

CONCORSO PUBBLICO, PER TITOLI ED ESAMI, A N. 1 POSTO DI CATEGORIA EP, POSIZIONE ECONOMICA EP1, AREA TECNICA, TECNICO-SCIENTIFICA ED ELABORAZIONE DATI, PER LE ESIGENZE DEL DIPARTIMENTO DI SCIENZE MEDICHE TRASLAZIONALI DELL'UNIVERSITÀ DEGLI STUDI DI NAPOLI FEDERICO II (COD. RIF. 2006)

QUESITI ESTRATTI E NON ESTRATTI ALLA PROVA ORALE DEL 29 SETTEMBRE 2020

ELENCO QUESITI ESTRATTI

- 3. Maturazione delle cellule staminali ematopoietiche in senso linfocitario;
- 3. Metodiche di laboratorio per lo studio dello sviluppo del timo;
- 3. Interazione tra matrici extracellulari sintetiche e cellule;
- 3. Applicazioni di metodiche di analisi molecolare allo studio della fisiopatologia del timo;
- 3. Piattaforme per la ricerca bibliografica in ambito biomedico;
- 3. Generazione di grafici da dati mediante excel.

ELENCO QUESITI NON ESTRATTI

- 1. Descrizione dello sviluppo dei linfociti T;
- 1. Vantaggi delle analisi mediante next generation sequencing rispetto a metodiche convenzionali nella diagnosi di immunodeficienze congenite;
- 1. Geni implicati nello sviluppo del timo;
- 1. Metodiche per l'allestimento di organoidi in vitro;
- 1. Piattaforme informatiche per la ricerca di bandi di finanziamenti;
- 1. Utilizzo del power-point per la preparazione di presentazioni scientifiche;

- 2. Tecniche di immuno-fenotipizzazione per lo studio dello sviluppo dei linfociti T Geni implicati nello sviluppo del timo;
- 2. Tecniche per l'inquadramento diagnostico di pazienti con sospetta immunodeficienza;
- 2. Applicazioni dello studio di organoidi nello studio della fisiopatologia del timo;
- 2. Strategie per la ricerca su piattaforme informatiche di bandi per finanziamenti;
- 2. Inserimento dati in excel da ordinare cronologicamente

BRANI ESTRATTI E NON ESTRATTI OGGETTO DELLA PROVA IN LINGUA INGLESE

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Ensuring continuity of care for children with inherited metabolic diseases at the time of COVID-19: the experience of a metabolic unit in Italy

Nicola Brunetti-Pierri, MD^{1,2,3}, Simona Fecarotta, MD, PhD^{1,2}, Annamaria Staiano, MD^{1,2}, Pietro Strisciuglio, MD¹ and Giancarlo Parenti, MD^{1,2,3}

Genetics in Medicine (2020) <https://doi.org/10.1038/s41436-020-0831-4>

In December 2019, a novel and highly pathogenic strain of coronavirus (SARS-CoV-2) caused an outbreak in Wuhan city, Hubei province in China, and rapidly spread worldwide. Following China and South Korea, Italy has been among the first countries affected by coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2. After the first cases identified in Lombardy (Northern Italy), the outbreak rapidly spread to other Italian regions. Under these circumstances, Italian clinical centers involved in the diagnosis and management of chronic disorders, such as inherited metabolic diseases (IMDs), had to face new and unprecedented challenges. Here, we report the experience of the Unit of Metabolic Diseases, Federico II University Hospital over the past month, following the first directives from the central government (decrees of the prime minister [DPCM] dated 8 March and 10 March 2020) that mandated social distancing, home confinement of people, discontinuation of most commercial and productive activities—the so-called lockdown—including ordinary and deferrable hospital activities not related to the care of COVID-19 patients.

Our center has been involved in the care of patients affected by IMDs since the early 1980s. Currently, our unit follows approximately 400 patients (half of whom are below the age of 18 years), affected by a broad range of IMDs, including defects of amino acid, urea cycle, organic acid, carbohydrate and energy metabolism, and organelle disorders (lysosomal storage diseases and peroxisomal diseases). In addition, our unit is the referral center for the expanded newborn screening program for the region of Campania, which has approximately 48,000 births per year.¹

Although the COVID-19 outbreak has involved large countries like China for at least three months, challenges imposed by this pandemic on the care of IMD patients have not been discussed so far.

Under ordinary conditions IMDs are neglected disorders. These diseases are rare, have limited awareness among general

practitioners and pediatricians, and thus IMD patients are typically followed by specialized physicians in a few expert centers. It may be anticipated that under the COVID-19 pandemic, the efforts and the time dedicated to the care of IMD patients may decrease further. Nevertheless, most of these patients continue to require dietary and therapy interventions, and close monitoring of their clinical status, which are critical for their health and in some cases for their lives. During major catastrophic events, provision of health care to IMD and rare disease patients in general poses additional and unique challenges, as previously highlighted by the experience of genetic/metabolic services in Louisiana during Hurricanes Katrina and Rita in 2005.² In addition, some groups of IMD patients are likely to be particularly fragile and at risk of life-threatening acute metabolic decompensation in case of SARS-CoV-2 infection. These categories especially include patients with defects of amino acid and organic acid metabolism, urea cycle defects, and disorders of carbohydrate and energy metabolism, which are highly prevalent in our clinic. Other patients, such as those with substantial neuromuscular involvement, such as Pompe disease, are likely susceptible to greater risks in case of respiratory disease and need for ventilatory assistance.

