

Welcome!

Thank you for joining us!
The webinar will begin shortly.



WEBINAR





Lunch & Learn: Specific Antibody Deficiency

January 20th, 2023

IDF's Mission

Improving the diagnosis, treatment and quality of life of people affected by primary immunodeficiency through a community empowered by advocacy, education and research.



iDF Immune
Deficiency
Foundation



Core Services Partners

CSL Behring

GRIFOLS



KEDRION
BIOPHARMA

accredo[®]



X4
PHARMACEUTICALS

AstraZeneca



octapharma



Housekeeping



Zoom Webinars

Attendees will not have access to their mic or webcam throughout the event.



Slides

To see the full slides, select "side-by-side" in the dropdown menu at the top of your Zoom screen.



Questions

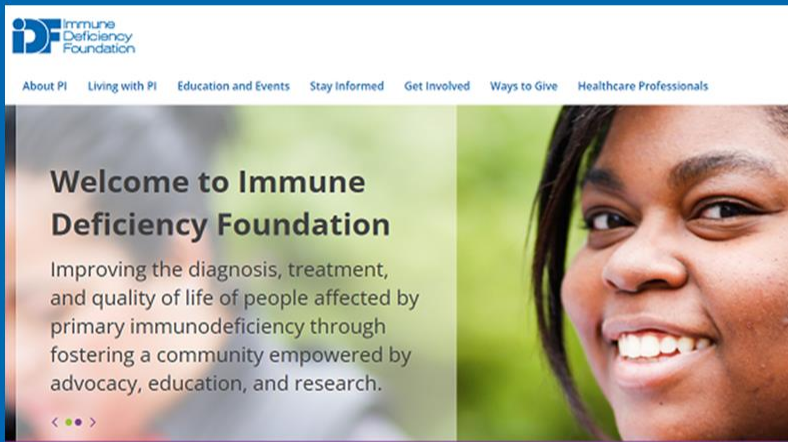
Submit your questions throughout the session via the Q&A Box.

DISCLAIMER

Immune Deficiency (IDF) education events offer a wide array of educational presentations, including presentations developed by healthcare and life management professionals invited to serve as presenters. The views and opinions expressed by guest speakers do not necessarily reflect the views and opinions of IDF.

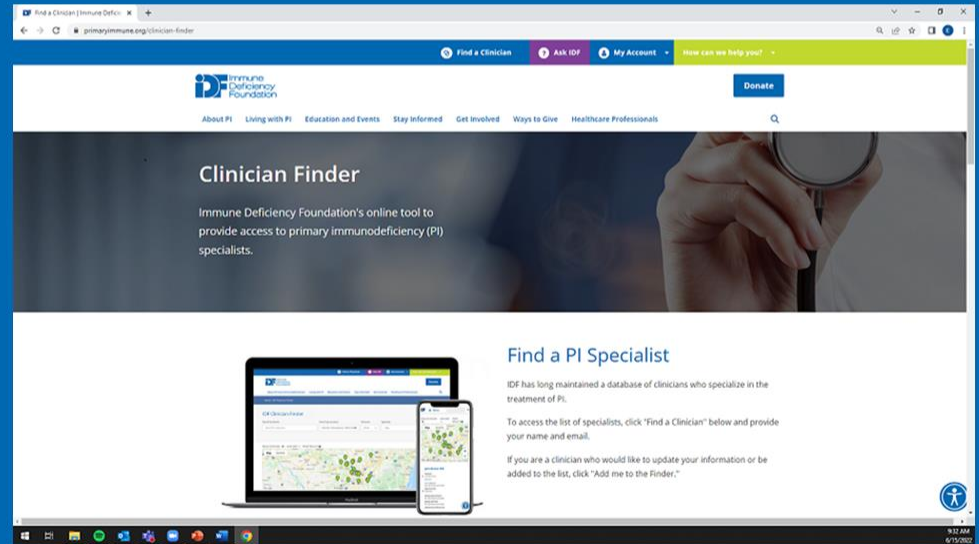
The information presented during this event is not medical advice, nor is it intended to be a substitute for medical advice, diagnosis or treatment. Always seek the advice of a physician or other qualified health provider with questions concerning a medical condition. Never disregard professional medical advice, or delay seeking it based on information presented during the event.





Welcome to Immune Deficiency Foundation

Improving the diagnosis, treatment, and quality of life of people affected by primary immunodeficiency through fostering a community empowered by advocacy, education, and research.



Clinician Finder

Immune Deficiency Foundation's online tool to provide access to primary immunodeficiency (PI) specialists.

