VIRUS RESEARCH AS ESSENTIAL TO THE NIDCR STRATEGIC PLAN

► The NIDCR and the dental profession need to proactively develop and implement viral pandemic strategies. The organizations need to rapidly respond to better understand the current pandemic and support critical studies to address/prevent the next pandemic virus.

► Research personnel. Professionals in our disciplines need to be better educated to deal with viral pandemics including basic, clinical and public health researchers and providers.

TESTING AND CHARACTERIZING SARS-COV-2 INFECTION—SHORT TERM/HIGH IMPACT

► Saliva or breath for rapid testing for infection (virus) and immunity (IgA, IgG), considering the durability of antibody response, viral load and transmission including markers of asymptomatic infection (i.e., sequence isolates) and the impact of co-morbidities.

► Do loss of taste and smell translate into early diagnostic molecular sentinels?

► Oral intradermal mucosal vaccine to create local and systemic immunity and compare to a nasal vaccine.

► Optimize virus detection platforms including electric-field induced release and measurement (EFIRM), which is an electric chemical analytical platform optimized for salivomics target detection (technology developed with NIDCR support). Preliminary data indicate that the S1 viral antigen is exquisitely sensitive for EFIRM detection (CLIA certified).

► Develop tests to be used in the dental office by dental personnel to accurately test personnel and screen patients (i.e., point-of-service tests).

FUNDAMENTAL AND FOUNDATIONAL STUDIES

► Mapping oral/oropharyngeal/nasal sites with ACE-2 receptors

► Mechanism of Cov-2 entry/infection into oral/oropharyngeal and salivary epithelial cells. Can COVID-19 proliferate and survive in oral epithelial cells and induce immune response? In addition to the ACE2 receptor, we need to examine the spike protein processing proteases (i.e., endosomal cathepsins, cell surface transmembrane protease/serine (TMPRSS) proteases, furin and trypsin) in oral/tongue epithelial cells.

► Use mechanisms of coronavirus infection to better understand the acquisition of other respiratory and ingested infectious agents (i.e., influenza, other coronaviruses, enterovirus and bacterial agents such as Listeria and Salmonella spp.).

► Role of mucosal microflora on susceptibility to coronavirus infection; promoting dysbiosis

► Phagocyte response to SARS-CoV2 in oral mucosa. As the first line of immune defense, how do neutrophils, monocytes/macrophages and dendritic cells respond to SARS-CoV2? Can myeloid cell responses be pharmacologically enhanced for a more efficient eradication of the virus?

► Roles of dendritic cells (DC) and T cell functions in SARS-CoV2 infection in the oral cavity. How do the functions of oral mucosal DCs and T cells determine SARS-CoV2 infectivity and host responses?

► Role of T-resident memory cells in the oral mucosa in immunity/preventing recurrence

► Role and regulation of innate immunity in response to SARS-CoV-2

► Genetic factors in SARS-CoV-2 infection: resistance vs. susceptibility. Develop an understanding of inter-individual differences (e.g., linked to age, gender, ethnicity, etc.) and correlations with susceptibility to infection.

► Blocking oral/oropharyngeal/nasal sites for infection (i.e., ACE-2 inhibitors, blocking agents) as a potential preventive strategy in high risk populations

► Route of oral/oropharyngeal transmission; reservoirs of virus; post-receptor/downstream signaling pathways mediate SARS-CoV2 infectivity in oral mucosa?

► Contribution of oral/oropharyngeal SARS-CoV-2 infection to systemic cytokine storm

► Role of saliva: neutral, inhibitory, augmenting infectivity.
Fundamental and Foundational Studies (continued)

► Why does Cov-2 affect taste, smell? Does COVID-19 affect the chemosensing by taste receptors, relationship to ACE-2 receptors on the tongue, or interfere with signal transduction or other pathways?

► Generate critical reagents for studies of Cov-2 and host cell interactions; i.e., producing and sharing pseudovirions with reporter constructs for visualization, receptor-binding domain proteins, spike proteins, cell lines and organoids, mouse and other animal models of oral/oropharyngeal infection.

► Natural history studies to determine the effect of COVID-19 on the pathobiology of oral, oropharyngeal and salivary gland tissues and their contributions to pulmonary and systemic outcomes and cytokine storm.

EPIEMIOLOGIC STUDIES

► What are the long-term effects of COVID-19 and treatment on oral health and associated systemic diseases, including autoimmune diseases such as RA and Lupus?

