Dear Friends of the Foundation,

Welcome to the PFF Summit 2013: From Bench to Bedside. This is our second biennial scientific healthcare conference. We are once again quite fortunate in being able to assemble an outstanding, international faculty. We hope that fostering this type of collaboration will lead to improved diagnosis, better patient care, and help stimulate the research needed to find better treatments—and ultimately, a cure—for idiopathic pulmonary fibrosis (IPF). We are pleased to once again provide sessions for both professionals and patients and caregivers. Education is an important part of our mission, and in order to reach as many people as possible, webinars of all sessions will be available post-Summit.

As many of you know, the Foundation was the brainchild of my father, Albert Rose, and his brother, Mike Rosenzweig, who had IPF. Their sister, Claire, died from the disease and they were both personally driven to help find a cure. My father died in 2002, but his brother continued to work passionately to help find a cure until he passed away in 2012. I am extremely honored to carry on our family legacy as Chief Executive Officer and Chairman of the Board of Directors for the Foundation. Over the past twelve years, the Foundation has become a beacon for those afflicted with this deadly disease. Summit 2011 was highly successful and created many new in-roads for international collaboration, enabling us to provide more information and support to patients, and to help clinicians and researchers around the world make meaningful connections with one another.

Many people have worked hard to organize this year’s Summit. I would like to thank the Foundation’s staff and our partner, National Jewish Health, for what was truly a team effort to make this event a success. Of course, many thanks must go to our “all star” faculty for sharing with us their knowledge and expertise. Lastly, I would like to thank both our individual and corporate sponsors for their generosity.

Since we last gathered for Summit 2011, there has been an increase in interest in drug development for IPF. There are a number of exciting therapies that are in early development while others are working their way through the clinical trial process. It is critically important for patients to participate in clinical trials. This is the only way we can develop new, effective treatments. I am continually impressed and motivated by the courage and commitment of the patients and their family members. They are a constant source of inspiration to all of us, and I assure everyone that we will continue to work tirelessly to help find a cure for IPF.

Warmest Regards,

DANIEL M. ROSE, MD
CHIEF EXECUTIVE OFFICER AND CHAIRMAN OF THE BOARD OF DIRECTORS
PULMONARY FIBROSIS FOUNDATION
Dear Patients and Caregivers,

It is a true pleasure to welcome you to the *PFF Summit 2013: From Bench to Bedside*. Despite two decades of progress, our understanding of the pathobiology, and more importantly, our ability to treat pulmonary fibrosis (PF), remains a challenge. In order to address this deficit we held the first *Summit* in 2011 to expand our collective knowledge and encourage the development of new treatment options. This year, physicians, researchers, patients, family members, and industry representatives are gathering together again to learn, collaborate, and share information.

The Pulmonary Fibrosis Foundation and National Jewish Health have organized the *PFF Summit 2013* to provide the most up-to-date material to the medical and research communities and much-needed information and support to those affected by this disease. This innovative conference includes a faculty of distinguished experts in the field of pulmonary fibrosis from around the world who have created an outstanding program. The *Summit* gives us an opportunity to combine our talents and dedication to work towards a single goal: making a difference to those who suffer from PF.

We are honored and excited to be the Program Chairs for the *PFF Summit 2013*, and thank each of you for attending and sharing your experience, knowledge, and expertise. Your engagement and input during the *Summit* will help shape the next decade of pulmonary fibrosis research, and through our collective efforts we can improve the future of those affected by these terrible diseases.

Sincerely,

**GREGORY P. COSGROVE, MD**  
NATIONAL JEWISH HEALTH & UNIVERSITY OF COLORADO DENVER

**MARTIN KOLB, MD, PHD**  
MCMASTER UNIVERSITY

**PATRICIA J. SIME, MD**  
UNIVERSITY OF ROCHESTER MEDICAL CENTER
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OUR MISSION

The mission of the Pulmonary Fibrosis Foundation (PFF) is to help find a cure for idiopathic pulmonary fibrosis (IPF), advocate for the pulmonary fibrosis community, promote disease awareness, and provide a compassionate environment for patients and their families.

CURRENT INITIATIVES

The PFF’s strategic plan includes initiatives to:

• Increase funding for PF research through independent foundation grants, and partnership grants with the American Thoracic Society, the American College of Chest Physicians, and the National Institutes of Health.

• Facilitate collaboration between the academic research community and the bio-pharma industry.

• Establish a Pulmonary Fibrosis Foundation Care Center Network and Pulmonary Fibrosis Foundation Patient Registry.

• Foster interaction and innovation among physicians, researchers, allied health professionals, patients, and caregivers at our biennial international conference, *PFF Summit: From Bench to Bedside*.

• Expand our support group network to include the international PF community, assist in the development of local support groups, and improve access to the PFF online support groups.

• Implement new patient education and disease awareness programs utilizing webinars, online support services, and social media platforms.

• Support the needs of our constituents through legislative advocacy.

• Increase disease awareness though education, traditional media, social media, and community events.
HISTORY

The Pulmonary Fibrosis Foundation (PFF) is a 501(c)(3) nonprofit organization that was founded in 2000 by two brothers, Albert Rose and Michael Rosenzweig, PhD. Their sister Claire died from idiopathic pulmonary fibrosis (IPF), and both brothers were later diagnosed with the disease. Their vision shaped the PFF to become the leader in the pulmonary fibrosis community for research, advocacy, awareness, and patient support. In February of 2002 Albert Rose succumbed to the disease.

Dr. Rosenzweig was the Foundation’s first President and Chief Executive Officer. He worked tirelessly and passionately to build the Foundation, fund research, and create a financially viable entity. He also helped recruit an outstanding Medical Advisory Board, which has provided keen insight and direction.

Daniel M. Rose, MD, the son of Albert Rose and chairman of the Board of Directors, assumed the positions of President and Chief Executive Officer in March 2009 when Dr. Rosenzweig retired due to the progression of his disease. Dr. Rose had previously been a practicing cardiothoracic surgeon and Chief of Cardiothoracic Surgery at St. Vincent’s Medical Center in Bridgeport, Connecticut, for 19 years. Having had three relatives afflicted with IPF, he brings to the Foundation a family member’s passion and motivation, along with a broad medical background and a profound desire to lead the PFF in its second decade.

Dr. Rosenzweig lost his courageous battle against IPF on June 23, 2012. Dr. Rose and the Foundation’s staff are honored to carry on his vision of finding successful treatments and hopefully a cure for pulmonary fibrosis. Learn more about how the PFF is making a difference to the PF community at www.pulmonaryfibrosis.org.
the foundation
about the pulmonary fibrosis foundation

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National Jewish Health
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*Member of the Research Advisory Committee
One of the primary goals of the Pulmonary Fibrosis Foundation (PFF) is to fund research that will lead to successful therapies for pulmonary fibrosis (PF). As part of this commitment, the Foundation supports new research through grants funded solely by the PFF and through partnership grants with other organizations.

The PFF Research Fund was established with the primary goal of funding innovative grants that offer a high likelihood of advancing research that could translate into successful therapies.

**PRIMARY OBJECTIVES**

**FUND INNOVATIVE AND PROMISING RESEARCH**

- **I.M. Rosenzweig Young Investigator Awards:** These awards of up to $50,000, given over a two-year period, encourage young investigators* to maintain and enhance their interest in PF research during the early stages of their academic careers. (*individuals within five years of completion of their formal training)*

- **Albert Rose Established Investigator Awards:** These awards of up to $50,000, given over a two-year period, allow established investigators* to explore innovative areas of research that may not yet be eligible for federal grants. (*individuals who have demonstrated a clear record of successful independent research as defined by publication record and current or previous funding from a major organization)*

- **Special Needs Awards:** These awards, granted periodically as needs arise, provide funds for investigators and institutions to “fill the gaps” of financial need where unique circumstances exist and additional funding will help advance an exceptional research effort.

- **Partnership grants with the American Thoracic Society and the American College of Chest Physicians:** These unique partnerships allow the PFF, in collaboration with leading lung health organizations, to jointly award grants focusing on PF.

**PROVIDE DONOR GRANT GUIDANCE AND ADMINISTER DONOR-ADVISED FUNDS**

The Foundation provides oversight for a donor wishing to make a restricted gift to a specific institution (or institutions) or support a specific research project. The Foundation receives a small percentage of the total grant to administer the grant and to provide oversight.

**FOSTER FUNDING OPPORTUNITIES FOR PF RESEARCH**

The Foundation continually seeks ways to increase research funding through partnerships with industry, governmental agencies, and other foundations.

Learn more at [www.pulmonaryfibrosis.org/research/PFFgrants](http://www.pulmonaryfibrosis.org/research/PFFgrants).
LET THE WORLD KNOW SEPTEMBER 2014

www.globalPFawareness.org
save the date!

NOVEMBER 12–14, 2015

We’ve set the date, now help us choose the location.

Cast your vote at the Registration Desk or email summit@pulmonaryfibrosis.org with the city of your choice in the subject line.

To receive information about the *PFF Summit 2015*, or to be placed on the pre-registration list, please email summit@pulmonaryfibrosis.org or call 888.733.6741 or +1 312.587.9272.
NAME BADGE

Your name badge is your admittance to activities during the conference. Please wear your badge for the duration of the conference.

GENERAL SESSION, EXHIBIT/POSTER HALL, AND MEALS

You must have a name badge to enter the sessions, Exhibit/Poster Hall, and to participate in the Welcome Reception, Networking Dinner, and meal functions. The Exhibit/Poster Hall is located in the Vicino Ballroom and is open during the following hours:

- Thursday, December 5: 5:00 p.m. – 8:00 p.m.
- Friday, December 6: 7:00 a.m. – 5:45 p.m.
- Saturday, December 7: 6:45 a.m – 3:00 p.m.

Breakfasts, lunches, and breaks are for meeting registrants only.

CELL PHONES AND PAGERS

Please be courteous to fellow participants and turn your phones and pagers to silent during the sessions.

“TOGETHER WE WILL MAKE A DIFFERENCE IN PF . . .”

MESSAGE BOARD AND COMMUNITY MAP

Connect. Collaborate. Inspire. The Message Board is a place for conference attendees to leave inspirational messages.

The Community Map is a visual representation of how the PF community has assembled at the Summit. Mark your hometown with a color-coded pin that indicates your interest in PF.

We want all of you to have an impact and “make a difference!” Both boards are located near the Registration Desk.