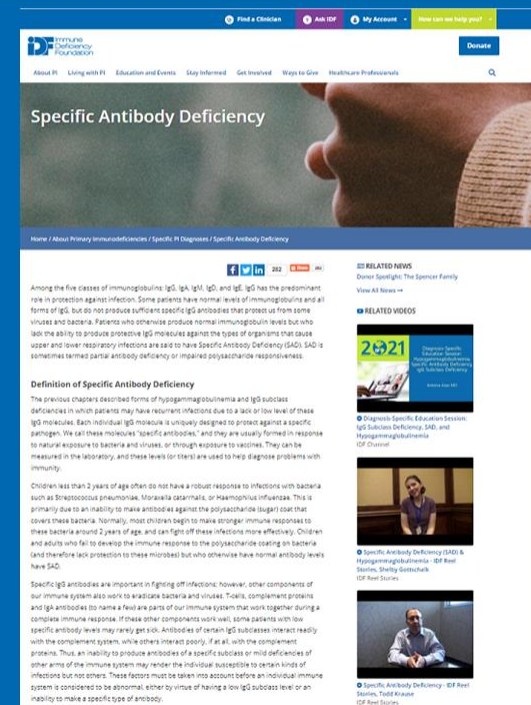
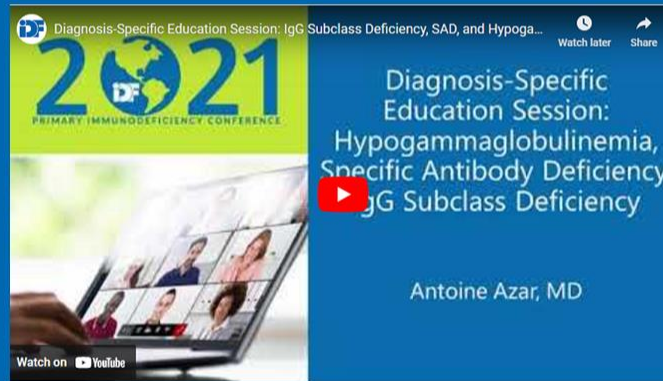
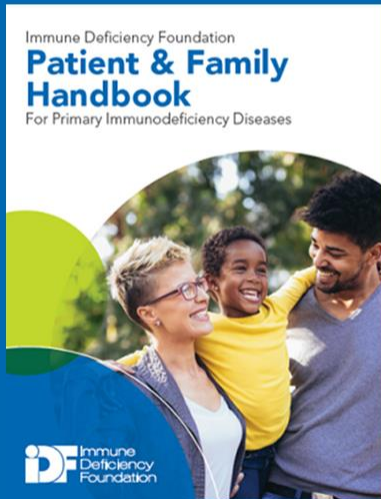
Find a PI Specialist

IDF has long maintained a database of clinicians who specialize in the treatment of PI.

To access the list of specialists, click "Find a Clinician" below and provide your name and email.

If you are a clinician who would like to update your information or be added to the list, click "Add me to the Finder."

<https://primaryimmune.org/resource-center>



Connect & Collaborate



Monthly Lunch & Learns

Medical experts provide education on various diagnosis-specific topics.



IDF Webinars

Top Clinicians present on medical and lifestyle topics most pressing to the PI Community.



Get Connected Groups

Individuals and families living with PI can connect with others in their local community or online.



ASK IDF

Submit your questions about insurance, treatment options and more!



Annual PI Conference

Attend presentations from top immunology experts and engage with others in the PI Community.

WELCOME!

Francisco Bonilla, MD PhD
Northeast Allergy, Asthma & Immunology





FRANCISCO A. BONILLA, M.D., PH.D.
NORTHEAST ALLERGY ASTHMA & IMMUNOLOGY

IMMUNE DEFICIENCY FOUNDATION
LUNCH AND LEARN
JANUARY 2023

Specific antibody deficiency

Incidence and prevalence of antibody deficiency

- ▶ Estimated for all immune deficiencies:
 - ▶ Prevalence - 1/1,000-2,000 based on registries/surveys
- ▶ For antibody deficiency (roughly half of all primary immunodeficiencies):
 - ▶ Prevalence - 1/2,000-4,000

Symptoms of antibody deficiency

- ▶ Recurrent otitis media, sinusitis, pneumonia
- ▶ Also cellulitis, osteomyelitis, meningitis, etc.
- ▶ Frequent viral infections
- ▶ Enteric infections (especially enteroviruses)
- ▶ Onset of infections may be delayed
 - ▶ *Protection by maternal Ab*
 - ▶ *Syndrome of late onset*
- ▶ Allergy (some)
- ▶ Autoimmune disease (some)
- ▶ Malignancy (some)

