



EUROPEAN NETWORK FOR INFECTIOUS DISEASE

REPORT of the THIRD ANNUAL MEETING

May 24 2007, Rome, Italy

GLOSSARY

EUNID	European Network for Infectious Diseases
HIDs	Highly Infectious Diseases
HIUs	High Isolation Units
EU	European Union
PPE	Personal Protective Equipment
HCWs	Health-Care Workers
IT	Information Technology
INMI	Istituto Nazionale per le Malattie Infettive (National Institute for Infectious Diseases)
E-CDC	European Centres for Disease Prevention and Control

SUMMARY

1. The third meeting of EUNID, a European project aiming to create a network of infectious disease experts with expertise in highly infectious diseases, was attended by national officials and national representatives from 11 of the 16 states involved in the project;
2. EUNID participants may view the presentations made at the meeting on www.eunid.com;
3. Among co-opted experts, Dr. Philippe Brouqui from France was present. Moreover, Dr. Philip W. Smith, head of Biocontainment Unit of the University of Nebraska, USA, and Dr. Michael Borg, head of Infectious Diseases Department at St. Luke's Hospital in Malta (partner in the next project, EuroNHID) were present;
4. The EUNID meeting was included in a whole week of events focused on bio-safety, bio-security and management of HIDs: the final meeting of EuroNET-P4 project (an EC co-funded network of P4 laboratories in Europe, coordinated by INMI), and a meeting of the GHSAG-Lab (Global Health Security Action Group – Laboratories) were scheduled in the same week. In the middle of the week we organized an International Workshop on “Critical Aspects of Highly Infectious Diseases”, where all the participants of the three meetings shared their ideas and experiences;
5. The main results of 3rd EUNID meeting included:
 - a final agreement, after a discussion moderated by Dr. Bannister and Dr. Smith, on technical and logistic specifications of HIUs;
 - a final agreement, after a discussion moderated by Dr. Brouqui, on criteria for patient's admission in HIUs;
 - a final agreement, after a discussion moderated by Dr. Brouqui and Dr. Smith, on recommendations for some specific medical procedures to be performed in HIUs. The analyzed procedures have been: endotracheal intubation, bronchoscopy, endoscopy, radio-imaging (CT Scanning and MRI), renal dialysis and post-mortem evaluation;
6. Moreover, a strategy for the accomplishment of a “List of experts” in Europe on isolation and infection control procedures was developed with all the attendants;
7. National officials or their representatives from Belgium, Italy and Spain presented their facilities and national strategies for isolation and management of patients with HIDs;
8. All participants agreed to continue to collaborate and exchange knowledge and experiences, both through the next network co-funded by EU and coordinated by INMI, EuroNHID (European Network for Highly Infectious Diseases), and through personal contacts.

1. BACKGROUND

The European Network of Infectious Disease Physicians (EUNID) is a European project, funded by the European Commission, DG SANCO Public Health through the work programme 2003. EUNID consists of partners from 16 member states (the original 15 EU member states, plus Estonia), who together have broad, multi-disciplinary experience of the management and control of highly infectious diseases. The main aims of EUNID are to enhance and maintain co-operation, communication, and exchange of information on highly infectious diseases among infectious disease clinicians, in order to enhance preparedness and response within Europe to health threats from HIDs, whether naturally occurring, newly emergent, or deliberately released. The project started in mid 2004; this was the third and final meeting of national officials and/or their representatives. EUNID members may review the meeting presentations on the EUNID website (www.eunid.com).

