THE EUROPEAN DIRECTORATE FOR THE QUALITY OF MEDICINES & HEALTHCARE (EDQM)
Tissue donation from deceased donors during COVID19 pandemic

Webinar
Agenda

15:00-15:05 Opening Remarks & Introduction, Susanne Keitel, Director EDQM, and Laurent Mallet, Head of Department of Biological Standardisation, OMCL Network & HealthCare (DBO)

15:05-15:15 Introduction by the Chairs

15:15-16:05 Experiences from tissue establishments in different countries
   15:15-15:25 Eliana Porta, Centro Nazionale Trapianti, Italy
   15:25-15:35 Isabelle Martinache, Agence de la Biomédecine, France
   15:35-15:45 Ralf Reinhard Tönjes, Paul Ehrlich Institute, and Martin Börgel, Deutsche Gesellschaft für Gewebetransplantation, Germany
   15:45-15:55 Jorge Gayoso, Organización Nacional de Trasplantes, and Anna Vilarrodona, Banc de Sang i Teixits, Spain
   15:55-16:05 Kyle Bennett, National Health Services Blood and Transplant, United Kingdom

16:05-16:30 Questions & Answers

16:30-16:45 Risk of transmission through tissues from deceased donors and testing practices, Dragoslav Domanovic, European Centre for Disease Prevention and Control (ECDC)

16:45-17:20 Open Discussion

17:20-17:30 Conclusions & Closing Remarks
Welcome Address

Dr Susanne Keitel
Director of the EDQM, Council of Europe
Number of registrants by country
Welcome Address

Dr Laurent Mallet
Head of Department of Biological Standardisation, OMCL Network & HealthCare,
EDQM, Council of Europe
Tissue donation from deceased donors during COVID19 pandemic Webinar
Akila CHANDRASEKAR

Co-Chair European Committee on Organ Transplantation
Co-Chair Guide to the Quality and Safety of Tissues and Cells

JPAC Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee
Introduction

• Substance of Human Origin (SoHO) : Blood, Organs, Tissues or Cells:
  • Many years of clinical use
  • There is always concern about risk of infection transmission (TTI) and consequences to the recipients

• Tissue Establishments strive to make them as safe as possible
  • Donor selection
  • Testing (for known TTI)
  • Processing (including sterilisation) & Storage
  • Monitoring

• Unknown Infections: New Infection or New Territory (geographical spread)
New or Emerging Infections

• **Monitor: Horizon Scanning – National & International**
  - World Health Organization (WHO)
  - Centers for Disease Control and Prevention (CDC)
  - European Centre for Disease Control (ECDC)
  - EU Rapid Alert System: Eurosurveillance
  - European Infectious Diseases (EID) Monitor group of the European Blood Alliance (EBA)
  - Public Health Authorities
  - Competent Authorities Alerts

- **Examples:**
  - SARS: (2002-2003), H1N1: (2009-2010),

- **Actions**
  - Exclude donors with travel history/symptoms,
  - Exclude contacts
  - Pandemic plan
SARS CoV 2 Outbreak - What is different?

New Strain Corona virus - SARS Cov 2 (virus) – COVID 19 ( infection)

- **Timeline**:
  - ? Nov/ Dec 2019 : first reported in China
  - January 2020 : first Report in Europe
  - Feb- March 2020 : Europe epicentre (with cases in China declining)
  - 11th March 2020 : WHO declared pandemic- Global spread

- **Challenges to tissue establishments**:
  - Rapid spread overwhelming healthcare system in Europe
  - Pressure on intensive care beds, cancellation on planned surgical procedures
  - Social distancing/lock down
  - ? Challenges in donor selection with community spread/ testing

- **Guidance & Support**
  - Local : NHSBT Position statement/Risk Assessment
  - National : JPAC (UK)
  - European : ECDC
  - International ( Scientific Associations)
Jacinto SÁNCHEZ

Co-Chair Guide to the Quality and Safety of Tissues and Cells
President European Association of Tissue and Cell Banks
SARS CoV 2 Outbreak - Scientific Associations

COVID-19 Update

COVID-19 AND BLOOD ESTABLISHMENTS

GLOBAL ALLIANCE

COVID-19 and BMT

EBMT
European Society for Blood and Marrow Transplantation

ALERT UP-DATE: Coronavirus (COVID-2019) and Ocular Tissue Donation.

ESHRE COVID-19 working group

In view of the rapidly growing number of reports and the impact of the COVID-19 coronavirus on public health, ESHRE has formed a specialist working group to keep track of bibliography and published scientific reports relevant to reproductive medicine, pregnancy and newborns.
SARS CoV 2 Outbreak- Challenges to tissue establishments

• **Donor evaluation / Safety of Recipients:**
  - No known transmission from donor to recipient through Transfusion or Transplant
  - Period of viraemia – not known
  - Immunosuppressed recipients: and increased risk?