EVALUATION FORM

Your feedback is important to us and will help us plan future Summits. Please remember to complete your evaluation form and return it to the Registration Desk.
OXYGEN STATION

Oxygen refills will be available during Summit hours on Friday, December 6 and Saturday, December 7 to patients with valid prescriptions and who have made an advanced request.

MEDICAL EMERGENCIES

If you are experiencing a medical emergency, please call 911. There is no physician or nurse on site who can legally see or care for a patient with a medical emergency.

PHOTOGRAPHY, FILMING, AND RECORDING OF PFF SUMMIT 2013

The PFF Summit 2013 will be photographed, videotaped, and/or recorded in its entirety by staff and third party vendors. All sessions will be available post-conference on, but not limited to, the Pulmonary Fibrosis Foundation’s and PFF Summit’s websites. Crews will be videotaping and taking still photographs of all sessions, meals, and periphery Summit activities. Conference video, still photographs, and quotes may be used and/or repurposed in promotional materials for the PFF and future Summits, including but not limited to the websites, print materials, and social media. All attendees will be asked to sign a Release at registration. For those who do not wish to be filmed or photographed, please be sure to get an orange name badge lanyard at registration for identification. Recording of any session by attendees is strictly prohibited.

DISCLAIMER

The views of the speakers do not necessarily reflect the views of the presenting, partnering, or endorsing organizations. The Pulmonary Fibrosis Foundation and National Jewish Health present this information for educational purposes only. The content is provided solely by faculty who have been selected because of recognized expertise in their field. Participants have the professional responsibility to ensure that products are prescribed and used appropriately on the basis of their own clinical judgment and accepted standards of care. The Pulmonary Fibrosis Foundation and National Jewish Health assume no liability for the information herein.

QUESTIONS OR ASSISTANCE

If you have any questions or need assistance, please visit the Registration/Information Desk.
meeting info and space map(s)
navigating the summit

THURSDAY

1. INFORMATION DESK
   GRAND FOYER

2. EXHIBIT HALL
   VICINO BALLROOM

3. POSTER HALL
   VICINO BALLROOM

A. WELCOME RECEPTION AND
   POSTER PRESENTATIONS
   VICINO BALLROOM
meeting info and space map(s)
navigating the summit

FRIDAY

1 REGISTRATION/INFORMATION DESK
   GRAND FOYER

2 EXHIBIT HALL
   VICINO BALLROOM

3 POSTER HALL
   VICINO BALLROOM

4 PATIENT AND CAREGIVER SESSIONS
   AVENTINE BALLROOM A, B, C

5 PROFESSIONAL SESSIONS
   AVENTINE BALLROOM D, E, F, G

6 PATIENT AND CAREGIVER SESSIONS
   OVERFLOW
   PALATINE

7 PROFESSIONAL SESSIONS OVERFLOW
   PORTOFINO

8 SPEAKER READY (FACULTY AND STAFF ONLY)
   PALMERO

9 OXYGEN REFILLS
   FOYER II

A ONLINE > OFFLINE MEET + GREET
   (PATIENTS AND CAREGIVERS ONLY)
   FOYER II

B NETWORKING DINNER RECEPTION
   ASTERIA TERRACE, FOYERS

C NETWORKING DINNER
   AVENTINE BALLROOM
meeting info and space map(s)
navigating the summit

SATURDAY

1. REGISTRATION/INFORMATION DESK
   GRAND FOYER

2. EXHIBIT HALL
   VICINO BALLROOM

3. POSTER HALL
   VICINO BALLROOM

4. PATIENT AND CAREGIVER SESSIONS
   AVENTINE BALLROOM A, B, C

5. PROFESSIONAL SESSIONS
   AVENTINE BALLROOM D, E, F, G

6. PATIENT AND CAREGIVER SESSIONS OVERFLOW
   PALATINE

7. PROFESSIONAL SESSIONS OVERFLOW
   PORTOFINO

8. SPEAKER READY (FACULTY AND STAFF ONLY)
   PALATINE

9. OXYGEN REFILLS
   FOYER II
# Friday > Sessions

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<td>8:00 a.m.– 9:00 a.m.</td>
<td>REGISTRATION AND CONTINENTAL BREAKFAST</td>
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<td>9:00 a.m.– 9:15 a.m.</td>
<td>WELCOME AND INTRODUCTION</td>
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<tr>
<td></td>
<td>Daniel M. Rose, MD</td>
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<td>CEO and Chairman of the Board, Pulmonary Fibrosis Foundation</td>
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<tr>
<td>9:15 a.m.– 9:45 a.m.</td>
<td>OPENING SESSION KEYNOTE ADDRESS</td>
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<td>Robert J. Beall, PhD</td>
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<td>President and CEO, Cystic Fibrosis Foundation</td>
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<tr>
<td>9:45 a.m.– 10:15 a.m.</td>
<td>WHAT IS PULMONARY FIBROSIS, WHAT ARE THE CAUSES, AND HOW IS IT TREATED?</td>
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<td>Harold R. Collard, MD</td>
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<td>10:15 a.m.– 10:45 a.m.</td>
<td>VISIT EXHIBITS AND VIEW POSTERS</td>
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<tr>
<td>10:45 a.m.–11:15 a.m.</td>
<td>WHAT IS AUTOIMMUNE RELATED PULMONARY FIBROSIS?</td>
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<td>Richard T. Meehan, MD</td>
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<tr>
<td>11:15 a.m.– 11:45 a.m.</td>
<td>WHAT IS PULMONARY HYPERTENSION AND HOW IS IT RELATED TO PF?</td>
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<td>Serpil C. Erzurum, MD</td>
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<td>11:45 a.m.–12:15 p.m.</td>
<td>VISIT EXHIBITS AND VIEW POSTERS</td>
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<tr>
<td>12:15 p.m.–12:45 p.m.</td>
<td>SPECIAL LUNCHEON SPEAKER</td>
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<td>WHEN DRUG RESEARCH IS PERSONAL: THE IMPORTANCE OF PATIENT ADVOCACY IN</td>
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<td>DRUG DEVELOPMENT AND INNOVATION</td>
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<td>John F. Crowley, JD, MBA</td>
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<td>Chairman and CEO, Amicus Therapeutics</td>
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<tr>
<td>12:45 p.m.– 1:00 p.m.</td>
<td>BREAK</td>
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<tr>
<td>1:00 p.m.– 1:30 p.m.</td>
<td>OCCUPATIONAL AND ENVIRONMENTAL CAUSES OF PULMONARY FIBROSIS</td>
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<td>Cecile S. Rose, MD</td>
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<td>Time</td>
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</table>
| 1:30 p.m.–2:15 p.m. | **ROUNDTABLES: QUESTIONS AND ANSWERS WITH THE EXPERTS**  
|               | **PF SPECIALIST:** Harold R. Collard, MD  
|               | **RHEUMATOLOGIST:** Richard T. Meehan, MD  
|               | **OCCUPATIONAL AND ENVIRONMENTAL SPECIALIST:** Cecile S. Rose, MD, MPH  
|               | **PAH SPECIALIST:** Serpil C. Erzurum, MD  
|               | **ILD NURSE SPECIALIST:** Susan S. Jacobs, RN, MS  |
| 2:15 p.m.–2:30 p.m. | **CLOSING REMARKS**  
|               | Dolly Kervitsky, RCP, CCRC  
<p>|               | Vice President, Patient Relations and Medical Affairs, Pulmonary Fibrosis Foundation |
| 5:30 p.m.–6:30 p.m. | <strong>ONLINE &gt; OFFLINE PATIENT MEET &amp; GREET</strong> |
| 6:30 p.m.–10:00 p.m. | <strong>NETWORKING DINNER</strong> |</p>
<table>
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<td>Daniel M. Rose, MD&lt;br&gt;CEO and Chairman of the Board, Pulmonary Fibrosis Foundation</td>
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<tr>
<td>9:15 a.m.–9:45 a.m.</td>
<td>RESEARCH TRIALS, STEM CELL THERAPIES, AND THE DRUG PIPELINE</td>
<td>Erica L. Herzog, MD, PhD</td>
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<td>9:45 a.m.–10:15 a.m.</td>
<td>LUNG TRANSPLANTATION AND PF</td>
<td>Errol L. Bush, MD</td>
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<tr>
<td>10:15 a.m.–10:45 a.m.</td>
<td>VISIT EXHIBITS AND VIEW POSTERS</td>
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<tr>
<td>10:45 a.m.–11:15 a.m.</td>
<td>THE FINAL STAGES OF PULMONARY DISEASE</td>
<td>Molly Bourne, MD</td>
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<tr>
<td>11:15 a.m.–11:45 a.m.</td>
<td>TOOLS FOR LIVING BETTER WITH PULMONARY FIBROSIS</td>
<td>Susan S. Jacobs, RN, MS</td>
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<tr>
<td>11:45 a.m.–12:00 p.m.</td>
<td>EFFECTIVE ADVOCACY FOR PULMONARY FIBROSIS</td>
<td>Brian Baird, MS, PhD</td>
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<tr>
<td>12:00 p.m.–1:00 p.m.</td>
<td>LUNCH</td>
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<tr>
<td>1:00 p.m.–1:15 p.m.</td>
<td>THE ROLE OF THE US FDA IN THE PROCESS OF DRUG DEVELOPMENT</td>
<td>Eugene J. Sullivan, MD</td>
</tr>
<tr>
<td>1:15 a.m.–1:30 p.m.</td>
<td>US FOOD AND DRUG ADMINISTRATION—PATIENT-FOCUSED DRUG DEVELOPMENT PROGRAM</td>
<td>Richard M. Klein</td>
</tr>
</tbody>
</table>
### ROUNDTABLES: QUESTIONS AND ANSWERS WITH THE EXPERTS

**PF SPECIALIST:** Erica L. Herzog, MD, PhD

**PALLIATIVE AND HOSPICE CARE:** Molly Bourne, MD

**LUNG TRANSPLANT SPECIALIST:** Errol L. Bush, MD

**FAMILIAL PF, GENETIC COUNSELING:** Robin R. Deterding, MD; Janet Talbert, MS, CGC

**ILD NURSE SPECIALISTS:** Kathleen O. Lindell, PhD, RN; Susan S. Jacobs, RN, MS

**ADVOCACY:** Brian Baird, MS, PhD; Richard M. Klein; Eugene J. Sullivan, MD

### 2:30 p.m.–2:40 p.m.  CLOSING REMARKS

Dolly Kervitsky, RCP, CCRC

Vice President, Patient Relations and Medical Affairs,

Pulmonary Fibrosis Foundation
program faculty

**GREGORY P. COSGROVE, MD**
**CO-CHAIR**
National Jewish Health
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AS OF NOVEMBER 16, 2013

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The Pulmonary Fibrosis Foundation is grateful to our generous sponsors for helping us fulfill our mission. Their support helps us assist the entire PF community in so many ways. Thank you to our sponsors for assisting us in funding research, advocating on behalf of the PF community, raising awareness and providing education, and playing a critical role in the lives of thousands of patients and families with whom we connect each year. Together we will win the fight against pulmonary fibrosis.
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CHILD (CHILDREN’S INTERSTITIAL AND DIFFUSE LUNG DISEASE)
NORMAN, OKLAHOMA

Our Mission is to accelerate research to cure all forms of Children’s Interstitial and Diffuse Lung Disease (chILD) and to provide compassionate support, education, and hope to children and families affected by these life-altering diseases. chILD is not a single disease. Instead it is a group of several rare disorders that affect infants and children, and some of the underlying causes may be linked to adult lung disease.