Dr. Vincenzo Puro, INMI “Lazzaro Spallanzani”, scientific coordinator of the project, opened the meeting and welcomed the participants. Dr F. M. Fusco, INMI “Lazzaro Spallanzani”, Rome, EUNID project coordinator, gave a presentation on the current stage of the project and the expectations of the meeting. He reviewed rapidly the results already accomplished, and spent more time on the planned agenda of the meeting: the expected results of the day included:

- the final agreement on the definition of technical and logistic specifications and personnel requirements for HIUs/referral centres in Europe;
- the final agreement on recommendations/expert’s opinions for the management of HIDs, including criteria for patient’s admission in a HIU/referral centre and specific medical procedures (procedures analysed: Intensive Care, bronchoscopy, gastroscopy, imaging exams - CT scan and RMI, Chest X rays and Ultrasound -, renal dialysis and post-mortem examinations);
- the final agreement on the strategy to be applied to accomplish a list of physicians with expertise in infection control and management of patients with suspected/probable/confirmed HIDs, including isolation, in European countries.

2. PARTICIPANTS

Participants from infectious disease units, national institutions, and/or public health authorities in Belgium, Denmark, Estonia, Germany, Ireland, Italy, Luxembourg, Spain, Sweden, the United Kingdom were present at the 3rd EUNID meeting; national officials and/or their representatives from Austria, Finland, Greece, the Netherlands, and Portugal were not able to attend. Prof. Philip

W. Smith, from Nebraska University, USA, Dr. Michael Borg, from St. Luke's Hospital, Malta, and Dr. Enrico Girardi, from INMI, Italy, were present, too. See appendix 1 for further details

3. XDR-TUBERCULOSIS IN EUROPE: EPIDEMIOLOGICAL ASPECTS

(Dr. Enrico Girardi, INMI, Italy)

Dr. Enrico Girardi gave a presentation about emerging aspects of Extensively-Drug-Resistant Tuberculosis (XDR-TB). He preliminary gave an overview of changes in TBC epidemiology in the last years, with special focus on the emergence of Multi-Drug-Resistant (MDR) strains of *Mycobacterium tuberculosis*, and on recent recognition of XDR-TB as a separate entity.

Subsequently, he showed the results of 2 studies in which he participated.

The first one, recently published on Emerging Infectious Diseases (Migliori GB, Ortmann J, Girardi E et al. Extensively Drug-resistant Tuberculosis, Italy and Germany. *Emerg Infect Dis* [serial on the Internet]. 2007 May [date cited]. Available from <http://www.cdc.gov/EID/content/13/5/780.htm>), reviewed the clinical records in 6 referral centres for tuberculosis (3 in Italy and 3 in Germany), and tested drug susceptibility of all the strains for first- and second-line anti-TB drugs. In this study, 4.4% resulted MDR strains, and 0.4% resulted XDR strains. The main findings of the study are:

- XDR-TB causes an higher risk of death than MDR-TB (Relative Risk 5.5 - 95% CI 2.04-16.04; $P < 0.01$);
- XDR-TB causes longer hospital admission and infectiousness.

The second study (Migliori GB, Besozzi G, Girardi E et al. Clinical and operational value of the XDR-TB definition. *Eur Respir J*. 2007 Aug 9) analyzed data from all culture confirmed TB cases diagnosed consecutively by the 9 TB clinical reference centres in Italy, Germany, Estonia and Russia. The final outcome of 3 groups of patients (patients with XDR-TB, “complicated” MDR - resistant to all 1st-line drugs -, “other” MDR - susceptible to at least one 1st-line drug -) is compared. This study evidenced that the XDR-TB clinical outcome is worse than “complicated” and “other” MDR (there is a “continuum” of severity).

After the presentation the participants discussed about the opportunity to include XDR-TB among HIDs. MDR-TB was included in the original list of HIDs discussed in 2005, during the first meeting. Members from Germany said that, in their opinion, and according to German national guidelines, TB is not “highly infectious”, because is not easily transmissible from person to person. Dr. Girardi, Dr. Puro and Dr. Brouqui said that it is true for not-MDR or XDR strains. In the case of MDR- or XDR-TB the poor efficacy of therapy causes longer period of sputum positivity, and

consequently an increased infectiousness. Although the knowledge about MDR- and XDR-TB transmissibility is currently poor, we can not exclude that it is higher than not-MDR- and not-XDR-TB strains. Finally, all the participants agreed to include in the list XDR-TB.