• **Safety of staff in TE and procurement team:**
  - Transmission through respiratory droplets, contact, faecal/oral route, ? Aerosol
  - Staff absence/availability – particularly small tissue establishments

• **Sufficiency:**
  - Several unknowns – asymptomatic infection in donors
  - Is testing required/ what test/when to test
  - Decline in demand for planned procedures

• It is highly likely experiences in tissue establishments vary- and the purpose of this webinar is to learn from each other
Speakers

• Eliana Porta : Italy
• Isabelle Martinache : France
• Ralf Reinhard Tönjes, Martin Börgel : Germany
• Jorge Gayoso, Anna Vilarrodona : Spain
• Kyle Bennett : United Kingdom

• Dragoslav Domanovic : European Centre for Disease Prevention and Control (ECDC)
ITALY

Eliana PORTA
Impact of COVID-19 on healthcare activity in general and on tissue donation activity in particular

On April 24th: 192,994 total cases, 25,969 deaths on a population of 60,431,283

-23.5% organ donors compared to the same period of 2019 (Feb 27th - Apr 16th)

- We observed a significantly lower opposition rate.
- No relevant decrease in the number of donors for skin, heart valves, vessels and musculoskeletal tissue compared with the first quarter of 2019 but a reduction in March 2020 is expected, the same way as it happened with corneas (50% of corneas retrieved compared to 2019).
- Such a decrease is expected to continue for as long as the emergency goes on.
- A relevant reduction of living donations has been observed.

General situation in the country

Overload of the Intensive Care Units

Re-organisation of many departments to face the epidemic

Overload of the Intensive Care Units
Situation of tissue donation from deceased donors

In addition to the usual selection criteria, since March 3rd:

- **Deceased tissue donor**
  - Oropharyngeal or nasopharyngeal swab taken within 24 hours from donor death on all donors notified in all Italian regions.
  - The test results must be available before the tissues are released
  - If positive, donor must be deferred.

As of April 22nd: 9 actual donors were found positive.
There are no specific recommendations at national level.

- Usual procedures (protective clothing, procurement techniques) are considered adequate to face the risk of contamination of the staff; even if some initial concern had been expressed.

- Many tissue establishments performed some training on PPE and the measures aimed at reducing the transmission of the disease to the personnel involved in procurement activities.
There are no specific recommendations at national level.

Taking into account:

- Decontaminating procedures put in place during transportation and processing;
- The low probability to find the virus in the retrieved tissues;
- The unlikely occurrence of aerosols/droplets during processing;
- Clothing that is required during processing (for all tissues, except for corneas, a GMP class A environment with a class B background is required – for corneas, clothing requirements include a surgical mask, goggles, double gloves, long-sleeved water-resistant gown).
Availability of personnel in tissue establishments

- No specific measures for tissue establishment personnel have been introduced.

- In Italy, tissue establishments are inside public hospitals and all countermeasures aimed at reducing the transmission of the disease are applied to anyone entering healthcare facilities.

- Administrative staff from tissue establishments are working from home, if possible.

- For people working in the laboratories, rules on correct clothing and distancing (as recommended nationally following ECDC indications) are respected.

- Tissue establishments with high activity and high number of personnel are evaluating a reorganisation of the activities, introducing working shifts.

- The risk of a reduction in the availability of the personnel due to COVID is real, but at the moment the number of personnel in tissue establishments guarantees the continuity of the activity.
Clinical application of tissues from deceased donors

- There has been a decrease in the demand of corneas, because of the provision given nationally to postpone all non-urgent surgical operations.
  
  (March 2020: 33% less of cornea transplantations than on March 2019, but 80% less in the last two weeks).

- CNT has recommended that hospitals capable of doing so maintain their cornea transplant programmes.

- For all other tissues, a less relevant reduction in transplantation activity has been observed and no difficulties in transportation have been reported.
Provisions to control tissue availability

- No specific provisions for tissue availability were made:
  - Tissue procurement is going on with no significant reduction.
  - There is no reduction in the stocks, for all tissues that can be stored for long.
  - The decrease in the procurement of corneas causes some concern, as far as the post-epidemic phase is concerned, and CNT together with the Eye Banks and the regional centres is defining measures to limit the problem.
  - At the moment, there is a surplus of corneas that is being managed at CNT level.
  - A good network is in place to face an emergency in skin demand or the request of ‘rare’ tissues (heart valves with unusual size).
FRANCE

Isabelle MARTINACHE
General situation in the country

COVID 19 situation

66 987 244 Inhabitants
120 804 Cases
21856 Deaths

Situation 24/04/2020

European Centre for Disease Prevention and Control
An agency of the European Union

Tissue donation activity

Between 16/03/2020 and 23/04/2020

<table>
<thead>
<tr>
<th>Deceased donors</th>
<th>Bones</th>
<th>Skin</th>
<th>Vessels</th>
<th>Valves</th>
<th>Cornea</th>
</tr>
</thead>
<tbody>
<tr>
<td>O&amp;T</td>
<td>48</td>
<td>4</td>
<td>5</td>
<td>26</td>
<td>13</td>
</tr>
<tr>
<td>T</td>
<td>22</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>total</td>
<td>70</td>
<td>4</td>
<td>6</td>
<td>26</td>
<td>13</td>
</tr>
</tbody>
</table>

Source : CRISTAL database
Situation as regards tissue donation from deceased donors

Donor evaluation: investigation & questionnaire update

• Absence of symptoms suggestive of SARS-CoV-2 infection < 28 days.
  • Influenza Syndrome (headache, arthralgia and fever)
  • Respiratory infection (fever, cough, shortness of breath)
  • Digestive symptoms (vomiting, diarrhea, loss of taste or smell)
  • Eye symptoms (conjunctivitis)