INSPIRE
PRINCETON, NEW JERSEY

Inspire is the patient engagement company. We build and manage online peer-to-peer support communities for more than 400,000 patients and caregivers, and help industry connect to members for the purpose of research. We partner on our communities with more than 100 nonprofit patient advocacy organizations, including the Pulmonary Fibrosis Foundation, Genetic Alliance, Ovarian Cancer National Alliance, and National Psoriasis Foundation. Find out more at http://corp.inspire.com or by contacting us at team@inspire.com.

INTERMUNE
BRISBANE, CALIFORNIA

InterMune is a biotechnology company focused on the research, development and commercialization of innovative therapies in pulmonology and orphan fibrotic diseases. In pulmonology, the company is focused on therapies for the treatment of idiopathic pulmonary fibrosis (IPF), a progressive, irreversible, unpredictable and ultimately fatal lung disease. InterMune’s research programs are focused on the discovery of targeted, small-molecule therapeutics and biomarkers to treat and monitor serious pulmonary and fibrotic diseases. For additional information about InterMune and its R&D pipeline, please visit www.intermune.com.
MAYO CLINIC
ROCHESTER, MINNESOTA

At Mayo Clinic, over 3,800 doctors and scientists and over 58,000 allied health staff work together to care for people from all walks of life, joined by common systems and a philosophy of “the needs of the patient come first.” Mayo Clinic is a nonprofit organization; for more Mayo news visit www.mayoclinic.org/news.

NATIONAL JEWISH HEALTH
DENVER, COLORADO

Our mission since 1899 is to heal, discover, and to educate as a preeminent healthcare institution. We serve by providing the best integrated and innovative care for patients and their families; by understanding and finding cures for the diseases we research; and by educating and training the next generation of healthcare professionals to be leaders in medicine and science.

National Jewish Health is the leading respiratory hospital in the nation, treating patients from all over the country and conducting innovative and groundbreaking research to improve health worldwide.

PATIENTSLIKEME
CAMBRIDGE, MASSACHUSETTS

PatientsLikeMe® (www.patientslikeme.com) is an online patient network that improves lives and a real-time research platform that advances medicine. Patients connect with others who have the same disease or condition and track their own experiences. In the process, they generate data about the real-world nature of disease that help researchers, pharmaceutical companies, providers, and nonprofits develop more effective products and services. PatientsLikeMe is a trusted source for real-world information and has published more than 35 peer-reviewed articles.

PULMONARY FIBROSIS FOUNDATION
CHICAGO, ILLINOIS

The mission of the Pulmonary Fibrosis Foundation (PFF) is to help find a cure for idiopathic pulmonary fibrosis (IPF), advocate for the pulmonary fibrosis community, promote disease awareness, and provide a compassionate environment for patients and their families. The PFF collaborates with physicians, organizations, patients, and caregivers worldwide. For more information visit www.pulmonaryfibrosis.org.
**SCLERODERMA FOUNDATION, GREATER SAN DIEGO CHAPTER**
SAN DIEGO, CALIFORNIA

Scleroderma is a rare autoimmune disease for which there is no known cause or cure. Symptoms range from extreme fatigue and joint discomfort to life threatening, hardening of skin and various organs. Treatments exist to alleviate certain symptoms, but we strive to find a cure. Our three-fold mission is providing Support, Education and Research for patients and families affected by scleroderma. We offer monthly Support Group meetings, Education Days, walkathons for Research, and more.

**UNIVERSITY OF SOUTHERN CALIFORNIA, CENTER FOR ADVANCED LUNG DISEASE**
LOS ANGELES, CALIFORNIA

The USC Center for Advanced Lung Disease is dedicated to helping patients to breathe easier, live longer and enjoy a better quality life by providing excellent, innovative and patient-centered care. Our lung experts provide highly specialized evaluations and treatment options for all patients suffering from complex lung diseases, regardless of their transplant status. Referring physicians have rapid access to physicians who offer vast experience in treating the most severe cases of advanced lung disease. Our personalized interdisciplinary approach consists of many specialties, resulting in comprehensive and individualized diagnostic and treatment plans that produce optimal outcomes.
sessions overview
friday and saturday

friday

OPENING SESSION KEYNOTE ADDRESS
Robert J. Beall, PhD
President and CEO, Cystic Fibrosis Foundation

WHAT IS PULMONARY FIBROSIS,
WHAT ARE THE CAUSES, AND HOW
IS IT TREATED?
Harold R. Collard, MD

WHAT IS AUTOIMMUNE RELATED
PULMONARY FIBROSIS?
Richard T. Meehan, MD

WHAT IS PULMONARY HYPERTENSION
AND HOW IS IT RELATED TO PF?
Serpil C. Erzurum, MD

SPECIAL LUNCHEON SPEAKER
WHEN DRUG RESEARCH IS PERSONAL:
THE IMPORTANCE OF PATIENT ADVOCACY
IN DRUG DEVELOPMENT AND INNOVATION
John F. Crowley, JD, MBA
Chairman and CEO, Amicus Therapeutics

OCCUPATIONAL AND ENVIRONMENTAL
CAUSES OF PULMONARY FIBROSIS
Cecile S. Rose, MD, MPH

ROUNDTABLES:
QUESTIONS AND ANSWERS WITH THE EXPERTS
Harold R. Collard, MD
Serpil C. Erzurum, MD
Susan S. Jacobs, RN, MS
Richard T. Meehan, MD
Cecile S. Rose, MD, MPH

saturday

RESEARCH TRIALS, STEM CELL THERAPIES,
AND THE DRUG PIPELINE
Erica L. Herzog, MD, PhD

LUNG TRANSPLANTATION AND PF
Errol L. Bush, MD

THE FINAL STAGES OF PULMONARY DISEASE
Molly Bourne, MD

TOOLS FOR LIVING BETTER WITH PULMONARY FIBROSIS
Susan S. Jacobs, RN, MS

EFFECTIVE ADVOCACY FOR PULMONARY FIBROSIS
Brian Baird, MS, PhD

THE ROLE OF THE US FDA IN THE PROCESS OF
DRUG DEVELOPMENT
Eugene J. Sullivan, MD

US FOOD AND DRUG ADMINISTRATION—
PATIENT-FOCUSED DRUG DEVELOPMENT PROGRAM
Richard M. Klein

ROUNDTABLES:
QUESTIONS AND ANSWERS WITH THE EXPERTS
Brian Baird, MS, PhD
Molly Bourne, MD
Errol L. Bush, MD
Robin R. Deterding, MD
Erica L. Herzog, MD, PhD
Susan S. Jacobs, RN, MS
Richard M. Klein
Kathleen O. Lindell, PhD, RN
Eugene J. Sullivan, MD
Janet Talbert, MS, CGC
Opening Session Keynote Address

ROBERT J. BEALL, PHD
PRESIDENT AND CEO, CYSTIC FIBROSIS FOUNDATION

Cystic Fibrosis Therapeutic Development
A Game Changer
December 6, 2013
Partnering for Cures

Cystic Fibrosis Foundation:
Enabling Success

Discover Magazine
September 2013

Therapeutics Era Begins in 1990’s

Doorway to a Cure
“...The Foundation imposed an urgency and focus that a biotech or pharmaceutical company functioning alone could not muster.”
September 2013

2012 - FDA Approves Ivacaftor
Drug Development for Cystic Fibrosis

**Statement of Problem:** How do you convince the biopharmaceutical industry to develop drugs for a disease with a population of less than 30,000 patients in the United States, and 70,000 worldwide?

**Solution:** Therapeutics Development Program, initiated in 1998 to provide financial and resource support to pharmaceutical partners to encourage development of new drugs for cystic fibrosis.

---

**Therapeutics Development Program “Elements of Diversity”**

- Working Hypothesis
- Access to Patients/Patient Data
- Ability to Conduct Clinical Trials
- Access to Expertise
- Financial _________
- Research _________
- Phase IV _________
### Opening Session Keynote Address (CONTINUED)

**Genotype Data**

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</table>

*Includes patients with one or two copies of the mutation.

**Harvard Business School Highlights Venture Philanthropy**

- Successful CF Foundation collaboration with Vertex selected as case study
- Validation of CF Foundation’s business model
- The CF Foundation has “really paved the way for other small disease nonprofits to take drug discovery into their own hands.”

— Harvard Professor Robert Higgins

**Cystic Fibrosis Therapeutics Development Network (CF-TDN) Established in 1998**

- Conduct Phase 1 and 2 trials for development of new therapies
- Conduct therapeutic trials of approved drugs or biologics ("low hanging fruit" studies)
- Conduct non-therapeutic studies to improve outcome measures and design better future trials
- Funding:

**High-throughput Screening**

>10,000 Primary Assays/day

**CFFT Therapeutics Development Network 2013**

**Vertex Screening for CFTR Modulators**
The CF Foundation and Kalydeco in the News

"Vertex drug is breakthrough for handful of CF patients, offers hope to many more"

"FDA approves new cystic fibrosis drug"

"Game changer" CF drug receives FDA approval

"Vertex gets early OK for new drug"

"Cystic fibrosis drug wins approval"

"Vertex receives U.S. FDA approval for Kalydeco to treat cystic fibrosis"

"FDA approves Vertex cystic fibrosis drug"

"U.S. approves Vertex cystic fibrosis drug Kalydeco"

"FDA approves Vertex’s cystic fibrosis drug"

"How science and strategic collaboration led to a new, ‘personalized’ cystic fibrosis treatment for some patients"

What About the Most Common Mutation - F508del?