4. ADMINISTRATIVE TOPICS

(Mrs. Ramona Iacovino, Project Secretary)

Mrs. Iacovino, project secretary, gave a brief explanation on some administrative topics. She explained the correct way to fill in the time sheet, and underlined the necessity to send it to her at INMI before the end of the project. Some partners required further details, and Mrs. Iacovino answered to all questions.

5. INVENTORY OF ISOLATION FACILITIES IN EUROPE: SITUATION IN SPAIN

(Dr. Sarah Lafuente, Hospital Clinic, University of Barcelona, Spain)

Dr. Sarah Lafuente, Hospital Clinic, University of Barcelona, gave 2 brief presentation. The first one briefly showed the situation of HIUs in Spain: the current number of HIU o High Isolation Room (single hospital room with at least anteroom and negative pressure) is unknown. There are some hospital, in Madrid and Barcelona, designated as “referral centres” for suspected cases of HIDs. Two Special High Security Labs (BSL4) are present in Madrid and Barcelona, but only for veterinary purposes. The Centro Nacional de Microbiologia in Majadahonda is designated as Special human pathogens Lab, but it is not a BSL4 facility.

The second presentation was focused on the Hospital Clinic, University of Barcelona. It is one of the “referral centre” for HIDs, and it a reference centre for influenza and tropical diseases, too. This hospital has diagnostic and management protocols for HID, also at the Emergency Ward, and has an Infection Control Team trained in HID. The hospital is equipped with 4 single isolation rooms, with negative pressure but without anteroom

6. DEFINITION OF TECHNICAL AND LOGISTIC SPECIFICATIONS AND PERSONNEL REQUIREMENTS FOR HIUS/REFERRAL CENTRES IN EUROPE

(Dr. Barbara Bannister, Royal Free Hospital, London, UK and the Coordination Team)

The Coordination Team planned a session for the achievement of the definitive agreement on a deliverable already discussed in London, during the second EUNID meeting: “Definition of

technical and logistic specifications and personnel requirements for HIUs/referral centres in Europe”. The session is conducted by Dr. Barbara Bannister, Royal Free Hospital, London, UK, and by Dr. Vincenzo Puro and Dr. Francesco M. Fusco. Coordination Team prepared a step-by-step working document that include all the items to be discussed, including agreement already reached in London and some proposal and suggestions for the open points. The points discussed were: definition of HIU, diseases that should be handled, logistic issues (including number, location and use - sporadic vs. day-by-day -), characteristic of personnel including external consultant, hotel service and security, management of not medical procedures (including transport of patients, transport of samples, diagnostic services, waste management and environmental disinfection), and technical requirements in the patient’s room and in the building.

Each points has been extensively discussed, and a final agreement has been reached for all points. In some cases the accomplishment of consensus has been difficult than other cases. There was a considerable debate on the diseases that should be handled in the HIUs: partners from Luxembourg and Ireland suggested to not include H5N1 influenza strain, because not transmissible from person-to-person, while other partners agreed with the inclusion, because suggested by WHO and CDC in order to reduce the risk of recombination with seasonal influenza human virus. Finally, the group decided to modify the proposed statement containing H5N1 to “each emerging, highly human pathogen influenza strain”. The group also agreed to include in the list each unknown, human highly pathogen agent causing epidemic events. Another point strongly discussed was the use of HIU. Some partner proposed to use it routinely, while some other preferred to use it only when a real need emerge (with appropriate maintenance procedures). Finally the group decided to state that HIU should be used sporadically or routinely (for patients’ care or for training) but in both case procedures should be in place in order to make it completely operative within few hours.