• Absence for contact with a person at COVID risks < 28 days

Donor testing update

• Systematic COVID testing on OTC donors
  • SARS-CoV-2 by nose/throat swab are accepted with a negative nucleic acid testing (NAT) result.
Precautionary measures for tissue procurement

COVID Neg donor: Standard protocols & protective clothing

- Cleaning of working surfaces, appropriate and effective disinfectant, scrubbing as for surgery, procurement under aseptic conditions
- Sterile gown, sterile gloves, protective mask

If unknown: Complementary recommendations

- Waterproof overshirt + single-use plastic apron.
- Single-use FFP2 mask
- Protective glasses.
- Compliance with the undressing procedure.
- Particular attention to hand hygiene each time gloves are removed /at the end of the handling.
Precautionary measures for tissue processing

Living donors
- Nasopharyngeal tests vs donor risk assessment interview and quarantine only: 
  ➔ under evaluation

Organ donors
- Systematic nasopharyngeal tests results before procurement: COVID – donors only

Deceased Tissue donors
- Systematic nasopharyngeal tests
- At the time of procurement and as close to death as possible within 24
- Under storage and transport conditions validated
- Results: 
  ➔ If negative before procurement: ok
  ➔ If positive: no procurement
  ➔ If ongoing: procurement and quarantine awaiting results prior to processing

Processing tissues COVID neg under usual conditions
## Availability of personnel in tissue establishments

<table>
<thead>
<tr>
<th>Problems</th>
<th>Social distancing</th>
<th>Contingency planning in case of infected personnel</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cessation of activity</strong> (monotissue bank) technical unemployment</td>
<td>In line with recommendation &amp; adapted to the size of the team and the premises</td>
<td>Quarantine of 14 days after recovery in accordance with medical prescription</td>
</tr>
<tr>
<td><strong>Reduced activity &amp; staff</strong> in line with containment recommendation promoting homeworking &amp; with due respect of emergency needs:</td>
<td>- mask mandatory in the presence of other persons - separation of office workstations, - hydroalcoholic gels available - wearing of gloves, - 1m physical distance, - disinfection of containers coming from outside, - regular decontamination of workstations.</td>
<td>If infected personnel, request for testing of all personnel who have been in contact. If staff suspected of infection but not tested, quarantine for a minimum of 14 days and adjust according to symptomatology.</td>
</tr>
<tr>
<td>- Half team</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Binomes (responsible/technician)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partial activity</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Current status

Routine and non-emergency transplantations postponed

- Postponement of all functional transplants (corneas, cancellous bone) since the 16th of March 2020
- Following National recommendations
- New schedule and transplant programs being defined

Emergency maintained on a case-by-case basis

- Corneas for perforation: 5-6 per week.
- Distributions of skin, vessels, heart valves and amniotic membranes have been recorded.
Provisions to control tissue availability

Monthly national inventory (tissue from deceased donor) 16 TE/21

- Very low cornea stocks ⇔ emergency stock (<1 to 3-4 corneas in organoculture/TE + a larger one at -40°C
- Other tissues : low number of entries ⇔ low number of exits

<table>
<thead>
<tr>
<th>Tissues osteoligamentaires</th>
<th>DROIT</th>
<th>GAUCHE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femur</td>
<td></td>
<td></td>
</tr>
<tr>
<td>entier</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>diaphyse</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>épiphyse supérieure</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td>épiphyse inférieure</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>rotule</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Tibia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>entier</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>diaphyse</td>
<td>1</td>
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<tr>
<td>épiphyse sup</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>épiphyse inf</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Numéreus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>entier</td>
<td>16</td>
<td>8</td>
</tr>
<tr>
<td>épiphyse inf</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Carpe</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DROIT GAUCHE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peau cm²</td>
<td>337681</td>
<td></td>
</tr>
<tr>
<td>Valves cardiaques</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pulmonaire ≤ 17 mm</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>pulmonaire 18-24 mm</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>pulmonaire ≥ 25 mm</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>aortique</td>
<td>180</td>
<td></td>
</tr>
<tr>
<td>Valiseaux</td>
<td></td>
<td></td>
</tr>
<tr>
<td>carrefour (bifurcation aorto bi iliaque)</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>artère femorale (axe ilio-femoro-poplite)</td>
<td>145</td>
<td></td>
</tr>
<tr>
<td>artère thoracique</td>
<td>81</td>
<td></td>
</tr>
<tr>
<td>veine</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>-------</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>Vaisseaux</td>
<td></td>
<td></td>
</tr>
<tr>
<td>artere thoracique</td>
<td>81</td>
<td></td>
</tr>
</tbody>
</table>
Thank you for your attention
How safe are tissue preparations in the context of SARS-CoV-2?

- A transmission of respiratory viruses by transplantation of human tissues has not been described yet.

- As there is currently no evidence that SARS-CoV-2 can be transmitted through the transplantation of tissue preparations, the PEI proposes the following precautionary measures:

  1. Exclusion of potential tissue donors upon contact with people with confirmed SARS-CoV-2 infection within 14 days before the donation.

  2. Exclusion of potential tissue donors with confirmed SARS-CoV-2 infection within 14 days after completion of the recovery.