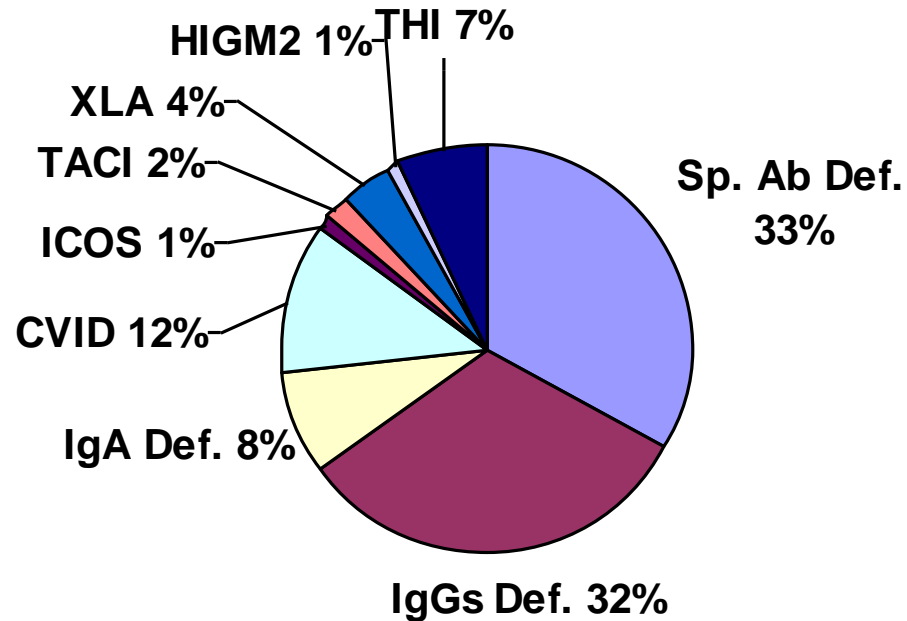
Antibody deficiency: Infectious organisms

- ▶ Bacteria: pneumococcus, H. influenzae type B (HIB), Moraxella, meningococcus, Staphylococcus aureus, Pseudomonas, Campylobacter
- ▶ Mycoplasma, ureaplasma
- ▶ Viruses: Rhinovirus, Influenza, RSV, SARS-CoV-2, enteroviruses, rotavirus, Norovirus
- ▶ Protozoa: giardia, cryptosporidium

Antibody Deficiencies

- ▶ Agammaglobulinemias, XL, AR
- ▶ Class-switch defects ("hyper-IgM" syndromes)
- ▶ Common variable immunodeficiency
- ▶ IgA deficiency
- ▶ IgG subclass deficiency
- ▶ Specific antibody deficiency
- ▶ Transient hypogammaglobulinemia of infancy

Antibody deficiencies



Immunoglobulins

- ▶ A class of antibody (Ab) or immunoglobulin (Ig), produced by B cells (plasma cells)
- ▶ Five main types of Ig:
 - ▶ IgG, IgA, IgM, IgD, IgE
- ▶ IgG has the highest concentration in the blood
- ▶ Four kinds (subclasses) of IgG:
 - ▶ IgG1, IgG2, IgG3, IgG4
- ▶ Two subclasses of IgA
 - ▶ IgA1, IgA2

Antibody

- ▶ Immunoglobulin that is **SPECIFIC** for an **ANTIGEN**
- ▶ Part of a germ or microbe/pathogen
- ▶ For example, COVID spike protein, etc.

Immunological evaluation: humoral immunity

- ▶ Immunoglobulin levels, IgG, IgA, IgM, IgE, IgG subclasses (IgG1, 2, 3, 4)
- ▶ Specific antibody titers (tetanus, diphtheria, Hib, pneumococcus, meningococcus, isohemagglutinins, other)
- ▶ Response to immunization (tetanus and diphtheria toxoids, Hemophilus influenzae B, Pneumovax, Prevnar, Menactra)

Pneumococcal responses (provisional criteria)

- ▶ Protective level - 0.35-1.3 mcg/mL
 - ▶ Depends on type of vaccine
- ▶ Adequate response (single serotype) - >4 fold rise in titer
 - ▶ *Rise in titer is less if pre-immunization level is high*
- ▶ Adequate response (multiple serotypes)
 - ▶ < 2 years - unreliable
 - ▶ 2-5 years - $\geq 50\%$ of serotypes
 - ▶ > 5 years - $\geq 70\%$ of serotypes
- ▶ May depend on method of measurement

Specific antibody deficiency (with normal immunoglobulins)

- ▶ Recurrent sinopulmonary infections
- ▶ Normal IgG, IgA, IgM, IgG subclasses
- ▶ Impaired vaccine response (polysaccharide)
- ▶ Impaired antibody response to natural infection with encapsulated bacteria
- ▶ Normal B cell number
- ▶ Normal T cell number and function
- ▶ Impaired memory B cell development?