7. PRESENTATION BY SOME PARTNERS ABOUT THEIR INTERNAL PROCEDURES FOR THE MANAGEMENT OF HIDS

- a) Italy (Dr. Simone Lanini, INMI, Rome, Italy): Dr. Simone Lanini presented some examples taken from the manual of internal procedures currently in use at INMI for the management of HIDS. This manual, known as “Libro Giallo” (Yellow Book), include the internal procedures for the hospital management of anthrax, botulism, plague, smallpox, Viral Haemorrhagic Fevers, tularaemia, SARS and Avian Flu. For each diseases, in the book are described: generality (including etiology, pathology, public health issue, epidemiology and clinical features), case management (including case identification, case definition, clinical

diagnosis, laboratory diagnosis, sample collection and handling, treatment), infection control measures (including isolation measures, PPE, environmental disinfection, human remains handling) and contact/HCW management (including contact case definition, surveillance, post exposure prophylaxis). For each point, Dr. Lanini gave a brief example. Finally, he presented some operative flow-charts illustrating the complete clinical management, currently in use at INMI.

- b) Belgium (Dr. Renaat Peleman, University Hospital of Gent, Belgium): Dr. Renaat Peleman presented the pandemic influenza preparedness plan developed in his hospital. He showed the adopted case definition for suspected/probable/confirmed cases, and showed some flow-chart for severity assessment and hospital admission of the cases, such procedures are different on the basis of the number of patients (more or less than 3). Finally, he shared with participants some infection control procedures applied in the University Hospital of Gent, including isolation precautions, PPE, patient care equipment, patient transport, environmental cleaning and disinfection, waste disposal and disposal of laundry and dishes, and specimen handling.
- c) USA (Dr. Philip W. Smith, University of Nebraska, USA): Dr. Smith, head of Bio-Containment Patient Care Unit at University of Nebraska Medical Center, gave an brief overview of the procedures used in his institution, giving some examples. He said that about 65 unit specific written policies/procedures and 11 practice guidelines are used, in addition to Federal and State Regulations, laboratory standards, infection control and hospital standards. He gave some example on the selection and use of PPE, presenting the procedure for the donning of Biological Protective Gown and PAPR (Powered Air Purifying Respirator). Finally he just listed the medical care procedures in use.

8. DEFINITION OF SAFE PROCEDURES INSIDE HIGH ISOLATION UNITS, INCLUDING CRITERIA FOR PATIENT'S ADMISSION AND SAME SPECIFIC MEDICAL PROCEDURES

(Dr. Philippe Brouqui, BSL3 Unit, AP-HM, Marseille, France)

Dr. Brouqui, head of BSL3 Clinical Ward at the Public Health University Hospital in Marseille, conducted this session. Initially he gave a presentation about his Unit in Marseille. In this presentation he showed the structure of French for HIDs, the procedures for the admission Emergency Department attached to BSL3 Clinical Ward. He gave details about transportation of patients from their house to isolation ward. About it, he showed a 15-minutes video illustrating a

simulation of patient's transportation, with the aim to show all the applied infection control procedures. In the second part of the presentation, Dr. Brouqui showed diagnostic and patient care facilities available in his unit. He pointed up diagnostic capabilities inside the Unit, showed the Unit's structure, with 8 isolation beds available, and finally gave some example about patient's care facilities, including Intensive Care, Radio Imaging, Paediatric equipments, and bronchoscopy and gastroscopy.

After this presentation, Dr. Brouqui presented the results of his work on guidelines for specific medical procedures to be performed in HIUs. He selected some procedures considered of interest by himself and/or by the other members of EUNID project, as emerged by discussion made during first and second EUNID meeting, and he completely revised the available literature for each HID. Finally, he developed a draft, containing guidelines/recommendations for patient's admission and for the specific medical procedures. Procedures selected included intensive care procedures, bronchoscopy, gastroscopy, imaging exams - CT scan and RMI, Chest X rays and Ultrasound -, renal dialysis, delivery/pregnancy and post-mortem examination. Guidelines proposed by Dr. Brouqui were discussed point by point for many hours. Some common agreement have been reached: first of all, because of lack of evidence due to the limited number of patients with HIDs decrypted in the scientific literature, it was decided to not consider the final results as guidelines, but as recommendations and/or expert's opinions. The reaching of the agreements for each point has been very difficult. Indeed, because of the scarcity of data, evidence-based recommendations are impossible to develop, and consequently these can be based on personal experiences and expert's opinions, that not always are convergent. When a final consensus has no been reached on some points, EUNID members decided to include in the final document the different opinions.