For these reasons, continuity of care and a high level of attention to the needs of these patients should be ensured, even under situations of emergency, such as those imposed by the SARS-CoV-2 outbreak. Strategies should be implemented to address the criticalities related to the care of IMD patients and to minimize the impact of the COVID-19 pandemic on this fragile group of individuals.

With the rapid spreading of SARS-CoV-2 infection in Italy, most of the human and financial resources of the Italian National Health Service are being shifted to COVID-19 patients. Our hospital was identified as the regional pediatric referral center for children with COVID-19 and specific areas

¹Dipartimento di Scienze Mediche Traslazionali, Federico II University, Naples, Italy; ²Azienda Ospedaliera Federico II, Naples, Italy; ³Telethon Institute of Genetics and Medicine

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BRUNETTI-PIERRI *et al*

of the building became exclusively dedicated to these patients. This decision had major consequences on the activities of our unit, which is embedded into the pediatrics division. We predict that most metabolic clinics worldwide will be also affected and will face a similar scenario. To minimize the impact of these changes on the activities of our clinic, we applied a number of measures. First, we had to rearrange, reduce, or discontinue our standard activities (e.g., outpatient clinics, follow-up evaluations, enzyme replacement therapies, and clinical trials) to comply with government directions and to prevent unnecessary exposure of our patients to the risk of infection while preserving the health of our fragile patient population and allowing timely diagnosis of new cases. Next, we converted the vast majority of our follow-up visits into remote visits through regular phone calls, Skype calls, or emails to ensure continuing monitoring of patient conditions and access to medical consultation. During these interactions, we recommended strict observation of home confinement for patients and their caregivers. Moreover, consultations for other hospitals (such as neonatal intensive care units for newborns with a suspicion of IMD) or services in our department were converted, whenever possible, into telemedicine activities. Although helpful and accurate, these remote consultations do not easily allow for monitoring of biochemical parameters that are essential in the follow-up of several IMDs. Therefore, we are currently addressing this issue by exploiting home care services made available by the National Health System (the Integrated Home Assistance program) allowing nurses to visit patients at their home to obtain vital parameters and draw blood samples. We hope that some of these activities might be maintained even after the COVID-19 pandemic to improve the quality of life of IMD patients. A similar approach has been undertaken for enzyme replacement therapies in patients with lysosomal storage diseases. Nevertheless, IMDs typically require multidisciplinary assessments and anticipatory evaluations by several specialists and using imaging to allow timely diagnosis of well-established disease complications. Should this emergency last for longer periods of time, limited access to such evaluations might have a serious impact on the health of our IMD patients and to avoid this, we would need to implement further contingency plans.

An additional but not marginal risk related to hospital rearrangement is the reduced availability of non-COVID-19 beds. This could determine reduced possibility to assist patients with intercurrent metabolic decompensation who require hospital admissions. To overcome this problem, we have ensured that a minimum of non-COVID-19 beds remain available, should patients with IMD or other chronic illness require hospital admissions.

For ongoing clinical trials, new recruitments were put on hold and all the activities focused on already enrolled subjects. For ongoing trials of gene therapy (ClinicalTrials.gov identifiers NCT03173521 and NCT03466463), our center has been enrolling patients from different countries, but travel bans made the trial visits unfeasible. Therefore, scheduled

visits were replaced with visits to local IMD physicians and shipping of the most relevant biological samples to a central lab. This was an additional burden on the clinical trial staff who had to reorganize several new activities.

Being not deferrable and potentially associated with emergency, all activities related to expanded newborn screening were preserved. Neonates with a positive result on newborn screening are brought to either inpatient or outpatient services accompanied by only one parent following directions on social distancing and use of personal protective devices. The heavy psychologic burden on parents coming to the hospital under these special circumstances for testing their newborn for a suspected severe, lifelong disease also needs to be considered.

Other activities, including drug prescriptions, adjustments of dietary protocols, and disease certifications were remodulated, mostly through telemedicine tools.

In summary, we report the experience of a single center involved in the care of IMD patients. It is reasonable to think that many other centers involved in the care of chronic and fragile patients (e.g., immunodeficiencies, cystic fibrosis, cancer, and others) are facing similar challenges and are taking immediate action to ensure the best standard of care to their patients during the COVID-19 pandemic.

None of our IEM patients has developed COVID-19 and it remains to be established whether IMDs are at particular risk during SARS-CoV-2 infection. However, a single center experience is not going to be able to address this question. The Chinese Center for Disease Control and Prevention has published the largest case series to date of COVID-19 in mainland China including 72,314 cases (updated through 11 February 2020). The overall case-fatality rate was 2.3% but no deaths occurred in the group aged 9 years and younger, which included 416 cases.³ In another study, among the 366 children (≤ 16 years of age) hospitalized for respiratory infections from 7 January to 15 January 2020, in an hospital serving an area located 14 km to 34 km from central Wuhan, COVID-19 was detected in 6 patients (1.6%) all presenting with moderate-to-severe respiratory illness.⁴ A similar experience with very few SARS-CoV-2 positive children has been recently reported in a pediatric unit in Lombardy.⁵ In summary, COVID-19 in children appears to be relatively mild compared with adults and this could explain the lack of reports of fatalities in children with IMD and our experience with no cases of IMD children presenting acutely with decompensation and SARS-CoV-2 infection. This positive outcome might also be dependent on hygiene and social distancing measurements that typically patients with IMD and their families routinely follow. Being at risk of life-threatening acute decompensation following even common infections, patients and their caregivers are used to following measurements for minimizing risk of infection very carefully and on a routine basis. However, in the growing population of adults with IMD, the risks are likely to be much higher and they need special attention.

Per ordine del Presidente della Commissione
Il Segretario
f.to dott.ssa Mariarosaria Casale