- Tissue preparations that undergo a validated pathogen reduction process for enveloped viruses are not affected by these precautionary risk-minimizing measures.

Source: https://www.pei.de/EN/newsroom/dossier/coronavirus/coronavirus-node.html
General situation in the country (2)

<table>
<thead>
<tr>
<th>Confirmed cases</th>
<th>Deaths</th>
<th>Deaths (%)</th>
<th>Recovered</th>
</tr>
</thead>
<tbody>
<tr>
<td>148,046 (+2,352*)</td>
<td>5,094 (+215*)</td>
<td>3.4%</td>
<td>ca. 103,300**</td>
</tr>
</tbody>
</table>

Summary (as of 23/04/2020, 12:00 AM)
- In total, 148,046 COVID-19 cases and 5,094 deaths due to COVID-19 have been electronically reported to the Robert Koch Institute in Germany.
- The incidence (cases per 100,000) of COVID-19 is highest in Bavaria (301), Baden-Wuerttemberg (266), Saarland (242) and Hamburg (233).
- Most cases (67%) are between 15 and 59 years old; men (48%) and women (52%) are almost equally affected.
- 87% of deaths, but only 19% of all cases, occurred in persons aged 70 years or older.
- COVID-19 related outbreaks in nursing homes and hospitals continue to be reported. In some of these outbreaks, the number of deaths is relatively high.

Source: Daily situation Report RKI, 23.04.2020

In Germany, approximately 0.18% of the population (83 million) is or was infected with SARS-CoV-2; reproductive number R=0.9 (23.04.2020)
Since the beginning of the COVID-19 pandemic, the number of donors and retrieved tissue in the DGFG network has approximately decreased by half, (Source: DGFG, 22.04.2020).
Situation as regards tissue donation from deceased donors (1)

Source of information for German tissue establishments:

Paul-Ehrlich-Institute (PEI), Robert-Koch-Institute (RKI), European Eye Bank Association (EEBA), European Association of Cell and Tissue Banks (EACTB), Global Alliance of Eye Bank Associations (GAEBA), German Ophthalmologist Society (DOG) – section tissue, European Centre for Disease Prevention and Control (ECDC)
### Situation as regards tissue donation from deceased donors (2)

#### Exclusion of potential tissue donors...

<table>
<thead>
<tr>
<th>Condition</th>
<th>Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upon contact with people with confirmed or suspected SARS-CoV-2 infection within 14 days before the donation</td>
<td>With confirmed SARS-CoV-2 infection within 14 days after completion of the recovery (negative PCR) or 28 days free of symptoms</td>
</tr>
<tr>
<td>With following symptoms unexplained/unclarified pneumonia or respiratory infections, unexplained fever presence of an x-ray thorax with diagnosis &quot;Covid-19 pneumonia cannot be excluded&quot;</td>
<td></td>
</tr>
</tbody>
</table>

- Since every donor is thoroughly medically evaluated, the presence of several individual uncritical symptoms combined with background information may also lead to donor exclusion
- PCR-Testing of donor for SARS-CoV-2 not mandatory
- At current, other assays like testing for antibodies or tissue testing are not available or useful/valid at the moment
Situation as regards tissue donation from deceased donors (3)

Actual available tests for COVID-19:
• First tests for antibody detection are described
• Gold standard: SARS-CoV-2-PCR, only validated for respiratory specimens
• Current RKI advice for testing of patients using SARS-CoV-2-PCR (no information available for testing deceased persons):

„Testing is generally recommended for symptomatic individuals ... as well as in the context of differential diagnosis, if there is a clinical suspicion based on medical history, symptoms or findings compatible with a COVID-19 disease and a diagnosis for another disease is missing, which sufficiently explains the clinical picture.

Due to the unclear significance of a negative result and in order to save test capacities, we generally advise against testing asymptomatic persons.

A negative PCR result does not completely rule out the possibility of infection with SARS-CoV-2. False-negative results cannot be ruled out, e.g. due to poor sample quality, improper transport or unfavourable timing (in relation to the course of the disease) of sample collection. ...

The most suitable test material depends on the time of collection during the course of the disease. In the case of deep respiratory tract infections, the testing of sample material from the oro- and nasopharynx alone is not suitable to exclude an infection, since in this phase of the disease only material from the lower respiratory tract or stool may be positive in the PCR."(RKI Website, 30.03.2020)
Conclusions for testing deceased donors:

- Since there is no re-testing possible for deceased donors, it would be **dangerous to rely on a single swab test** for COVID-19 risk assessment.
- Due to the required invasive **smear technique**, the **retrieval staff** is exposed to a **significantly higher risk of infection**.
- The **risk to transmit Covid-19 via corneal transplantation is very low** even in the case of a positive donor.
- For evaluation of deceased tissue donors a **thorough risk assessment can be sufficient** if enough information about the donor is available.
- If resources allow for the carrying out of a **SARS-CoV-2 PCR test** to give additional information (but still not 100% safe) this can be done, but should **not be mandatory**.
Precautionary measures for tissue procurement

Tissue procurement:

- **No specific requirements** for tissue procurement regarding COVID-19 described
- **All previously known standards** for minimizing cross-contamination and for the protection of staff continue to be complied with, e.g.
  - Hand disinfection with alcohol-based disinfectants
  - Personal protective equipment: Face mask, gown, gloves, hood
  - Protective goggles for the eyes are recommended
  - Staff members have to be trained in the use of personal protective equipment and safe retrieval techniques
  - Protective clothing must be discarded after use
  - Covering of the retrieval area with sterile tissues
  - Decontamination of retrieval area with pvp-iodine
  - The procurement is performed with sterile instruments, direct contact with the donor should be avoided

! **Current challenges due to COVID-19**: Limited availability of hand disinfectants and face masks (which are required in shops and public transportation in Germany as of 27 April)
Precautionary measures for tissue processing

Tissue processing:

• **No specific requirements** for tissue banks regarding COVID-19 described

• **All previously known standards** for minimizing cross-contamination and for the protection of staff continue to **be complied** with, e.g.
  ✓ All processing steps with open tissue must be performed in a laminar flow hood with background of class D
  ✓ Protective clothing like face mask, gown, gloves
  ✓ Protective clothing has to be discarded after use
  ✓ Some tissue banks use reusable clothing that is safely reprocessed (with exception of gloves)
  ✓ Regular disinfection of the work space with virucidal / limited virucidal disinfectants
  ✓ To prevent cross-contamination, instruments must be changed after each donor
  ✓ Biological waste is disposed of safely

! **Current challenges due to COVID-19:** Limited virucidal disinfectants and face masks
Availability of personnel in tissue establishments

• Decrease of potential donors and recipients lead to a significant reduction in the working hours of the staff

• Staff members are told to work in home office if possible

• If home office is not possible: teams are half divided up, in the case that one team member is infected, the other team can be completed and may continue working
Clinical application of tissues from deceased donors

- Cancelation of many elective surgeries lead for to a decreased demands for ocular tissue
- Current, many postponed surgeries are planned in the near future
- Due to reduced donation numbers during the last weeks an adequate transplant supply becomes difficult
- In Germany, so far there are no problems / limitations in the transportation of tissues
Provisions to control tissue availability

INFORMATION TO INCLUDE: Are any in place and for which tissues (e.g. live saving tissues such as heart valves, skin)

For Germany, no provisions are taken or are planned up to now.
SPAIN

Jorge GAYOSO

Anna VILARRODONA

aebt
Asociación Española de Bancos de Tejidos
General situation in the country

**Cumulative cases per notification date**

- **TOTAL CASES**: 219764
- **CASES last 24h (PCR +)**: 12756
- **Recovered**: 93255
- **Deaths**: 22824
- **National Alarm Declaration**

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**Clinical situation daily evolution**

- **ICU beds x3**
- **Emergency and in-patient wards collapse**
- **PPE and diagnostic tests shortage**

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**Total cases (24-APRIL-2020)**

**COVID-19 cases**

- 1 - 100
- 101 - 500
- 501 - 2000
- 2001 - 5000
- 5001 - 10000
- 10001 - 15000
- 15001 - 20000
- 20001 - 50000
- >50000

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**Cumulative incidence during last 14 days (24-APRIL-2020)**

**Cases/100.000 hab**

- 1.7 - 20
- 20 - 27.4
- 27.4 - 77.5
- 77.5 - 147.9
- >147.9

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**SPAIN population: 47,0 M**

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**Deaths TOTAL CASES CASES last 24h Recovered ICU beds x3 Emergency and in-patient wards collapse PPE and diagnostic tests shortage**

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**National Alarm Declaration**

**March**

- **Recuperados**
- **Hospitalizados**
- **UCI**
- **Fallecidos**

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**April**

*Datos en curso Carutella*

Fuente: RENAVE, ISCIII-CCAES

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**Cumulative incidence during last 14 days (24-APRIL-2020)**

Fuente: RENAVE, ISCIII-CCAES

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General situation in the country

**Cumulative cases per notification date**

- **TOTAL CASES**: 219,764
- **Cases last 24h (PCR+)**: 12,796
- **Recovered**: 93,255
- **Deaths**: 22,824

**SPAIN population: 47,0 M**

**Total cases (24-APRIL-2020)**

- **COVID-19 cases**
  - 1 - 100
  - 101 - 500
  - 501 - 1,000
  - 1,001 - 5,000
  - 5,001 - 10,000
  - 10,001 - 15,000
  - 15,001 - 20,000
  - 20,001 - 30,000
  - >30,000

**Deceased donors and transplantation. SPAIN (23-APRIL-2020)**

- **National Alarm Declaration**

**All causes mortality rate. SPAIN (24-APRIL-2020)**

- **Deaths**
- **Cumulative cases per notification date**
- **Recovered**

**SPAIN population**: 47,0 M

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Situation as regards tissue donation from deceased donors

Weekly biovigilance report to our network from January 23th

Screening strategy according to the epidemic scenario

RT-PCR test on BAS/BAL/ nasoph samples obtained <24h donation

**ALGORITHM TO FOLLOW FOR DECEASED DONATION**

- **DECEASED DONOR**
  - Confirmed case of COVID-19
    - Lives/Has visited any affected area within the previous 21 days
      - Assess the clinical situation
        - Clinical symptoms compatible with COVID-19
          - No need for screening
            - Donation does not proceed
        - Without clinical symptoms compatible with COVID-19
          - Screening of SARS-CoV-2
            - Positive/Inconclusive
              - Proceed with donation
            - Negative
  - Exposed to a confirmed case of COVID-19 within the previous 21 days
  - No epidemiological risk
    - Lung and/or small bowel donation or clinical symptoms compatible with COVID-19
      - YES
      - NO
Situation as regards tissue donation from deceased donors