The main themes of discussion were:

- Endotracheal Intubation: all participants agreed that mechanical ventilation should be reserved to patient who failed NIV or who are contraindicated, the duration of the procedures should be reduced to a minimum, it should be performed by skilled persons, and meticulous infection control measures are mandatory, including the use of negative pressure room and appropriate PPE. There is a general consensus also about the necessity of a sedation in order to reduce cough. Not complete agreement there was about the opportunity to include Intensive Care capabilities in the design of HIUs, because some partners believe that rooms in existing Intensive Care ward, if equipped with negative pressure, are adequate.
- Bronchoscopy, Gastroscopy, Endoscopy: a general agreement has been reached about some statements. It is necessary to avoid unnecessary procedures, to wear appropriate PPE (higher

protection than usual is advisable for aerosol-producing procedures), to perform these procedures in an air controlled environment and by an expert operator. Some participants, including Dr. Ippolito, Dr. Puro and Dr. Sheehan, believe that for each procedure a clear protocol should exist, showing the added value of that procedure in the diagnostic process. The balance between risk for HCWs and benefits for the patient should be guided from the evidence, if any. Dr. Brodt and other participants disagree with this point, because in their opinion it is impossible to predict what is the added value of a diagnostic procedure before to do it.

- Radio Imaging: according to all Chest X ray and ultrasonography in patient with HIDs should be carried out at bedside in isolation rooms. Because CT scan or RMI is sometime mandatory for patient survival (CT scan should be always preferred) we should be prepared to reconfigure the radiology department in low and high risk area, to reprogramming examination, and to identify specific way and procedures for patient transportation. Training the radiology staff to infection control measures is strongly recommended.
- Renal dialysis: the group agreed that patients with HIDs who require dialysis should be hospitalized in HID unit and treated at bedside with either PD or haemodialysis, and that a particular attention should be carried out to infection control of dialysate effluents and decontamination of the machines. There was a little disagreement between Dr. Ippolito, who preferred peritoneal dialysis in these patients, and Dr. Brodt, who believed that parenteral dialysis is possible also in patients with HIDs.
- Post-mortem examination: according to all, post mortem examinations should be limited as more as possible. If necessary, post mortem biopsies are preferable to complete autopsy. these procedures should be performed in a BSL3 area or equivalent with adequate PPE. All the group agreed that autopsy should be done only in patients died without a diagnosis.
- Delivery/pregnancy: all the group noticed that the evidence are not existing and also the experiences are very few on this point. Dr. Brodt said that a caesarean delivery may be suggested, but according to Dr. Puro and the remaining participants, the group can't give this recommendation without any evidence.

About the criteria for patient's admission, Dr. Brouqui presented few slides showing his proposal. He pointed out some general situations that require patient's admission in a HIU, such as the provenience from an area where an outbreak of a HIDs is ongoing. Participants suggested other situations and criteria, for example Dr. Brodt suggested that all the hardly sick workers who are exposed to animals that are potential reservoir of HIDs should be admitted. Dr. Brouqui also

presented a list including 48 agents, proposing for each of them the class of risk, the proposed level of isolation in health care, and the level of evidence to justify it. All the group agreed to check carefully the list and to communicate proposal, changes and comments to coordination team.