50% of patients carry two copies of the F508del mutation

90% of patients carry at least one copy

Phase 3 Trial Lung Function Changes

- Two phase 3, randomized, double-blind, placebo-controlled, parallel-group, multicenter studies
- 500 subjects/study (enrollment ongoing)
- Population
  - >12 years old
  - Homozygous for F508del-CFTR mutation
  - FEV1 40% and ≤90% predicted at Screening
- Treatment duration: 24 weeks
  - With an optional open label extension
- Two daily doses of VX 809 (600 and 800mg)

Two Year Ivacaftor Lung Function Results

Possible CFTR Modulation Expansion

FIGURE 3: Mean Absolute Change from Baseline in Percent Predicted FEV₁
Ongoing Efforts to Identify the Next Generation ΔF508 CFTR Correctors

and more to follow

Benefits of TDP for Company

Access to:
• Non-diluting Capital
• Patient Population for Clinical Trials
• Clinical Trials Network
• Secondary Assays
• CF Expertise
• Population Data (patient registry)
• Access to Phase 4 Post-marketing Registry
• CFS Insurance Expertise and Launch Capability

Requirements for Adopting a TDP
• Working hypothesis about disease pathogenesis
• Targets for discovery efforts
• Significant dollars
• Establishment of accountability criteria (milestones)
• Access to patients and other resources (cell lines, secondary assays, animal models)
• Fortitude and determination (i.e., willingness to take risks)

Benefits of TDP for the CF Foundation
• New treatments
• Creation of pipeline
• Increased involvement of basic scientists in drug development
• Nucleus of major gifts program
• Creation of sense of hope and optimism with patients and families
• Leverage of discovery/development investment ($108M to $1.6B)

Lessons Learned: Life
Follow the wisdom of Wayne Gretzky:
• "You miss 100% of the shots you do not take!"
• "A good skater skates to where the puck is; a great skater skates to where the puck is going to be!"

Be willing to take risks in life:
• Every time we’ve moved ahead in IBM, it was because someone was willing to take a chance, put his head on the block, and try something new. (Thomas J. Watson)

Keep an eye out for serendipitous events – life is not a pre-planned roadmap
• "Do well and do good!"
• Relax and enjoy!

Lessons Learned: Leadership
• Have a vision—share your priorities!
• Be the architect of your organization
  ➢ Don’t be afraid to change the paradigm
  ➢ Don’t be afraid to create a new paradigm
• Be the change agent in your organization
  ➢ Take the pulse—look at customers, employees and business
  ➢ Do you have drift?
Thank you!
What is Pulmonary Fibrosis?

What is Pulmonary Fibrosis?
What Are the Causes and How is it Treated?

Harold R Collard, MD
Director, Interstitial Lung Disease Program
University of California San Francisco

Terminology

• **Pulmonary** = of or relating to the lungs
• **Fibrosis** = thickening and scarring

• “thickening and scarring of the lungs.”

Anatomy of the lungs

Lung tissue

Alveolar unit

Interstitium (tissue)

Alveolar spaces (air)
What is Pulmonary Fibrosis? (CONTINUED)

Terminology

- **Pulmonary fibrosis** is generally used in reference to thickening and scarring of the interstitium of the lung caused by diffuse interstitial lung diseases (diseases that affect most/all parts of the lungs).

What causes pulmonary fibrosis?

Consequences

- The lungs can’t breath deeply and bring in oxygen.

Normal:

```
O2
O2
O2
O2
O2
```

Fibrotic:

```
O2
```

Consequences

- Oxygen can’t move from the air to the blood.

Normal:

```
Air
O2
```

Fibrotic:

```
O2
```

Inflammation and Fibrosis

- In most cases, pulmonary fibrosis is caused by excessive inflammation in the lungs.

```
Air
O2
```

```
Blood
```

```
Lungs expand poorly and less oxygen enters
```

```
Lungs expand well and lots of oxygen enters
```

Inflammation and Fibrosis

- In most cases, pulmonary fibrosis is caused by excessive inflammation in the lungs.

```
Air
O2
```

```
Blood
```

```
Lungs expand poorly and less oxygen enters
```

```
Lungs expand well and lots of oxygen enters
```

What is Pulmonary Fibrosis? (CONTINUED)

Inflammation and Fibrosis
• In some cases, scar may occur on its own, absent inflammation.

Diagnosis: history and exam
• Description of symptoms
  – Rapid or slow onset?
  – Associated non-lung symptoms?
• Occupational and environmental history
  – Exposures to inorganic and organic dusts?
  – Cigarette smoke?
• Medications
• Family history

Inflammation and Fibrosis
• In some cases, scar may occur on its own, absent inflammation.

Diagnosis: High-resolution CT
• Thin slices of your chest and lungs
• Air is dark, tissue is grey/white
• Allows your MD to determine the cause of pulmonary fibrosis in ~50% of cases.

Categories of Pulmonary Fibrosis

Diagnosis: High-resolution CT
What is Pulmonary Fibrosis? (CONTINUED)

**Diagnosis: Surgical Lung Biopsy**
- Usually done with a small incision and camera
- Lung pieces taken from multiple sites
- Requires brief hospitalization

**How do we care for patients with pulmonary fibrosis?**

**Medical therapy**
- In diseases characterized by inflammation, drugs that reduce inflammation are used.
  - Prednisone
  - Imuran (azathioprine)
  - Cellcept (mycophenolate)
  - Cytoxan (cyclophosphamide)

**Diagnosis: Surgical lung biopsy**

**Medical therapy**
- In diseases without evidence of active inflammation, treatment is less clear.
  - Esbriet (pirfenidone)
  - Experimental therapies
What is Pulmonary Fibrosis? (CONTINUED)

Medical therapy
- Pirfenidone
- Enrollment in a clinical trial
- Immunomodulator (imuran, cellcept, cytoxan)
- Enrollment in a clinical trial
- Removal from the exposure (if known)
- Prednisone
- Immunomodulator (imuran, cellcept)

Lung Transplantation
• For select patients, a final option

Non-Medical Treatment
• Pulmonary rehabilitation
• Vaccination
• Oxygen therapy
• Education

Expectations
• In general, inflammation can resolve, fibrosis cannot.

Thank You
What is Autoimmune Related Pulmonary Fibrosis?

RICHARD T. MEEHAN, MD

Connective Tissue and Autoimmune Disease and Pulmonary Fibrosis

Richard Meehan MD
Professor of Medicine
Department of Medicine, Rheumatology, National Jewish Health

Most common autoimmune illnesses associated with ILD or pulmonary fibrosis

- Rheumatoid Arthritis
- Systemic Sclerosis “Scleroderma”
- Inflammatory myositis; Dermatomyositis and polymyositis
- Sjogrens’ syndrome
- Systemic Lupus Erythematosus “SLE”
- Undifferentiated CTD

40% of patients referred to tertiary centers with an IPF diagnosis actually have an underlying CTD related ILD which mimics IPF on high resolution CT scan

The prognosis and responsiveness to immunosuppressive therapy is much better for CTD-ILD than IPF

Systemic autoimmune diseases are the result of immune system dysregulation with resulting loss of self tolerance.

Since immune cells are mobile, any organ system including the lungs can be involved with diverse symptoms.

Clinicians should suspect and search for underlying autoimmune disease in “IPF patients” since pulmonary fibrosis may be the first symptom and non-pulmonary manifestations may be subtle.

ACR/EULAR Criteria for Classification of RA (6 of 10 = definite)

- Joint Involvement (0-5) tender & swollen
  - 2-10 median - large joint (S, E, A, H) 1
  - 1-3 small joints (MCP, PIP, IP) 2
  - 4-10 small joints 3
  - > 10 joints, at least one small 5

- Serology RF or ACPA (0-3)
  - One low positive (1.5x ULN) 2
  - One high positive 3

- Duration of synovitis (0-1) self reported
  - < 6 weeks 1

- Acute phase reactants (0-3) 1
What is Autoimmune Related Pulmonary Fibrosis? (CONTINUED)

SSC-Systemic Sclerosis “scleroderma”:

- **Skin**: tight, Raynaud’s, finger ulcers, skin calcification, dilated blood vessels (telangiectasia), abnormal nail fold, capillary microscopy
- **GI manifestations**: esophageal dysmotility (severe GERD or aspiration)
- **Laboratory**: + ANA, + SCL 70
- **Chest**: Pulmonary fibrosis (NSIP or UIP), pulmonary hypertension (cardiac echo abnormalities or heart catheter)

Muscles: painless progressive proximal muscle weakness, difficulty swallowing, Abnormal EMG, muscle biopsy

Skin: “mechanics hands”, rashes

Laboratory: ↑CPK, ↑aldolase, + anti-synthetase antibodies, + ANA

Chest: esophageal dilation, pulmonary fibrosis with consolidation
What is Autoimmune Related Pulmonary Fibrosis? (CONTINUED)

Sjogren’s Syndrome:
• Sicca Symptoms: dry mouth, hoarseness, increased dental problems, dry eyes (abnormal schirmer test and corneal ulcers)
• Salivary gland enlargement, lymph node enlargement, sub labial lip biopsy may be positive
• Lab: + ANA, + SSA, + SSB,
• Chest: fibrosis, inflammation, airway thickening, cysts
**Systemic Lupus Erythematosus**

- **Skin:** rashes (malar, Discoid), photosensitive, oral ulcers,
- **Arthritis**
- **Lab:** + ANA, DS-DNA, + Sm antibodies, anti-cardiolipin Abs, low counts (red blood cells/hemolytic, white blood cells, lymphocytes, platelets),
- **Internal organ involvement:** kidney (excess protein), Brain (Seizures/psychosis),
- **Chest:** pleuritis, bronchiolitis, hemorrhage, ILD, pulmonary infiltrates.

