.time (s)	N exp.	DAP ($mGy.cm^2$)
	30	0.7	8
	18	4.5	156
1	115	6.0	285
	35	10.2	1898



Council Directive of 30 June 1997

on health protection of individuals against the dangers of ionising radiation in relation to medical exposure

- far -reaching
- implementation before 13 May 2000
- broader scope

Optimisation

- All doses due to medical exposures **ALARA**
  - in radiotherapy,**doses to non-target tissues**

- Members states shall :
  - **promote diagnostic reference levels**

- Shall include:
  - **selection of equipment**
  - **quality assurance**
  - **evaluation of patient doses**

Justification:

- **all individual** medical exposures:
  - prescriber and practitioner shall seek to obtain, where practicable, previous information
- **new types** of practices justified in advance
- **existing types** of practices may be reviewed when new elements

Procedures

- **written protocols** for every type of practice for each equipment
- recommandation concerning **referral criteria** available to prescribers (M.S.)
- **medical physics expert** :
  - closely involved in radiotherapy
  - available in nuclear medecine
  - involved, as appropriate, for consultation in radiology
- **clinical audits** carried out

Excellent directive

Implementation in the medical field:

Far from ideal!

Use of X-ray in medicine: vade-mecum

- FANC and Consilium radiologicum
- **Summary of regulation; answers to FAQ**
- ***Directives for patient dosimetry***
  - Triennal dose studies
  - On-line measurements or individual evaluations

Multicenter research (FANC)

- Finalized: 2 y study in interventional radiology (25 services: cardiology, radiology)
- In project:
  - Study on trigger values in interventional procedures (to avoid radiodermitis)
  - Study on extremity/lens doses (int. rad. and nucl. med.)
  - Study on doses to premature babys

New challenges

- Rapid technological evolutions with new RP problems (IMRT, Tomothérapie, cone beam CT,..): justification? RP design? RP guidance?
- *Strong increase in use of high-dose* radiological techniques (interventional radiology, new CT…)
- *opportunistic screenings* (self referral)
- Individual justifications: often pious hope!
- **Last but not least: new insights on radiation risk largely unknown**

Developments in Radiation Protection Standards

- Scientific Research: incl. EU FP
- Evaluation of the scientific data +

  Implications: 3 pitfalls
  - Value judgments even in scientific evaluation
  - Mandates
  - Weight of dominant paradigms
- Possible modification of the standards

The Article 31 Group of experts and the RIHSS Seminars

- Article 31 Group of Experts: Group of independent scientific experts referred to in Article 31 of the Euratom Treaty, that assist the European Commission in the preparation of Basic Safety Standards
- RIHSS : Art 31 WP on Research Implications on the Health and Safety Standards (chairman: Patrick Smeesters)
- Scientific Seminars *(*yearly):
  - Leading experts are asked to review the **state-of-the-art**
  - Invited experts act as *peer reviewers*
  - **Discussion of the potential regulatory implications**

Bridge between research and regulators

2nd Draft ICRP Recommendations

EU Scientific Seminar 2006

New Insights in Radiation Risk and BSS

1. Radiation-induced cancers and age/gender sensitivities

- New models for evaluation of the radiation-induced lifetime cancer risk: M. Little
- New epidemiological data (nuclear w., Techa R.): E. Cardis
- Large scale indoor radon studies (including leukemia): M.Tirmarche
- Biological aspects in relation to age/gender sensitivities and discussion of the potential implications: W.-U. Müller
- New biological data in relation with low dose risk: D. Averbeck

2. Radiation-induced genetic risk and non-cancer diseases

- Ionizing radiation, genetic risks and radiological protection: K. Sankaranarayanan
- New data on genetic risk : J. Angulo
- Radiation-induced cardiovascular diseases: NA (Mabuchi)
- Radiation-induced cataracts: new evidence: N. Kleiman

Proceedings of the EU 2006 Seminar

Available on the web site of the EC

http://ec.europa.eu/energy/nuclear/radioprotection/publication_en.htm

Radiation Protection no. 145

Cataracts
(EU Seminar 2006: N. Kleiman)

- New data from animal models and from exposed human populations (Chernobyl liquidators, A-bomb) suggests that lens opacities occur at doses far lower than those generally assumed to be cataractogenic
- Some observations are consistent with the possible absence of a dose threshold (genetic susceptibilities: Atm, Brca1 and Rad9 heterozygotes)

Cataracts among Chernobyl clean-up workers: implications regarding permissible eye exposures.

Worgul BV, Kundiyev YI, Sergiyenko NM, Chumak VV, Vitte PM, Medvedovsky C, Bakhanova EV, Junk AK, Kyrychenko OY, Musijachenko NV, Shylo SA, Vitte OP, Xu S, Xue X, Shore RE.