9. DEFINITION OF A LIST OF EXPERTS

(Dr. Francesco M. Fusco, INMI, Rome, Italy)

Dr. Fusco gave a presentation about another project deliverable, the definition of a list of physicians with expertise in infection control and management of HIDs including isolation in EUNID countries. He proposed to all participants to select some physicians in their own country on the basis of the EUNID approved core-curriculum. Furthermore, Dr. Fusco proposed to look for a link with E-CDC in order to include the EUNID list in the E-CDC expert list, as scientific advisers in the field of infection control and isolation and management of HIDs. All the participant agreed with this point.

APPENDIX 1 – LIST OF PARTICIPANTS

3rd EUNID MEETING Rome, MAY 24, 2007 National Institute for Infectious Diseases "L. Spallanzani"			
LIST OF PARTICIPANTS			
Coordination Team			
Giuseppe Ippolito	INMI "L. Spallanzani"	Italy	ippolito@inmi.it
Vincenzo Puro	INMI "L. Spallanzani"	Italy	puro@inmi.it
Francesco M. Fusco	INMI "L. Spallanzani"	Italy	fusco@inmi.it; eunid.coordinator.it
Simone Lanini	INMI "L. Spallanzani"	Italy	lanini@inmi.it
Fabio Soldani	INMI "L. Spallanzani"	Italy	soldani@inmi.it
Carla Nisii	INMI "L. Spallanzani"	Italy	nisii@inmi.it

Ramona Iacovino	INMI "L. Spallanzani"	Italy	eunid.secretary@inmi.it
Partners and Experts			
Name	INSTITUTE	COUNTRY	EMAIL ADDRESS
Bannister Barbara	Royal Free Hospital	United Kingdom	Barbara.Bannister@royalfree.nhs.uk
Brodth Hans-Reinhard	Johann Wolfgang Goethe Institut	Germany	reinhard@brodt.net
Brouqui Philippe	BSL3 Unit, AP-HM, Marseille	France	philippe.brouqui@medecine.univ-mrs.fr
Follin Per	Swedish Institute for Infectious Disease Control	Sweden	per.follin@imk.liu.se, per.follin@smi.ki.se, per.follin@lio.se
Gjorup Ida	Rigshospitalet	Denmark	schioedt@rh.dk; dorte.schioedt@rh.hosp.dk
Gottschalk René	Gesundheitsamt Stadt Frankfurt	Germany	rene.gottschalk@stadt-frankfurt.de
Hannan Margareth	Mater Misericordiae Hospital	Ireland	
Hemmer Robert	University Medical Center	Luxembourg	hemmer.robert@chl.lu
Jarhall Boo	Swedish Institute for Infectious Disease Control	Sweden	Boo.Jarhall@lio.se
Kutsar Kuulo	West Tallinn Central Hospital	Estonia	kuulo.kutsar@tervisekaitse.ee
Lafuente Sara	Universitat de Barcelona	Spain	SLAFUENT@clinic.ub.es
Peleman Renaat	University Hospital Gent	Belgium	renaat.peleman@ugent.be
Perronne Christian	Hopital Raymond Poincare	France	c.perronne@rpc.ap-hop-paris.fr, c.perronne@rpc.aphp.fr
Sheehan Gerard	Mater Misericordiae Hospital	Ireland	gsheehan@iol.ie
Skinhoj Peter	Rigshospitalet	Denmark	schioedt@rh.dk; dorte.schioedt@rh.regionh.dk
External Guests			
Smith Philip W	Nebraska Medical Center	USA	pwsmith@unmc.edu

Borg Michael	St. Luke's Hospital	Malta	michael.a.borg@gov.mt
Enrico Girardi	INMI "L. Spallanzani"	Italy	girardi@inmi.it

This report was produced by a contractor for Health & Consumer Protection Directorate General and represents the views of the contractor or author. These views have not been adopted or in any way approved by the Commission and do not necessarily represent the view of the Commission or the Directorate General for Health and Consumer Protection. The European Commission does not guarantee the accuracy of the data included in this study, nor does it accept responsibility for any use made thereof.