Therapy for antibody deficiency

- ▶ Avoidance
- ▶ Antibiotic therapy/prophylaxis
- ▶ Gamma globulin (immunoglobulin)

Goal of Treatment

- ▶ Prevent infection
- ▶ Reduce frequency of infections
- ▶ Reduce severity of infections
- ▶ Allow normal lifestyle

Treatment Options

- ▶ Recurrent Infections:
 - ▶ Improve vaccine responses: protein conjugated vaccines
 - ▶ Provides memory and efficiency of immune response to proteins
 - ▶ Limited to the vaccine being administered
 - ▶ Does not cover the large variety of possible pathogens

Treatment Options

- ▶ Recurrent Infections:
 - ▶ Preventative antibiotics
 - ▶ Lower but daily doses
 - ▶ Potential for growth of antibiotic-resistant bacteria (can rotate antibiotics)
 - ▶ Does not cover viral infections
 - ▶ Allergic reactions to antibiotic
 - ▶ Other side effects of antibiotic

Treatment Options

- ▶ Antibody replacement IVIG (every 3-4 weeks) or Subcutaneous IG (weekly)
- ▶ Protection against common pathogens (bacterial and viral)
- ▶ Side effects of Ig replacement
- ▶ Higher cost

Approach to Treatment

Ig replacement vs. antibiotic prophylaxis:

- ▶ Severity of infections (such as hospitalization or ICU for pneumonia, sepsis, meningitis)
- ▶ Complications of infections (hearing loss, speech development in young children)
- ▶ Quality of life and school/work attendance
- ▶ Failure of antibiotics to prevent infections

Safety of Ig products

- ▶ Plasma donation from healthy donors with 2 forms of identification and local address
- ▶ 60-day hold on all plasma donations until subsequent donation
- ▶ Most donors are repeat donors
- ▶ Ig products in US from US-derived plasma
- ▶ Antibody and PCR detection of viruses
- ▶ HIV was never transmitted
- ▶ Hepatitis C was transmitted in 1994
- ▶ Tests are now available for prions