► Oral health equity and social determinants of health related to COVID infection

► Identify social predictors of transmission in different communities and the impact of different interventions on disease prevalence using seroepidemiology and mapping studies

► Contact tracing — oral health care providers and patients

► Testing in dental offices; monitor potential virus contamination in the dental clinic given different infection control practices, types of ventilation and types of dental procedures (with and without generating aerosol)

► Understanding how COVID-19 may change dental practice

► Understanding social and cultural constraints of:
  – oral testing
  – oral screening
  – billing and insurance reimbursements

► Efficacy of dental treatment post-SARS-CoV-2 infection and/or development of COVID-19:
  – across the lifespan (pediatric, geriatric populations)
  – across the specialties/disciplines

  – ascertain effects of prior infection on procedural outcomes and healing (i.e., grafting materials, implants etc.)
  – ascertain risk factors (behavioral, social, genetic) that predict poor patient outcomes

INFORMATICS STUDIES

► Linkage of emerging and existing data sets to determine risk factors including oral risk factors for infection.

► Building a Bio/data repository.

STUDIES RELATED TO CLINICAL CARE

► Salivary detection of SARS-CoV2 in a dental setting:
  – Oral sensors: Can oral sensors be developed for fast detection of salivary SARS-CoV2?
  – Antibody testing: Can saliva be used for fast and non-invasive testing for antibodies (both IgM and IgG) against SARS-CoV2?
  – Define and characterize salivary and nasopharyngeal aerosols: Can viral particles and various surface proteins/accessory molecules of SARS-CoV2 be detected in salivary and nasopharyngeal aerosols?
  – Spread kinetics of virus particles in aerosols and saliva: Is 6-feet sufficient? Is there a diluting halo of dispersion of infectious SARS-CoV2; very critical determinant of viral spread and contamination?

► What is the impact of COVID-19 on oral health?
  – Periodontal health
  – Caries
  – Oralcancers
  – Bone/cartilage (including craniofacial structures and TMJ)
  – Diabetics and others with co-morbidities with COVID-19-associated coagulopathies

► Impact of antiviral medication usage on oral health:
  – Opportunistic infections associated with SARS-CoV2
  – Effects of antiviral medications with differing pharmacology
  – Effects of cytokine storm immunosuppressive agents on mucosal immunity
  – Novel treatment strategies for SARS-CoV2
Studies Related to Clinical Care (continued)

► Effective use of teledentistry in the context of the pandemic:
  – Determine rate of adoption and obstacles including state practice policies, reimbursement, patient and provider acceptance and utilization changes.

INFECTION CONTROL

► New, more efficient approaches to disinfection and sterilization in dental clinics (e.g. UV-disinfection, extroral suction units):
  – Hospital setting
  – Private clinics
► Determine the effectiveness and optimal design of face masks in protecting against transmission in the primary care setting
► Novel methods to minimize aerosolization and monitor infectious particles in the dental setting
► Effectiveness and means of UV decontamination
► Additional PPE and decontamination protocols
► Viral testing in water lines
► Ensuring staff and patient safety in delivering routine dental care
  – What are minimum requirements to reopen in terms of engineering of the office design (e.g., individual office operatory versus open bays, commercial vs hospital grade HVAC systems, minimum airflow, negative pressure rooms.)
  – Are dental offices located within in larger professional/medical or commercial office buildings safe for adjoining tenants?
  – Evidence needed to establish the new “Universal Precautions” with CDC/OSAP.
► Establish public-private partnership with dental manufacturers to develop new instrumentation to minimize all-source aerosols (e.g., handpieces, air/water syringe, high speed suction, etc).
► Establish a HIPAA-compliant patient registry of oral health personnel with COVID-19
  – Determine source of exposure, underlying health conditions and other risk factors

BEHAVIORAL STUDIES

► How does the pandemic change patient access/willingness/avoidance for care?
► Are these concerns/practices different for underrepresented and/or marginalized populations?
► Characterize stress on dental care professional and develop strategies to cope or treat
► Development of educational programs targeted at providers and patients
► Given (post-) pandemic concerns, which practice settings or environments are likely to be most effective; characteristics of providers that will be more effective:
  – Costs to dental practice of additional infection control procedures
► Establish an implementation sciences research agenda to determine that dental practices adopt these new infection control protocols and other changes.
  – Include public, private and academic settings
► Determine that oral healthcare delivery is managed optimally during and after the pandemic.
  – Impact to communities after dental practices close due to the pandemic and did not open (by geography, community population characteristics, size of practice, characteristics of provider etc.)

IMPACT ON DENTAL EDUCATION

► Effects of the pandemic on dental education
  – New virology/microbiology curricula for basic and clinical education
  – Develop online education and testing
  – Providers need to be trained to collect data to assess implementation of new protocols
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