**Pharmacologic Treatment**

- Prednisone: rapid onset used until immune suppressive therapy starts to work.
- Immune suppressive agents: azathioprine (Imuran), Mycophenolate mofetil (Cell Cept/Myfortec), Cyclosporine/tacrolimus
- Cytotoxic: cyclophosphamide (Cytoxan)

**Other treatment options**

- Reduce Complications from Infections:
  - Immunizations
  - IVIG replacement if low levels,
  - Monitoring WBC counts,
  - GERD treatment to prevent aspiration
  - DEXA-bisphosphonates to prevent fractures

- **Other treatment options**
  - Oxygen replacement
  - Sleep study
  - Pulmonary rehabilitation
  - Physical therapy
  - Treat co morbid conditions:
    - Pulmonary Arterial Hypertension
    - Obstructive Sleep Apnea
    - Diabetes Mellitus
    - Renal insufficiency

What is Autoimmune Related Pulmonary Fibrosis? (CONTINUED)
Prognosis of CTD-ILD

- In general much better survival than IPF
- Best prognosis if diagnosed early, fibrosis is minimal and improvement in PFTS observed during therapy
- Improved prognosis if NSIP rather than UIP pattern on hrCT or BX, and if Pulmonary hypertension is not present

Conclusions

- All patients with pulmonary fibrosis should have CTD-ILD excluded with appropriate clinical, lab, imaging evaluation since prognosis and treatment is different than for IPF patients.
- A surgical lung biopsy may reveal evidence of an unsuspected CTD-ILD (lymphoid aggregates, vasculitis, pleuritis) in some patients with pulmonary fibrosis.
- A team approach of dedicated professionals is preferred for managing Patients with complex CTD-ILD (Pulmonology, Rheumatology, GI, Cardiology, PT, etc).

Prognosis of CTD-ILD

- Worse prognosis if despite aggressive immune suppressive therapy, failure to slow rate of deterioration is observed, includes: declining PFTs, increased O2 requirements and progressive fibrosis
- Transplantation is an option despite an underlying autoimmune disease

Research

- More effective, less toxic, targeted anti-fibrotic therapies are needed similar to biologic agents used to treat antibody mediated vasculitis with Rituximab (Rituxan)
- Research needed:
  - to identify genetic susceptibility for developing ILD among patients with systemic autoimmune illnesses
  - biomarkers to identify drug responsiveness among patients with CTD
notes
What is Pulmonary Hypertension and How is it Related to PF?

SERPIL C. ERZURUM, MD

Classification of Pulmonary Hypertension

1. PULMONARY ARTERIAL HYPERTENSION (PAH)
   - Idiopathic, Heritable, Drug- and toxin-induced
   - Associated with Connective tissue diseases, HIV, Portal hypertension, Congenital heart disease, Horner's syndrome
   - Persistent pulmonary hypertension of the newborn
   - Pulmonary veno-occlusive disease

2. PULMONARY HYPERTENSION DUE TO LEFT HEART DISEASE
   - Chronic obstructive pulmonary disease, Interstitial lung disease, Sleep-disordered breathing, High altitude

3. CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

4. PULMONARY HYPERTENSION -OTHER DISEASES- MULTIFAC TUAL

Pulmonary Hypertension: Clinical Definition

Mean pulmonary arterial pressure (mPAP) >25 mm Hg at rest, or >30 mm Hg during exercise, with a normal PCWP

Associated with adverse changes
- in the pulmonary vasculature (vasculopathy), and
- at the level of the right ventricle (hypertrophy)

Concept for the development of pulmonary hypertension in Pulmonary Fibrosis

Concept for the development of pulmonary hypertension in Pulmonary Fibrosis

Epithelial injury

- Development: Rho-kinase activation

- Fibrosis: ECM deposition, collagen

- Vascular remodeling: Intimal thickening, arteriolarization

- EC dysfunction: p27kip1, angiotensin, TGF-beta, PDGF, PD-1

PA wall remodeling

- Endothelial cell injury

- Smooth muscle cell activation

- ECM deposition, collagen

- Vascular remodeling

Pulmonary Hypertension
What is Pulmonary Hypertension and How is it Related to PF? (CONTINUED)

**Echocardiography**

**Right Heart Catheterization**

**Current Therapies in Pulmonary Hypertension based on Pathobiology of Endothelium**

---

**STEP-IPF (Sildenafil Trial on Exercise Performance in IPF)**

- Patient with idiopathic pulmonary fibrosis, in advanced stage, defined by diffusion capacity < 35%, studied during two periods: period 1 was a 12-week double-blind, placebo-controlled study of sildenafil; period 2 was a 12-week open-label extension with all patients receiving sildenafil.
- Sildenafil-treated patients had physiological improvement as compared with placebo-treated patients; sildenafil improved ventilation-perfusion matching in patients with pulmonary fibrosis. Patients in the sildenafil group improved DLCO and the partial pressure of oxygen in blood and arterial oxygen saturation as compared to placebo.
- Quality of Life scores stable in sildenafil group, but worsened in placebo.
- Subgroups of patients with right ventricular dysfunction benefitted from sildenafil.

SPECIAL LUNCHEON SPEAKER

When Drug Research is Personal: The Importance of Patient Advocacy in Drug Development and Innovation

JOHN F. CROWLEY, JD, MBA

Slides not available at time of printing.
Occidental and Environmental Causes of Pulmonary Fibrosis

CECILE S. ROSE, MD, MPH

The diagnosis of IPF requires exclusion of other known causes of interstitial lung diseases such as drug toxicities, environmental and occupational exposures, and connective tissue diseases.

(IPF Diagnosis and Treatment: ATS/ERS International Consensus Statement, AJRCCM 2000;161:646]

Idiopathic means an exposure hasn’t been identified... not that it didn’t occur.

Some epidemiologic and mineralogic studies link exposures and IPF.

There are important exposure triggers and co-factors that may increase the risk for lung fibrosis.

- Smoking
- Infections

- Pneumoconioses
  - Asbestosis
  - Silicosis
  - Coal worker’s pneumoconiosis (CWP)
- Chronic beryllium disease (CBD)
- Hypersensitivity pneumonitis (HP)
- Other
  - WTC sarcoidosis
  - Metals: plutonium, aluminum, cobalt, indium
  - Flock worker’s /textile fiber lung
  - Sequela of acute lung injury (eg, nickel fume pneumonitis)

- Drugs/radiation
- Collagen vascular diseases (CVD)
- Vasculitides
- Sarcoidosis
- Idiopathic pulmonary fibrosis (IPF)
- Smoking-related diffuse lung disease (RB-ILD, DIP, Langerhans cell histiocytosis/EG)
EPIDEMIOLOGIC STUDIES
- Increased IPF risk in agricultural workers and those exposed to metals, paints, oils. [Vergnon, Lancet 1984]
- IPF rates 2x higher in those with jobs with dust and solvent exposures; esp. in miners, agricultural and metal workers, and in those with wood dust exposure. [Baumgartner, Am J Epi 2000; Hubbard, Lancet 1996]
- Deposits of silica/silicates increased in lung tissue of some patients with IPF. [Monso, Envir Health 1990]
- Population Attributable Risks (PAR) for IPF: smoking 49%, farming 21%, livestock 4%, wood dust 5%, metal dust 3.4%, stone/sand/silica 3.5%. [Taskas & Coultas, Clin Chest Med 2008]

CO-FACTORS
- Smoking is a risk factor for IPF, familial pulmonary fibrosis, acute eosinophilic pneumonia and RA-ILD.
- Sarcoidosis, hypersensitivity pneumonitis and chronic beryllium disease are more common in non-smokers.
- Infections may be important in triggering some interstitial and granulomatous lung diseases.

Why is it often so hard to link occupational and environmental exposures with an ILD diagnosis?

Why is it important to distinguish ILD from exposure to occupational and environmental agents from idiopathic ILD?

- Clinical features are often overlapping with and even indistinguishable from non-exposure related ILDs.
- Long latency diseases – exposures may be remote.
- Workers may not know to what they have been exposed.
- Workers may be exposed to unknown hazards (e.g., metal recycling or food industry ingredients).
- Exposure history-taking is time consuming and requires skilled listening (workplace, residential, avocational, community environments).
- There may be a public health response required.
Occupational and Environmental Causes of Pulmonary Fibrosis (CONTINUED)

**Asbestososis**
- Long (20+ yrs) latency
- PFTS: Classically restrictive
- Imaging often accompanied by pleural abnormalities (10% without)
- Differential diagnosis: IPF, CVD

**SILICOSIS**
- NIOSH estimates 2 million total US workers potentially exposed to respirable silica
- Types: Simple, complicated, accelerated, acute
- PFTs: classically restrictive
- DDx: sarcoidosis, IPF

**Coal Worker’s Pneumoconiosis (CWP)**
- Upper lobe nodular and lower lobe linear inters’al fibrosis
- Latency >10 years
- Duration/intensity of exposure and coal rank predict risk
- PFTs: normal, obstructive, restrictive
- DDx: sarcoidosis, IPF

**Trends in CWP prevalence among underground coal miners, 1970-2006**

**Jobs with silica exposure**
- Agriculture
- Mining
- Sandblasting
- Glass
- Ceramics
- Foundries
- Construction
- Cement prod.
- Bricks, ‘le, pottery, porcelain, dental
- Sand molder, core knock-out
- Excavation, blasting, sandblasting, concrete and brick work, roofing

**Amphibolic asbestos fibers exposure questions**
- Exposure in the Navy/aboard ship?
- Work in building and construction trades (plumber, pipefitter, insulator, laborer, boilermaker, gravel worker)?
- Work at nuclear test site?
- Work or residence in Libby, Montana?
- Are you aware of any previous workplace asbestos exposure (please describe)?
- Family members with asbestos exposure?
Occupational and Environmental Causes of Pulmonary Fibrosis (CONTINUED)

Pulmonary Fibrosis

CHRONIC BERYLLIUM DISEASE (CBD)
- 134,000 current US workers and up to 1 million former US workers exposed to beryllium (10% CBD)
- Latency >10 years
- PFTs: restrictive, obstructive, mixed
- DDx: sarcoidosis

Industries with beryllium
- Aerospace
- Nuclear
- Computers, phones
- Automotive
- Dental alloy
- Metal machining
- Aluminum smelting or metal recycling
- Beryllium mining/milling

Pulmonary Fibrosis

3 major categories of antigen exposures that cause HP:
1. Microbial bioaerosols
   - Indoor pool or hot tub use? Humidifier or cool mist vaporizer?
   - Moisture intrusion, water damage, visible mold or mildew?
   - Agricultural exposures (or other organic dusts)?
   - Metal working fluid exposures?
2. Animal proteins
   - Bird in home or at work?
   - Feather pillows, duvets, decorations?
3. Low molecular weight chemicals
   - Work with isocyanates (foam production, painting, bathtub refinishing)?
   - Can we say they cause PF?
     - Probably not. The medical evidence may not show a link or it hasn't been adequately studied.