Eye Radiation and Environmental Research Laboratory, Columbia University, New York, New York 10032, USA.

The eyes of a prospective cohort of 8,607 Chernobyl clean-up workers (liquidators) were assessed for cataract at 12 and 14 years after exposure. The prevalence of strictly age-related cataracts was low, as expected (only 3.9% had nuclear cataracts at either examination), since 90% of the cohort was younger than 55 years of age at first examination. However, posterior subcapsular or cortical cataracts characteristic of radiation exposure were present in 25% of the subjects. The data for Stage 1 cataracts, and specifically for posterior subcapsular cataracts, revealed a significant dose response. When various cataract end points were analyzed for dose thresholds, the confidence intervals all excluded values greater than 700 mGy. Linear-quadratic dose-response models yielded mostly linear associations, with weak evidence of upward curvature. The findings do not support the ICRP 60 risk guideline assumption of a 5-Gy threshold for "detectable opacities" from protracted exposures but rather point to a dose-effect threshold of under 1 Gy. Thus, given that cataract is the dose-limiting ocular pathology in current eye risk guidelines, revision of the allowable exposure of the human visual system to ionizing radiation should be considered. **Radiat Res. 2007 Feb ;167(2):233-43.**

FANC AFCN

Postoperative cataract cases among atomic bomb survivors: radiation dose response and threshold.

Neriishi K, Nakashima E, Minamoto A, Fujiwara S, Akahoshi M, Mishima HK, Kitaoka T, Shore RE.

Department of Clinical Studies (Hiroshima), Radiation Effects Research Foundation, Japan. Neriishi@rerf.or.jp

Recent evidence argues against a high threshold dose for vision-impairing radiation-induced cataractogenesis. We conducted logistic regression analysis to estimate the dose response and used a likelihood profile procedure to determine the best-fitting threshold model among 3761 A-bomb survivors who underwent medical examinations during 2000-2002 for whom radiation dose estimates were available, including 479 postoperative cataract cases. The analyses indicated a statistically significant dose-response increase in the prevalence of postoperative cataracts [odds ratio (OR), 1.39; 95% confidence interval (CI), 1.24-1.55] at 1 Gy, with no indication of upward curvature in the dose response. The dose response was suggestive when the restricted dose range of 0 to 1 Gy was examined. A nonsignificant dose threshold of 0.1 Gy (95% CI, <0-0.8) was found. The prevalence of postoperative cataracts in A-bomb survivors increased significantly with A-bomb radiation dose.

The estimate (0.1 Gy) and upper bound (0.8 Gy) of the dose threshold for operative cataract prevalence was much lower than the threshold of 2-5 Gy usually assumed by the radiation protection community and was statistically compatible with no threshold at all. (Radiat. Res. 2007 Oct; 168(4): 404-408)

EU Seminar 2006: **Key points agreed** **by Article 31 GoE for transmission to ICRP**

Cataracts

- Current threshold concept and current yearly dose limit for lens are challenged
- ICRP should not postpone:
  - revisiting the relationship between the dose to the lens and the occurrence of cataracts
  - revisiting the protection system (for instance introducing lens dose constraints based on good practice)

In utero exposure: new data

- The (presumed “safe”) first days after conception could be at risk (1-14 d)
- Some individual genetic susceptibility seems to exist
- New unexplored mechanisms discovered
- Numerical values of threshold doses challenged

Ionizing radiation, genetic and embryonic risk: Chernobyl data and new insights
21 April 2006, Brussels, Belgium

Scientific seminar organized by FANC-AFCN, In cooperation with SCK.CEN

GENETIC SUSCEPTIBILITY TO RADIATION EFFECTS IN EARLY EMBRYOS

P. Jacquet, Laboratory of Radiobiology, Belgian Nuclear Research Centre, B-2400 Mol

Various results obtained during recent years have suggested that, like a number of chemicals, ionizing radiation could be potentially teratogenic in a few mouse strains, when administered as early as at the one-cell (or "zygotic") stage. The Japanese and German results also suggested that irradiation of later preimplantation stages could induce similar effects, though to a lesser degree. While the German studies have clearly shown that, in the Heiligenberger strain, a genetic predisposition exists for induction of gastroschisis, this is not necessarily so for the various malformations induced in other mouse strains.
Irradiation of early preimplantation embryos could also induce a genomic instability in the surviving foetuses…Mutations in genes concerned with cell cycle regulation, apoptosis or DNA repair could increase the radiation sensitivity of the embryo.

mechanisms

In these observations, the cause of the congenital malformation is not an increased loss of cells (classic deterministic effect) but rather the persistence of **unrepaired or misrepaired DNA-damaged cells**.