On the field:

- All National tissue establishments reported severe reduction of activities with deceased donors after the 2nd week of March
- Tissue establishments reported activities are mainly associated with living donors (Semen, cranial flaps, SED, breast milk, AM)
- The mandatory SARS-CoV-2 rRT-PCR tests were very limited and not always available to test potential donors (the situation seems to be improving)
- Transplant/Donor Coordinators were allocated to life saving tasks and not available to identify and evaluate potential donors
- ICUs and morgues were overwhelmed with COVID-19 patients

* Reported in the AEBT survey

Number of Deceased Donations (March + April)*
Precautionary measures for tissue procurement

Local Measures (implemented by the tissue establishments): Adoption of new procurement SOPs based on risk assessments

- Additional protective garments for professionals involved in procurement procedures (PPE, face shields ..)
- Protection of donors’ oral and nasal cavities during procurement procedures (BTB/BST)
- Limitation: Tissues from thorax will not be procured (BTB/BST).
- Extraordinary agreements with transport services and review their disinfection procedures (Leon)

On the field:
- Shortage of PPEs
- Health Professionals were not available to perform procurement
- Operating theatres were not available
Precautionary measures for tissue processing

Local Measures (implemented by the TEs):
Adoption of new SOPs for procurement based on risk assessments:
• Additional disinfection of material introduced in the clean rooms (Alcohol 70%) (Balearic Islands)
• Processing of MSK tissues procured (and stored) before Dec 2019

On the field:
• Shortage of PPEs
• Processing of tissues (other than MSK) has stopped almost completely
Availability of personnel in tissue establishments

National requirements:

- Presence of staff in tissue establishments was reduced due to sick leaves, self quarantine and lockdown rules;
- Home office for all non technical/non essential workers;

Locally:

- Some staff from tissue establishment was relocated to other services in the hospitals

On the field:

- The absence of staff (due to sick leave / national requirements) had very limited impact due to the significant decrease in the volume of the activities (procurement, processing and distribution were highly affected)
Clinical application of tissues from deceased donors

Clinical application at National Level:

- Elective surgeries were canceled
- Transport/distribution services seemed affected only between some countries (ex: Italy)

On the field:

- All transplant/implant of tissues ceased, except for urgent procedures.
- Alternative therapies were used (ex: Serum Eye Drops to Amniotic Membrane Ext.)

Distribution of Tissues
(Deceased Donors - March + April)*

* Reported in the AEBT survey
Provisions to control tissue availability

• **Demand is expected to recover faster than donation:** tissue establishments foresee a **severe shortage of tissues with short shelf life** when regular surgical activities return to normal.

• Stock of MSK tissues should not be affected, **if testing is available and new (validated) testing techniques are available soon**.

• Guidelines for the **risk assessment/lookback for the tissues donated in the period before the declaration of emergency** – Value of testing antibodies?

• **Suspension of autopsy procedures** may have resulted in a lost of knowledge related with the real incidence of the disease, and presence of virus in the different tissues and organs.

• New techniques for **viral inactivation** may play an important role in the future processing activities (ongoing research).

• **Financial impact** of the pandemic may result in difficulties for the sustainability of activities in the tissue establishments in the long term - **Collaboration Network between tissue establishments** will more valuable than ever.
UNITED KINGDOM

Kyle BENNETT

Blood and Transplant
General situation in the country (on 23 April 2020)

UK Population: 66.65 million

Total Number of COVID-19 associated UK deaths
in hospital by date reported = 18,100

Daily Number of COVID-19 associated deaths
in hospital by date reported = 759

Total Number of lab confirmed UK cases = 133,495

Daily Number of lab confirmed UK cases = 4,451

Data accurate as of 23rd April 2020 @ 09:00 (https://coronavirus.data.gov.uk)
Situation as regards tissue donation from deceased donors

Respiratory viruses are not known to be transmitted via tissue allografts, Precautionary measures are being applied until the pathogenesis of this new Coronavirus is known

**Donor Selection:** Follow UK Joint Professional Advisory Committee (JPAC) Donor Selection Guidelines (DSG)

**23 Jan 2020 : New coronavirus specific entry in DSG : Travel related**
Initially China but extended in early Feb to **8 other countries including airport stop overs** and then in early March further extended to include **Italy**

Less than 21 days from a donor’s return from a Coronavirus risk area or from the last contact with a person with Coronavirus infection. Less than three months since recovery from Coronavirus infection

**23 March : No longer travel risk (UK is an affected country) as increasing cases due to community spread in the UK**

**Confirmed or suspected COVID-19 infection** not to be accepted until at least 14 days after resolution of symptoms. Similar restrictions are applied to potential donors who may have been in contact with a person with COVID-19

https://www.transfusionguidelines.org/dsg/ctd/guidelines/coronavirus-infection-1

Any donor who had **respiratory symptoms at the time of death not accepted** unless Covid-19 had been excluded after testing at the hospital
NO routine testing: Asymptomatic, undiagnosed donors with COVID-19 may be accepted for tissue donation: NHSBT Tissue & Eye Services has documented a Position Statement after risk assessment to evaluate other steps that would inactivate/eliminate the SARS-CoV-2 in tissues.
Precautionary measures for tissue procurement

- Detailed **risk assessment on tissue procurement** with input from H&S professionals, Tissue Bankers and Clinical Virologists.