Pulmonary Fibrosis

HYPERSENSITIVITY PNEUMONITIS (HP)
- Variable clinical presentation (acute, insidious)
- Causal antigen identified in only 60%
- PFTs: restrictive, obstructive, mixed
- Gas exchange abnormalities common
- DDx: asthma, sarcoidosis, CTD, IPF

Pulmonary Fibrosis

DIAGNOSIS
- Thorough exposure history (home and work)
- Compatible clinical findings (imaging, pulmonary function)
- Adequate latency
- Consideration of other known causes
- Biopsy usually not necessary
**PHARMACOLOGIC TREATMENT**

- None known for the dust diseases/pneumoconioses
- Corticosteroids and immunosuppressive drugs (eg, azathioprine, methotrexate) may be helpful in more advanced cases of HP and CBD, where there is persistent inflammation and progressive loss of lung function.

**SOCIAL AND LEGAL ISSUES**

- Removal from exposure
  - Income and lifestyle implications
- Benefits counseling/legal referral
  - Worker’s compensation – state-based
  - DOL Black Lung benefits (coal miners)
  - DOJ Radiation Exposure Screening and Education Programs (RESEP) – uranium miners
- Impairment/disability assessment
- Medical follow-up and assessment of disease progression and complications

**MEDICAL MANAGEMENT**

- Treatment of co-morbid diseases
- Smoking cessation if needed
- Supplemental oxygen (based on rest and exercise oximetry or ABGs)
- Pulmonary rehabilitation
- Bronchodilators (if airflow limitation present)
- Antibiotic therapy for upper respiratory infections
- Vaccination (Pneumovax, yearly influenza)
- Lung transplant in end-stage disease

**SUMMARY: IPF vs O/E Pulmonary Fibrosis**

- The clinical manifestations of IPF and O/E fibrotic lung diseases are quite similar.
- Most occupational/environmental fibrotic lung diseases have a better prognosis than IPF.
- Early recognition and exposure removal is key.
- Medical management is similar to IPF but, depending on the disease, pharmacologic treatment options may differ.
- Substantial social and legal issues often arise when O/E lung diseases are diagnosed.

**PROGNOSIS**

- For most occupational and environmental lung diseases, risk for disease progression is related to dose.
- Early recognition and removal from causative exposure often improves the prognosis.
- O/E fibrotic lung diseases may progress, even after removal from exposure.
notes
Roundtables: Questions and Answers with the Experts
PF SPECIALIST: HAROLD R. COLLARD, MD
RHEUMATOLOGIST: RICHARD T. MEEHAN, MD
OCCUPATIONAL AND ENVIRONMENTAL SPECIALIST: CECILE S. ROSE, MD, MPH
PAH SPECIALIST: SERPIL C. ERZURUM, MD
ILD NURSE SPECIALIST: SUSAN S. JACOBS, RN, MS
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Research Trials, Stem Cell Therapies, and the Drug Pipeline

ERICA L. HERZOG, MD, PHD

Drugs in the Pipeline and Stem cells in IPF

Erica L. Herzog, MD, PhD
Assistant Professor of Medicine
Director, Translational Lung Research
Section of Pulmonary, Critical Care and Sleep Medicine

December 7, 2013

Definition of Idiopathic Pulmonary Fibrosis

• Exclusion of known causes of lung disease
  – Connective tissue disease
  – Occupational exposures
  – Environmental exposures
  – Medications

• Radiographic UIP pattern on HRCT
• Pathologic UIP pattern on biopsy

Disclosures

• I have received funding from the following commercial entities:
  Sanofi, Medimmune, Promedior, Galera

I also consulted for Boehringer-Ingelheim and Pfizer in the development of IPF therapeutics and hold two provisional patent applications for the use of therapies targeting Sema 7a, its receptors, and/or lymphocytes in lung fibrosis. These entities did not influence the data presented in today’s presentation.

UIP Pattern

Idiopathic Pulmonary Fibrosis

• A specific form of fibrotic interstitial lung disease
• Affects older adults
• Progressive dyspnea, cough and oxygen

IPF Incidence Higher than Many Cancers

Research Trials, Stem Cell Therapies, and the Drug Pipeline (CONTINUED)
**Research Trials, Stem Cell Therapies, and the Drug Pipeline (CONTINUED)**

### Drugs in the Pipeline for Lung Fibrosis

- **NAC**
- **GC-4419**
- **LPA1**
- **Anti-IL13**
- **Anti-IL-4/IL13**
- **Rituxan**
- **MMF**
- **PRM-151**
- **Arginase inhibition**
- **STX-100**
- **Anti-CTGF**
- **Anti-TGFB1**
- **Anti-LOX**
- **XL2**
- **Pirfenidone**
- **BIPF1120**

### Nintedanib (Triple Kinase Inhibitor)


### N-Acetylcysteine (NAC)


### Human Recombinant CTGF Antibody

- Preliminary results from open label trial
  - At 6 months, quantified lung fibrosis scores stable or improved for > 60% of subjects (persists at 12 months)
  - Incomplete dataset: FVC unchanged or improved in 23.0% at week 48
- Phase II RCT actively recruiting
  - Primary endpoint: change in FVC% predicted at week 48


### Pirfenidone (Small molecule)

- Lancet 2011; 377; 1580-60.

### Interleukin-13 Inhibition

- QAX576
  - Human monoclonal antibody against IL-13
  - Study completed, no results available
- Lebrikizumab
  - Human monoclonal antibody against IL-13
  - Phase II RCT actively recruiting
- Tralokinumab
  - Human monoclonal antibody against IL-13
  - Phase II RCT actively recruiting
TGF-β Inhibition

- STX-100
  - Humanized monoclonal antibody against αvβ6
  - Partial inhibition of TGF-β
  - Phase II RCT with dose escalation, actively recruiting
- GC1008
  - Antibody targeting all TGF-β isoforms
  - Phase I completed, results pending

Treatment of GERD

- 87% incidence in IPF patients
  - Testing by 24 hour pH probe
  - Only 47% with symptoms
  - Standard dose PPI did not control all patients
- Retrospective analysis:
  - Stabilization of previously declining PFTs after treatment of GERD
- Observational study:
  - GERD medication use associated with improved survival and decreased HRCT fibrosis score

Lysophosphatidic Acid (LPA-1) Inhibition

- Involved in many components of profibrotic process
  - Attracts fibroblasts to wound healing site
  - Affects cell proliferation and survival
  - Inhibits fibroblast apoptosis
  - Induces fibroblast proliferation
  - Induces vascular leak
- BMS-986020
  - Phase II RCT actively recruiting

Sildenafil in Advanced IPF

- STEP-IPF
  - Randomized, placebo controlled
  - DLCO < 35%
  - 12 wks sildenafil 20 mg TID vs. placebo then open label
- Results:
  - 20% increase in 6MWD (not significant)
  - Improved dyspnea and QOL
- Subset analysis:
  - Patients with right ventricular systolic dysfunction
  - Less decline in 6MWD and improved symptom scores

Thalidomide for Cough

- Double blind, 2-treatment, crossover trial
- 98 patients
- Single center
- Cough Quality of Life questionnaire scores significantly improved with thalidomide
- More adverse events with thalidomide
  - Constipation, bradycardia
  - Risk for thromboembolism, neuropathy

Other Novel Approaches

<table>
<thead>
<tr>
<th>DRUG</th>
<th>MECHANISM</th>
<th>STATUS</th>
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</thead>
<tbody>
<tr>
<td>Losartan</td>
<td>Inhibition of ANGII</td>
<td>Open label trial ongoing</td>
</tr>
<tr>
<td>Carbon monoxide</td>
<td>Inhibition of fibronectin and type 1 collagen production (?)</td>
<td>Phase II trial ongoing</td>
</tr>
<tr>
<td>Stem cell</td>
<td>Renewal of epithelial stem cells</td>
<td>Trial announced</td>
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<tr>
<td>Therapy</td>
<td></td>
<td>Not listed on clinicaltrials.gov</td>
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<tr>
<td>PRM-151</td>
<td>Recombinant Periostatin-2</td>
<td>Phase II trial announced</td>
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<tr>
<td></td>
<td>Alteration of macrophage phenotype</td>
<td>Not listed on clinicaltrials.gov</td>
</tr>
<tr>
<td>CNTD-888</td>
<td>Antibody against CCL2</td>
<td>Abstract ATS 2013: No measurable benefit</td>
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** Fibrosis Conference Session
Emerging Targets in Fibrosis: Friday 9:10 AM
Research Trials, Stem Cell Therapies, and the Drug Pipeline (CONTINUED)

Stem cells

• Treatment with Mesenchymal stem cells or adipose derived stem cells
• Lung Regeneration

Conclusions

• Multiple new therapies are in the pipeline for IPF
• These include novel drug therapies and regenerative approaches
• There is hope
Lung Transplantation and PF

ERROL L. BUSH, MD

Indications

- Chronic advanced lung disease
- Failed medical management
- Primary goal is improved duration of life but improved quality of life is also a major consideration
- Trading one medical condition for another

ADULT LUNG TRANSPLANTS
Major Indications By Year (Number)

<table>
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<tr>
<th>Year</th>
<th>CF</th>
<th>IPF</th>
<th>COPD</th>
<th>Alpha-1</th>
<th>IPAH</th>
<th>Re-Tx</th>
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<td>2012</td>
<td>2,645</td>
<td>3,340</td>
<td>3,800</td>
<td>1,385</td>
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<td>160</td>
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</tbody>
</table>

Number of Transplants Reported By Year and Procedure Type

<table>
<thead>
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<th>Procedure Type</th>
<th>Number of Transplants</th>
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</thead>
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<tr>
<td>Bilateral/Double Lung</td>
<td>2,645</td>
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<tr>
<td>Single Lung</td>
<td>3,340</td>
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</table>

UCSF Transplant Recipient Characteristics

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<tr>
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<tr>
<td>CF</td>
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<td>14.5</td>
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<tr>
<td>IPF</td>
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<td>47.5</td>
<td>45.8</td>
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<tr>
<td>COPD</td>
<td>17.4</td>
<td>31.9</td>
<td>29.9</td>
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<tr>
<td>Other</td>
<td>0</td>
<td>0.8</td>
<td>4.2</td>
</tr>
</tbody>
</table>
Timing of Referral