Whole pregnancy: cancer induction

- Embryo and fetus more sensitive
- Cancers appear in first 10 y or later
- No threshold dose!
- Risk dose-related (fatal cancers): LNT
  - 10 mSv (IV. Urogr.) : 1-2/1000
  - 100 mSv (some CT exams): **1-2/100**

EU Seminar 2006: **Key points agreed** by **Article 31 GoE for transmission to ICRP**

Pregnancy :

- the 100 mSv figure: due to the uncertainties and to childhood cancer risk, formulations which could be interpreted as 100 mSv during pregnancy being the « limit of concern » in medical exposures and prolonged exposure situations, would be unacceptable
- There is a real danger of such a 100 mSv figure being considered as a general threshold: ICRP has the responsability to warn against this misinterpretation

New epidemiological data:
Recent low dose studies
(EU Semin. 2006: E. Cardis)

- Nuclear Industry Workers (15-country study): low dose protracted exposures (most ≤ 100 mSv cumulative dose); results **statistically consistent** with A-bomb data (ERR higher! But smoking issue)

- Techa River Cohort (protracted exposures ext/int): results **statistically consistent** with A-bomb data (ERR higher! But dosimetric issues)

DDREF issue

- DDREF: reduction of risk coefficient at low dose and dose rate
- Human epidemiology: max 3-4 (UNSCEAR 2000)
- LSS: quasi-linear dose-response for solid cancers (means DDREF ~ 1)
- **ICRP (current regulation + recommend.): DDREF: 2**
- **BEIR VII (central estimate): DDREF: 1.5** (LSS DDREF) (1.1 - 2.3)

EU Seminar 2006: **Key points agreed** by **Article 31 GoE for transmission to ICRP**

DDREF (DOSE AND DOSE RATE EFFECTIVENESS FACTOR)

- The speakers presented central estimates of DDREF values clearly lower than 2
- From a Radiation Protection point of view, the position of BEIR VII (central value of 1.5) regarding DDREF seems to be more justified than the recommendation envisaged by ICRP.

Large scale indoor radon studies (EU Semin.2006: M.Tirmarche)

- 7 000 cases of lung cancers; 14 000 controls
- **Clear linear** DR relationship between radon in houses and lung cancer risk
- RR = 1.08 for 100 Bq/m3 CI 95% = [1,03 – 1,16]
- *significant relationship even if limited to those exposed to ≤ 200 Bq/m3*
- also a significant increase in the non-smoker population

EU Scientific Seminar 2006: some other important issues discussed

- Age at exposure
  - Children are not young adults!
  - Need to do something more to take this factor into account?
  - Organ dose limits/constraints, where necessary (thyroid, ..) would be an easy way
- Gender
  - Cancer risk women clearly higher v/men (BEIR VII)
  - The use of gender specific Wt is proposed by some, disputed by others
  - The question is whether such a decision should be made by ICRP or by the regulators (societal judgement)

Seminar RIHSS 2008

There are new data available pointing towards the possible induction by radiation of circulatory diseases at much lower doses than currently assumed.

Should we not explicitly take these data into account, particularly in the relatively high dose situations that may occur in medical applications and in prolonged exposures?