- **Guidance** from other sources such as the Association of Anatomical Pathology Technology (AAPT) and the Royal College of Pathologists (RCPath)

- Extensive **venue and donor risk assessment** is carried out prior to each tissue procurement activity and PPE is already in use

- **Main change**: introduction of Filtering Face Piece 3 (FFP3) masks for aerosol generating procedures such as bone, tendon and heart retrieval

- **Reduced Activity to reduce risk**: From 10 tissue donors per day to 3, with every potential multi tissue donor being referred to senior management for a decision on whether to proceed. This is based on donor characteristics (age, sex etc), potential tissue availability and donor location.

- Tissue retrievers are **working from home** where possible and are only being asked to work when there is a donor or a requirement for other duties to be carried out. This helps us meet the current **social distancing guidance**.
Precautionary measures for tissue processing

Tissue processing within NHS Blood & Transplant is carried out in accordance with The Human Tissue Act 2004 and the EU Tissue and Cells Directive (EUTCD) via the Human Tissue (Quality and Safety for Human Application) Regulations 2007.


**Tissue processing within NHS Blood Transplant continues during the pandemic.**

Current tissue processing practises have been reviewed with regards to COVID-19 taking into account up to date scientific advice and published data. This review has formed part of Risk Assessment. This outcome of the risk assessment can be categorised into two main areas:

1. **PPE:** The main change for tissue processing is with regards to *Aerosol Generating Procedures* such as bone cutting, blending or grinding. For these processes it has been recommended that current PPE is upgraded and the use of Filtering Face Piece 3 (FFP3) masks implemented. It is also a requirement that these masks are fit tested by a qualified tester.

2. **Virus Inactivation through processing:** A review of current processing techniques has been performed to identify potential COVID-19 risk reduction measures that are already in place. For example Polyvinyl Pyrrolidone (PVPI) is used in Cornea processing and there is evidence that PVPI inactivates a variety of both enveloped and non-enveloped viruses, including influenza A, MERS-CoV and SARS-CoV.
Social Distancing has been implemented across NHSBT Tissue & Eye Services with team members being asked to work from home, if their role permits this. Additional IT equipment has been provided to individuals to help facilitate this.

For individuals who have to work on an NHSBT site (such as tissue processors), we have introduced other measures to aid with social distancing such as,

- Staggered start and finish time
- Different shift patterns
- Staggered breaks
- Restrictions on meeting room use
- Meetings held via skype, zoom, Microsoft teams etc

Team members who have been identified as ‘high risk’ or ‘vulnerable’ have been asked to self-isolate at home for 12 weeks.

A meeting is held each morning to review staffing, activity, resources and other contingency planning.
Clinical application of tissues from deceased donors

• Elective surgery within the UK ceased in April with only emergency surgery taking place.
• Due to Elective surgery being cancelled we observed a large number of cancellations which unfortunately led to some clinical tissue time expiring (mainly corneas due to their short expiry).
• The only tissue that continues to be issued regularly is Heart Valves, Corneas and Skin, however corneas issues have significantly reduced.
• Delivery of tissue has been largely unaffected and we have been able to meet the demands of clinicians.

Provisions to control tissue availability

• All tissues processed within NHSBT Tissue & Eye Services have been deemed essential so processing continues
• Some tissues (heart valves, skin and corneas) have been classified as ‘emergency’ tissues and would take priority should staff availability reduce to a level that would prevent all tissue type being processed. This is as per existing business continuity/emergency plans.
• Processing of corneas has reduced in line with demand (due to tissue expiry dates). Heart Valve processing continues at pre COVID-19 levels. There is sufficient skin currently available to meet demand.
• NHSBT Tissue & Eye Services are now working on a ‘recovery’ plan to ensure sufficient tissue is available to clinicians post COVID-19 when elective surgery re-starts
The floor is yours!

Type your question in the chat window and indicate to whom it is addressed

Eliana PORTA  Isabelle MARTINACHE  Ralf Reinhard TÖNJES  Martin BÖRGEL

Jorge GAYOSO  Anna VILARRODONA  Kyle BENNETT
Risk of COVID-19 transmission through tissues from deceased donors and testing practice
Risks posed by COVID-19 pandemic to SoHO

Risk to the viral safety of SoHO
Risk to the SoHO recipients
Risk to the staff in SoHO establishments,
Risk to the sufficiency of SoHO supply
COVID-19 infection and patient

Route of infection
- Infection in community
- Nosocomial infection
- Transfusion and transplantation?