General Recommendations

- Early referral is highly desirable
- Consider when patient is symptomatic during daily activities (NYHA III or IV)
- When expected survival is 2-3 years
- Aids in the psychology of accepting and confronting life-threatening illness
- Aids in actively managing end-stage illness

Relative Contraindications

- Age > 65 years
- Critical or unstable condition
- Severely limited functional status
- Colonization with highly resistant or virulent bacteria
- Severe obesity: BMI > 30
- Severe osteoporosis

Pulmonary Fibrosis

Disease Specific Guidelines

- Most patients are referred late and this accounts for high wait list mortality
- UIP median survival is less than 3 years
- Factors associated with increased 5 year mortality
  - Male
  - Higher FEV1/FVC ratio
  - Lower FVC, TLC and DLCO
  - Other factors
    - FVC 10% drop in 6 months
    - DLCO < 35% - 39% predicted
    - O2 desaturation (<88%) during 6 MWT

Absolute Contraindications

- Malignancy
  - Within 2 years except basal and squamous cell of skin
  - 5 years disease free for breast CA > stage 2, colon > Dukes A, melanoma > level III or extra-capsular renal cell CA
  - Uncontrollable advanced organ dysfunction (kidney, heart, liver)
- Heart
- Cardiomyopathy
- Ungraftable CAD
- Significant chest wall/spinal deformity
- Major psychosocial derangement
- Current tobacco or drug use
- Non-curable extra-pulmonary infections: HIV, Hepatitis B and C.

Pulmonary Fibrosis

Refer Early
Lung Transplantation and PF (CONTINUED)

Day of Transplant

Donor Team
- Admission
  - H&P, Labs, CXR
- OR
  - Anesthesia
  - Monitors/Lines
  - Procedure
  - Incision
    - Sternotomy
    - Thoracotomy
  - Biopsy
  - Explant – removal of lung
  - Implant
  - Close

Implant Team
- Admission
- OR – Anesthesia
- Monitors/Lines
- Procedure
- Incision
  - Sternotomy
- Thoracotomy
- Biopsy
- Explant – removal of lung
- Implant
- Close

Extended Donor Criteria
- Age < 65 years
- > 20 pack year smoking history OK if no proven impairments
- chest trauma OK if no extensive parenchymal injury
- OK to use contralateral lung if there is unilateral infiltrate or injury
- Active donor management

Organ Bank

Donor Lungs Too Frequently Rejected
- Present criteria exclude more than 85% of lungs
- 29 pairs of rejected lungs were assessed by physiological, microbiological, and histological methods
- 83% had no or mild pulmonary edema, 74% intact alveolar fluid clearance, and 62% normal or mildly abnormal histological findings
- 41% of rejected lungs would have been potentially suitable for transplantation

Standard Donor Criteria
- Age < 55 years
- ABO blood group compatible
- Clear chest radiography
- Arterial oxygen pressure > 300 mmHg on FiO2 of 1.0 and PEEP of 5 cm H2O
- < 20 pack year smoking history
- Absence of chest trauma
- No aspiration or sepsis
- Sputum gram stain free of bacteria, fungus or significant number of WBCs

IPF Exacerbation
- Acute Deterioration due to right heart strain
- Intubation can make worse (positive pressure ventilation)

Traditionally lung transplantation has not been on option for those with respiratory failure
- Resistance because of concern for dismal outcome
- Allocation of lungs (based on time on wait list)
- Experience with ECLS and MV as well as change in LAS have shifted this paradigm
ECLS as a Bridge to Transplant appears to be on the Rise

Number of articles on ECLS and ECLS as a bridge to LTx published on PubMed for each year from 2000-2011

ECLS as a Bridge to Transplant

Efficiency of extracorporeal membrane oxygenation as a bridge to lung transplantation

Extracorporeal membrane oxygenation as a bridge to lung transplantation and recovery

ECMO Bridge to transplant

Lung Transplantation and PF (CONTINUED)
ECMO: PERMITS AMBULATION PRE-TRANSPLANTATION!

By simultaneously removing blood from both the SVC and IVC and returning blood to the Right Atrium, this instrument is able to match the body's natural flow ratios.

Avalon catheter

Ex-vivo Lung Perfusion, "Lung in a Box"
notes
The Final Stages of Pulmonary Disease

Margaret Bourne, M.D.
Medical Director
Hospice By The Bay

Why the discrepancy?

• We don’t like to talk about death
• Once housebound, 911 only option
• No crisis plan
• No plan for death
• Fear of Hospice

What do people want?

• Feel prepared
• Told the truth
• Die at home
• Avoid procedures, hospitalizations
• Die without pain
• Die without feeling of suffocation
• Not to die alone

With a little preparation:

• People live longer, increased quality of life
• Fewer hospitalizations, procedures
• Die at home
• More control over their lives
• Families feel patient’s wishes were honored
• Prevent the sensation of suffocation

What happens most of the time?

• Last year spent in and out of intensive care
• Use of ventilator for lung disease
• More than half die in the hospital
• Feel unprepared for death

What can patients do?

• Will disease likely be cause of death?
• Home care for infections, shortness of breath
• Talk with family about wishes
• File Durable Power of Attorney, POLST forms
• Talk with doctor about hospice, palliative care
• Request an informational visit from Hospice
Breathing Better

• Myth: “I need to breathe fast”
• Fact: Slowing down breathing increases quality of life and longevity
notes
Tools for Living Better with Pulmonary Fibrosis

SUSAN S. JACOBS, RN, MS

“How Does IPF Affect Your Life?”

Results of Interviews with 20 IPF Patients

- IPF therapy: oxygen, side effects of meds
- Sleep: disturbed sleep
- Exhaustion: lack of energy, fatigue
- Forethought: need to always plan ahead, mental energy
- Employment: finances, work, security
- Dependence: need to rely on others
- Family: impact on family relationships
- Sexual relations: limitations on activity
- Socialization/Leisure: social isolation
- Mental and spiritual: fear, worry
- Mortality: feelings about death

Quantity of Life: What Tools do We Have?

- Medications
- Oxygen
- Prevention of Exacerbations/Infections
- Drug research/clinical trials
- Lung transplantation
- Treatment of co-morbidities such as heart disease, pulmonary hypertension, gastroesophageal reflux

Quality of Life: What Tools Are Needed?

- Breathlessness
- Cough
- Fatigue
- Sleep quality
- Anxiety
- Depression
- Physical Activity
- Social Connectedness

Current Research on Quality of Life in Patients with Pulmonary Fibrosis/ILD

- “Patient-Reported Outcomes in IPF Research” (Savino et al.; CHEST 2016)
- “Health-Related QOL in IPF: where are we now?” (DeLeen et al.; Current Opinion Pulm Med 2017)
- “Palliative care needs for fibrotic ILD: A qualitative study of patients, informal caregivers and health professionals” (Rayson et al.; Palliative Med 2015)
- “Depression in patients with IPF” (Abkstes et al.; Chronic Resp Disease 2013)
- Health-related QOL does not predict mortality in IPF (Nakahama et al.; Sarrazid Vane Diffuse Lung Mx 2012)
- The minimal important difference of the King’s Brief ILD Questionnaire (K-ILD) and forced vital capacity in ILD (Punt et al.; Respir Med 2017)
- Pulmonary Rehab in Patients with IPF: A Review (Koza et al. Respir Res 2015)

Current Research on Quality of Life in Patients with Pulmonary Fibrosis/ILD

- Patient reported outcomes include questionnaires about your breathing, symptoms, energy, mood, etc...
- The FDA is paying more attention to how to include these measures in drug research trials
- The endpoint of a successful study might be improved physical and social activity, not just changes in the numbers on your breathing tests
- Data confirms that low breathing test numbers don’t necessarily correlate with a low quality of life.
- The most common quality of life issues are cough, SOB, and fatigue
Tools for Living Better with Pulmonary Fibrosis (CONTINUED)

**Tools to Manage The Cough**
- Cough is noted by over 80% of patients with IPF
- Cough is usually present by the time we first see a patient with IPF
- There is a constant urge to cough, but it is not relieved by coughing

**More on Cough**
- Cough is noted by over 80% of patients with IPF
- Cough is usually present by the time we first see a patient with IPF
- There is a constant urge to cough, but it is not relieved by coughing

**“If I Could Just Get Rid of the Cough”**
- Effect on family
- Embarrassment
- Sick to stomach
- Retching
- Incontinence
- Headache
- Ache all over
- Breathlessness
- Hurts to breathe
- Exhausted
- Unable to do activities
- Dizziness
- Rib fractures
- Sleep interruption
- Can’t phone, talk, sing, laugh
- Decreased socialization
- Change in lifestyle

**Research: “Objective Cough Frequency in Idiopathic Pulmonary Fibrosis”**
- **Goal:** To measure cough rates in patients with IPF and determine the association between cough frequency and quality of life, and also see how the severity of cough correlates to the severity of disease
- **Methods:** 19 patients with IPF underwent breathing tests, 24-hour cough recordings, quality of life questionnaires, and cough severity scores

**What Causes the Cough in ILD?**
- The pulling or stretching of fibrotic lung tissue stimulates the release of substances in the lung that trigger cough
- The cough receptors in airways of patients with ILD are ‘up-regulated’ compared to normal airways, ie, more sensitive
- Reflux/aspiration?
- We really don’t know for sure

**Objective Cough Frequency in IPF**
- The greater the cough frequency, the worse the patients’ rating of their cough-related quality of life
- There was no correlation between pulmonary function tests and cough frequency, except for total lung volume
- Patients’ estimation of cough severity correlated well with the cough counter device’s results
**Tools for Living Better with Pulmonary Fibrosis (CONTINUED)**

### Cough Evaluation
- First step is to eliminate the top 3 causes of cough for most people:
  - Rule out asthma
  - Aggressively treat and prevent GERD
  - Eliminate post-nasal drip

### Patient Tips on Managing Cough
- Try lozenges, honey and lemon, hot water (especially before making phone call, during ‘social times’)
- Avoid irritants, triggers
- ↑ oxygen during coughing as needed
- Hypnosis
- Yoga/relaxation techniques
- It is difficult to treat

### What we have learned about cough in ILD over the past 2 years?
- IPF patient estimates of how often they cough are extremely accurate (Key. Cough; 2010)
- Mechanical percussion on the chest wall produced cough in 85% of IPF pts. compared to 17% of healthy control subjects (Jones et al. BioMed Central 2011; April)
- Cough has not been improved by any of the investigational IPF drugs tested thus far.