Side effects of IVIG therapy

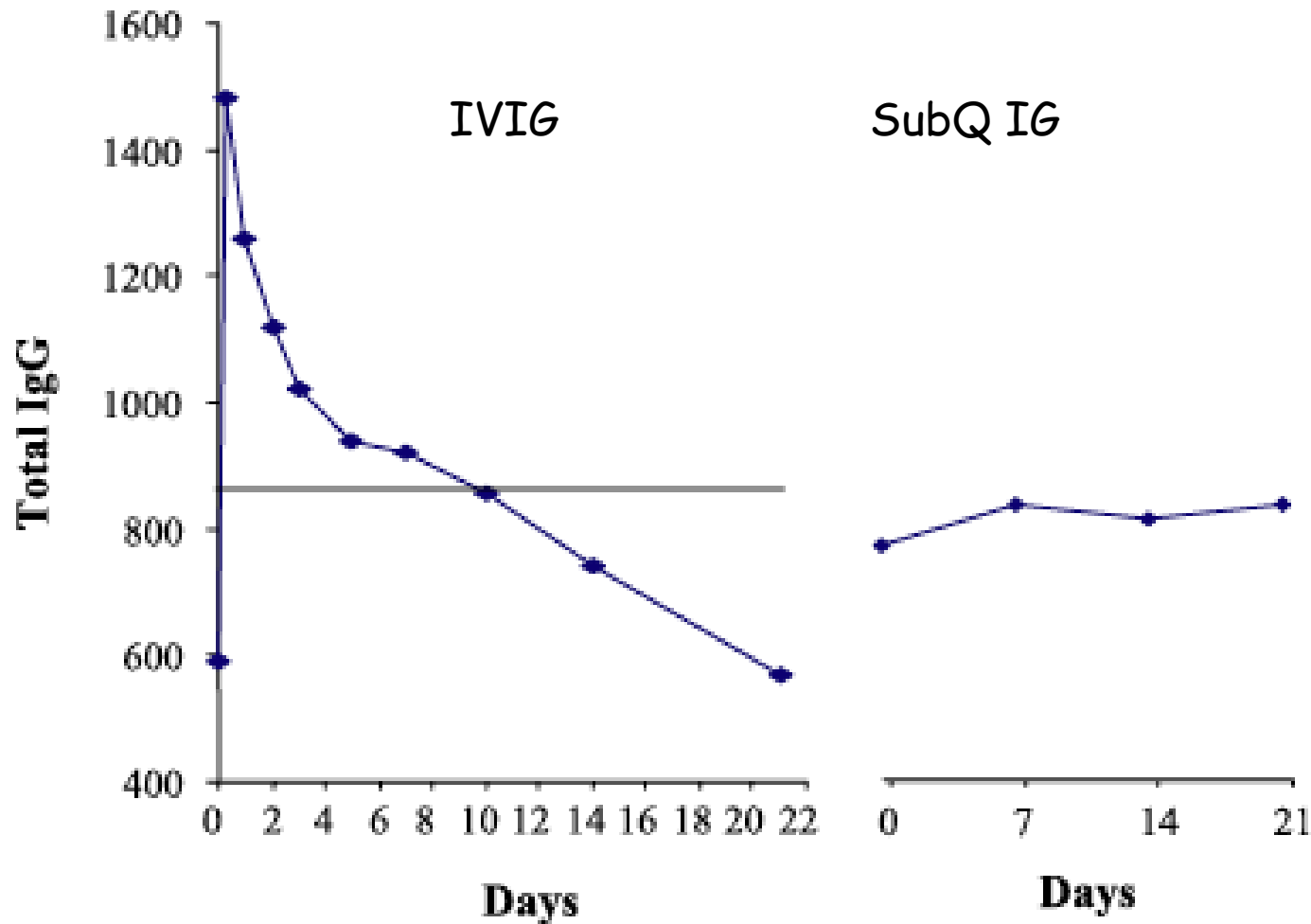
- Transfusion-like reactions: fever, chills
- Allergic reactions especially in totally IgA deficient patients (IgA in IVIG is recognized as a foreign protein, this is not common)
- Aseptic meningitis (Ibuprofen, slow rate of infusion)
- Renal dysfunction, thrombosis reported but rare
- Transient neutropenia
- Transmission of blood-borne viruses (none since Hepatitis C transmission in 1994)

Side effects of SubQ Ig therapy



- Limited to local side effects such as pain, redness and swelling at site of infusion
- Much fewer side effects as seen with IVIG

Comparison of IgG levels



Benefits of Ig Replacement

- ▶ Increased life expectancy
- ▶ Reduced frequency of bacterial infections
- ▶ Greater morbidity with delay in diagnosis and start of therapy
- ▶ Higher dose associated with decreased rate of infections

Conclusion

- ▶ Specific antibody deficiency leads to a susceptibility to recurrent infections
- ▶ Treatment of antibody deficiency is conceptually unchanged since the first described by Bruton in 1952 (Antibody Replacement)
- ▶ Improvement in Ig products: increased effectiveness with decreased side effects
- ▶ Early diagnosis and early start of treatment improves outcome and quality of life



IDF Immune
Deficiency
Foundation

Q & A

alt

THANK YOU!

Francisco Bonilla, MD PhD
Northeast Allergy, Asthma & Immunology



Additional Resources

- **ASK IDF:** www.Primaryimmune.org/ask-idf
 - 800-296-4433
- **IDF Resource Center:**
 - <https://primaryimmune.org/resource-center>
- **IDF Support Services:**
 - <https://primaryimmune.org/support-services>
- **IDF's YouTube Channel**
 - We record and upload all IDF Education sessions
 - <https://www.youtube.com/user/IDFvideos>





Upcoming Events

Walk for PI End of Year Celebration

Tuesday, 1/31/23

7:00-8:30PM ET

IDF Webinar: The Use of Prophylactic Antibiotics in Antibody Deficiencies

Ken Paris, MD, MPH

Thursday, 2/16/23

7:00-8:30PM ET



For a list of all upcoming IDF Events, visit:

https://community.primaryimmune.org/s/events?language=en_US



From all of us at IDF

Thank You!

Abe Frances CHRIS Lorraine Jarey ANGELA Katherine Rachel
 Lynn Mikhael Chuck Fci Stephanie Karen Zach
 Emma Kathy Alissa Jennifer Brian Cheryl Pat Tazary Aimee Sarah Christopher
 Amy Julieann Adam Wanda STEPHANIE Colleen Bianca Doreen Jamie
 Noora Kim

You make the IDF community stronger