Presence of the viral RNA
- Respiratory tract specimens
- Body fluids (tears, saliva, stool, urine)
- Blood (whole blood, serum, plasma)
- Tissues and organs (distribution of hACE2)?
Risk of COVID-19 transmission through SoHO

No report of COVID-19 transmission through SoHO
Low levels of detectable RNA in the blood - Infectivity not determined
RNA positivity of tissues and organs uncertain
Routine donor screening (medical and behavioural history and medical check) should detect donor with symptoms of acute respiratory illness
Disinfection, sterilization or pathogen reduction of some types of SoHO
Risk of COVID-19 transmission through SoHO is THEORETICAL but cannot be excluded
Suggested interventions – PRECAUTIONARY
Laboratory testing

NAT - rRT-PCR

- WHO have shortlisted three molecular detection assays through the Emergency Use Listing Procedure (EUL) and Foundation for Innovative New Diagnostics (FIND) has provided validation results for five more

Antigen detection tests

Antibody detection tests

Source of specimen

Lower respiratory tract
  • sputum
  • aspirate
  • lavage

Upper respiratory tract
  • nasopharyngeal and oropharyngeal swabs
  • nasopharyngeal wash/nasopharyngeal aspirate

Additional sources
  • stools, whole blood, urine, and if diseased, material from autopsy
Detection SARS-COV-2 RNA in Clinical Specimens by rRT-PCR of

<table>
<thead>
<tr>
<th>Specimens and values</th>
<th>Bronchoalveolar lavage fluid (n = 15)</th>
<th>Fibrobronchoscope brush biopsy (n = 13)</th>
<th>Sputum (n = 104)</th>
<th>Nasal swabs (n = 8)</th>
<th>Pharyngeal swabs (n = 398)</th>
<th>Feces (n = 153)</th>
<th>Blood (n = 307)</th>
<th>Urine (n = 72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive test result, No. (%)</td>
<td>14 (93)</td>
<td>6 (46)</td>
<td>75 (72)</td>
<td>5 (63)</td>
<td>126 (32)</td>
<td>44 (29)</td>
<td>3 (1)</td>
<td>0</td>
</tr>
<tr>
<td>Cycle threshold, mean (SD)</td>
<td>31.1 (3.0)</td>
<td>33.8 (3.9)</td>
<td>31.1 (5.2)</td>
<td>24.3 (8.6)</td>
<td>32.1 (4.2)</td>
<td>31.4 (5.1)</td>
<td>34.6 (0.7)</td>
<td>ND</td>
</tr>
<tr>
<td>Range</td>
<td>26.4-36.2</td>
<td>26.9-36.8</td>
<td>18.4-38.8</td>
<td>16.9-38.4</td>
<td>20.8-38.6</td>
<td>22.3-38.4</td>
<td>34.1-35.4</td>
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</tr>
<tr>
<td>95% CI</td>
<td>28.9-33.2</td>
<td>29.8-37.9</td>
<td>29.3-33.0</td>
<td>13.7-35.0</td>
<td>31.2-33.1</td>
<td>29.4-33.5</td>
<td>0.0-36.4</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: ND, no data.
Deceased tissue donors – testing practice

• Routine testing of all deceased tissue donors
• Testing of particular categories of deceased donors
• No testing
Deceased donors with an active confirmed COVID-19 at the time of death are not eligible for tissues donation – No testing

Rationale:
Precautionary intervention to prevent SARS-CoV-2 transmission which is based on possible presence of the virus in blood, body fluids and tissues of a deceased with active confirmed COVID-19 at the time of death
Deceased donors who have recovered from COVID-19 may donate tissues if tested negative for the presence of SARS-CoV-2 RNA in upper respiratory tract specimens more than 14 days before death or if became asymptomatic 28 days before death.

Rationale
Precautionary intervention to prevent SARS-CoV-2 transmission is based on the possible presence of the virus in blood, body fluids and tissues of a deceased donor who has recovered from the disease. Since the risk of the virus shedding after a patient tested negative for the presence of SARS-CoV-2 RNA in upper respiratory tract specimens is lower, we suggest 14 days deferral (maximum incubation period) before death. The risk of prolonged virus shedding after a patient became asymptomatic is higher, therefore, we suggest 28 days deferral (double maximum incubation period) before death.
Tissues should not be collected from deceased donors, who are without symptoms or diagnosis of COVID-19, and who lived in, or visited, areas of sustained community transmission of the virus unless:

- There is disinfection, sterilisation or a microbial inactivation step of procured tissues that is validated for enveloped viruses, or
- Donors tested negative for the presence of SARS-CoV-2 RNA in upper or lower respiratory tract specimens collected within 72 hours before procurement.

Rationale:

Precautionary intervention to prevent SARS-CoV-2 transmission is based on the possible presence of the virus in blood, body fluids and tissues of an asymptomatic or pre-symptomatic deceased donor.

Tissues that can be disinfected, sterilized or inactivated using a method validated for enveloped viruses during procurement and processing are excluded, because in such tissues the risk of diseases transmission negligible and acceptable.

Although testing of lower respiratory tract specimens are more sensitive than upper, both options are suggested to be not restrictive for those tissue procurement organizations who are not able to collect lower respiratory specimens.

The time criterion for the collection of lower or upper respiratory tract specimens for the detection of the viral RNA within 72 hours before tissue procurement allows to collect specimen before death without increased risk of donor infection in the period between specimen collection and death.
Open Discussion
Conclusions and Closing remarks

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Please take a minute to respond to our brief survey (coming up next)