Regulatory concerns

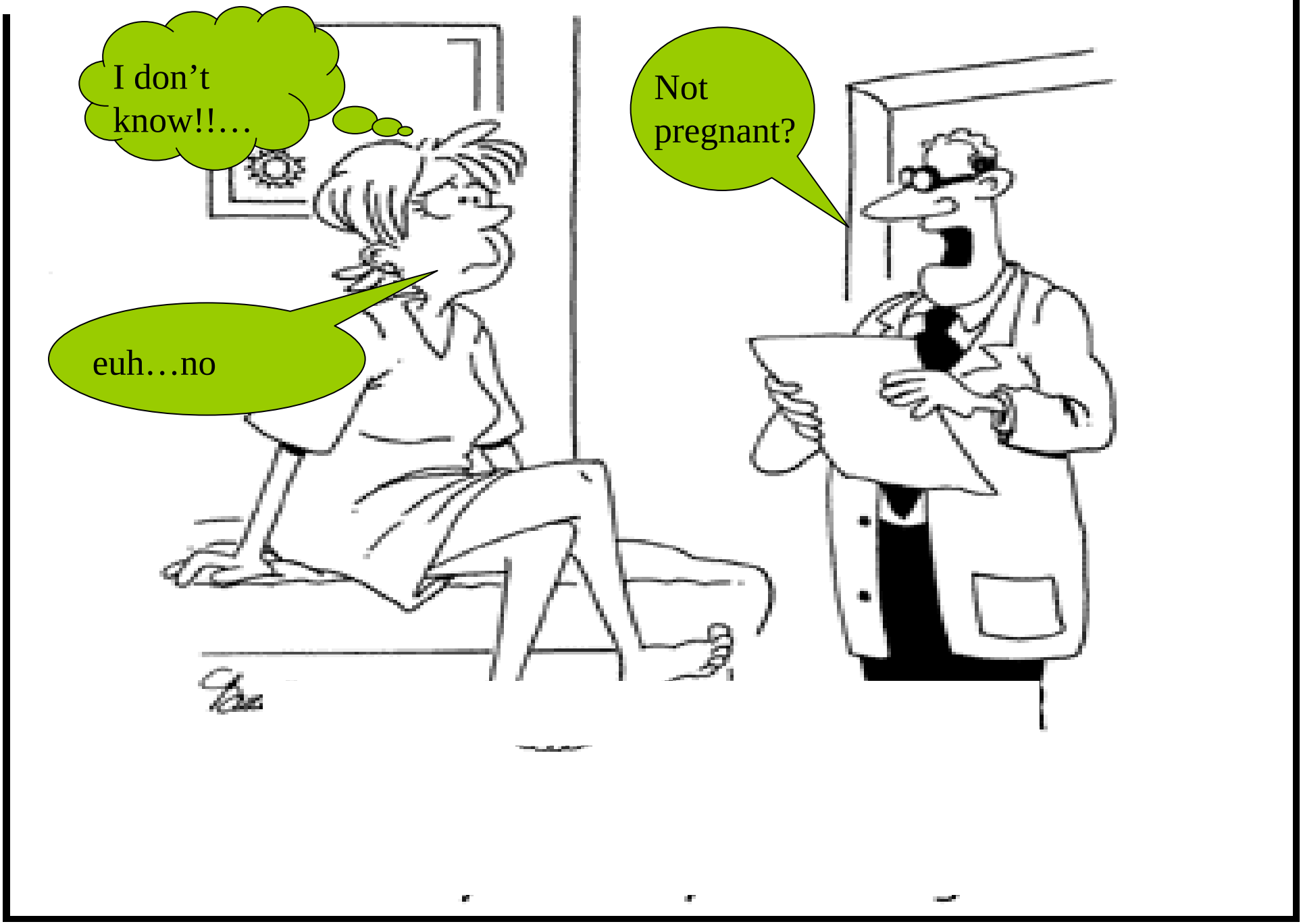
- Recent epidemiological and research results (incl. at SCK.CEN, funded by FANC) call for action
- EU process very long (many years)
- Possible need for initiatives by national regulators: tools exist (dose constraints..)

Regulatory (and medical) concerns

Can we wait with protective measures for the lens of the eye (dose constraints)?

Regulatory (and medical) concerns

- In utero exposure: can we wait for taking into account the new research data on the first days of pregnancy (radiological procedures, internal contaminations)?
- Due to these uncertainties and to the high cancer risk, can we accept the 100 mSv value being regularly presented as the limit of concern in medical exposures and prolonged exposure situations (cfr “seuil médical pratique”) ?


I don’t know!!…
euh…no
Not pregnant?

FANC AFCN
federaal agentschap voor nucleaire controle
agence fédérale de contrôle nucléaire

Veel zwangere vrouwen weten niet dat een onderzoek waarbij X-stralen te pas komen, schadelijk kan zijn voor haar ongeboren kind. Zelfs in het allervroegste stadium kan dit een risico zijn.
Uw arts zal u informeren, maar denk er zelf ook aan. Een gewaarschuwd mens telt immers voor twee!
Voor meer info: **www.fanc.fgov.be/netzwanger.mijdstraling**

Conclusions

- **ALARA culture: to develop urgently!**
- **Motivation of medical doctors**: key!!
  - Training is essential (existence! content! efficiency!)
  - Disastrous consequences of gaps in knowledge, prejudice (resistance to cognitive dissonance) and of quarrels between experts
- Doses in medicine: not low doses, nor low dose rates!!

« Scientific cautiousness »: primum non nocere !

- The « cautiousness » of the scientific world (UNSCEAR...): the main concern is to avoid concluding that a causal relationship exists before it is firmly proven.
- The « cautiousness » expected from national regulators, art 31 GoE, ICRP, …**and medical doctors**: the main concern is to protect health; when there is scientific plausibility of the existence of a risk of serious and irreversible harm (even if there is still uncertainty), the precaution principle must be applied.

- **« Lack of (human health) evidence does not mean evidence of lack of effect »**