### Medications to Treat Cough
- Inhaled steroids (Advair® combination, Symbicort®, QVar®)
- Guaiifenesin (Mucinex®)
- Benzonatate (Tessalon Perles®)
- Oral steroids (prednisone)
- Nebulized anesthetics (lidocaine)
- Opiates (codeine)
- Experimental: baclofen, gabapentin, thalidomide, tramadol, interferon alpha

### Tools to Manage Shortness of Breath

### Shortness of Breath: What Causes It?
- Increased ‘work’ to breathe due to stiffness of the inflamed or scarred lung tissue
- Possible receptors in lung that sense pressure and stretch of the lung tissue
- Low oxygen levels
- Deconditioning, weakness
- Contributing factors, such as anxiety and depression
Managing Shortness of Breath
• Exercise: Aerobic, Strengthening, Flexibility
• Fan/cold air/open windows
• Relaxation/visual imagery/meditation
• Distraction: headphones, social interaction
• Yoga (modified)
• Oxygen: if oxygen saturations are < 88-90%
• Opiates/Narcotics/Anti-anxiety drugs

Exercise as a Strategy to Treat Dyspnea, Fatigue, Anxiety, & Depression
• Regular, planned exercise can improve endurance, shortness of breath, quality of life and decrease panic, anxiety and depression
• Deconditioning can be more limiting than the level of disease reflected on breathing tests
• Exercise benefits are also a result of desensitization to SOB as well as motivation
• Adequate oxygenation during exercise remains a challenge for many patients with ILD
• Exercise has demonstrated more consistent benefits for decreasing SOB and increasing exercise capacity than any IPF clinical drug trials

Impact of Exercise on SOB
• Builds endurance
• Strengthens muscles
• “Desensitizes” you to SOB
• Improves mood
• Facilitates independence, travel, and socialization
• Maintains ideal weight
• Decreases anxiety, panic
• Does not change PFTs

Exercise as a Treatment for IPF Symptoms: Research Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample</th>
<th>±6MW, m</th>
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<th>QOL</th>
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<tbody>
<tr>
<td>Swigris 2011</td>
<td>21</td>
<td>2012</td>
<td>Fatigue improved</td>
<td>No chg SF36</td>
</tr>
<tr>
<td>Salti 2010</td>
<td>11</td>
<td>107</td>
<td>Improved</td>
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<td>Ferman et al 2009</td>
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<td>Improved</td>
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<td>Holland 2008 (RCT)</td>
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<td>55</td>
<td>Improved</td>
<td>Improved</td>
</tr>
<tr>
<td>Nishiyama 2008 (RCT)</td>
<td>28</td>
<td>46</td>
<td>No Change</td>
<td>Improved</td>
</tr>
<tr>
<td>Istrachekik 2006</td>
<td>5</td>
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<td>Improved</td>
<td>Improved</td>
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<tr>
<td>Naj 2006</td>
<td>26</td>
<td>NA</td>
<td>Improved</td>
<td>Improved</td>
</tr>
</tbody>
</table>


Exercise Stops the Downward Spiral of Dyspnea - Anxiety - Decreased Activity

Interrupt

Anxiety

Decreased Activity

Shortness of Breath

Anxiety

Shortness of Breath

Shortness of Breath

Decreased Activity

Treatment for ILD Symptoms:
Pulmonary Rehabilitation (PR) Programs
• PR programs combine social support, education and exercise to decrease symptoms and increase functional status
• Educational components include energy conservation, pacing techniques, nutritional education, breathing retraining, prevention of infection, relaxation training
• Exercise includes aerobics, strengthening, flexibility, oxygen monitoring and a ‘home exercise prescription’
• Measurable outcomes include less depression, anxiety and SOB plus increased exercise capacity and fewer hospitalizations
Summary: Top Ten Most Effective Tools to Live Well with Pulmonary Fibrosis

1. **Enroll in a Pulmonary Rehabilitation Program**

2. **Exercise Regularly:**
   - Pulmonary Rehab Maintenance programs
   - Sit and Be Fit
   - Water Aerobics
   - Yoga

3. **Stay Socially Connected:**
   - Find a local PF Support Group in your area and include caregivers / family
   - Join an on-line support group
   - Seek out Pulmonary Group activities (Better Breathers, Sea Puffers)

4. **Keep Spirituality in Your Life:**

5. **Seek Treatment for Depression:**
   - Medication
   - Counseling

6. **Have Ongoing Discussions** with your physicians/health providers regarding worsening symptoms and plans to manage them including Palliative Care and Hospice programs

7. **Seek Evaluation** at an Interstitial Lung Disease Clinic – even if for just a one-time consultation

8. **Enroll in Clinical Trial** as appropriate

9. **Be Involved** in management of all your health issues (weight, heart problems, reflux, medication mgmt, laboratory testing, etc...)

10. **Use Multiple Strategies** to stay healthy, active and socially connected
notes
Effective Advocacy for Pulmonary Fibrosis

BRIAN BAIRD, MS, PHD

**Effective Advocacy for Pulmonary Fibrosis**
Hon. Brian Baird Ph.D.
President, Antioch University Seattle

**Why Advocacy**
- Awareness of the disease and its consequences
- Increase funding for research
- Increase non financial support for research
- Increase funding for treatment and prevention
- SAVE LIVES!
- Save Money

**BUT I DON’T KNOW HOW**
- It is not that complicated – YOU CAN DO IT
- In Fact - Nobody can do it better than you

**How to Advocate**
- Get to the right people
- Tell the right story
- Repeat as necessary until you reach the goal

**Who are the most effective advocates?**
- YOU
- Your family
- Your friends
- Your health care providers
- Your elected representatives

**Finding the Right People**
- Federal Electeds
- Federal Appointeds
- State Electeds
- State Appointeds
- Local Electeds
- Local Appointeds
- Philanthropists
- Media
Effective Advocacy for Pulmonary Fibrosis (CONTINUED)

Federal Electeds – Who Are They
- How to find your Representatives and Senators
- House.gov
- Local Elections Auditors

What are the Asks
- Specific Legislation by name and number
- Funding
- Make the Ask explicit e.g. “Will you commit to supporting this legislation?”
- “Will you commit to reading the material, it’s only two pages long, and considering it?”
- Remind them of the commitment
- Thank them for their actions if they take action
- Publicize your support and appreciation if action is taken

How To Reach Them
- In Person is a Thousand Times More Effective Than Anything Else
- You must be polite but doggedly persistent – Your life and the lives of your loved ones are at stake.
- You will often meet with or speak to staff – THEY ARE IMPORTANT!
- Office visits
- Town halls
- Phone calls
- Letters

THE FUNDAMENTAL ASK NOW
- WILL YOU SUPPORT FUNDING BASED ON COMPARABLE IMPACTS?
- PF Prevalence
- PF Morbidity
- PF Mortality
- PF Increasing
- PF Costs
- PF Lack of known cause
- PF Lack of known cure

What is Your Message
- Short and compelling Tell Your Story
- The basic facts
- The facts in context
- What is your “Ask” – What should they do
- You will follow up

Advocating for Advocacy
- Encouraging others to advocate
- Working with your association
- Your support group and advocacy meetings
- Friends family and coworkers
- Letters to the editor
- Earned media
Effective Advocacy for Pulmonary Fibrosis (CONTINUED)

Political Involvement and Giving
- People help those who help them
- If someone is with you PF be with them on elections
- Individual financial support
- Group financial support
- Volunteering
- Letters to the editor

PERSISTENCE and DETERMINATION
- Time is of the essence
- But things take time
- This is a team sport and a relay race
- Never give up, never give out, never give in to defeat

Earned Media
- Building awareness through local media
- What kinds of events are interesting
- What is the MESSAGE?
- Make it meaningful, moving, and matter
- Tell Compelling Stories

Thanking Those Who Help
- If someone supports your efforts, be sure to thank them
notes
The Role of the US FDA in the Process of Drug Development

EUGENE J. SULLIVAN, MD

Legal / Regulatory Basis

- **Food, Drug, and Cosmetic (FD&C) Act**
  - Provides the legal authority for FDA’s activities
  - Written fairly broadly
  - e.g. the basis for approval: Substantial evidence (consisting of adequate and well-controlled investigations) which allows the conclusion that the drug will have the effect it purports to have

- **Regulations**
  - FDA interprets that Act and writes Regulations to more specifically define how the law is to be applied
  - Regulations have the rule of law

- **“Guidance Documents”**
  - Describe FDA’s current thinking on specific topics
  - Non-binding

My Background

- Pulmonary / Critical Care Medicine
  - University of Colorado
- Academic Medicine
  - Cleveland Clinic Foundation, 1995 - 1999
- FDA
  - Division of Pulmonary and Allergy Products, CDER
  - Medical Officer / Team Leader / Deputy Director
  - 1999-2006
- Pharmaceutical Industry
  - Chief Medical Officer, United Therapeutics and Lung Rx
  - 2006 - 2012
- Principal, EJS Consulting, LLC (current)
- Lymphangioleiomyomatosis (LAM) Foundation
  - Scientific Advisory Board, Board of Directors

The Drug Development Process

- Understanding causes/mechanisms of disease
- Identifying a potential “therapeutic target”
- Identifying/synthesizing a drug to affect the target
- Testing the drug in animal models of disease
- Testing the drug for toxicity in animals
- First introduction of drug into humans
- Exploring important aspects: safety/tolerability, blood levels, etc
  - Usually begins with single dose, then multiple dose
  - Exploring the effect of the drug in patients with the disease (safety and efficacy) and creating hypotheses regarding how the drug might benefit patients (“Phase 2”)
- Confirming those hypotheses and evaluating safety (“Phase 3”)
- Regulatory approval for marketing
- Ongoing surveillance to better understand safety in the “real world”

Overview

- Legal / Regulatory Basis of FDA’s Activities
- FDA’s Role During Drug Development
- The Efficacy Requirement
- Understanding the Risks

The Role of the US FDA in the Process of Drug Development (CONTINUED)

**FDA’s Involvement**
- No requirement for FDA involvement prior to human investigation
- In order to study the drug in humans, a firm must open an “IND” with the FDA (“Investigational New Drug” application)
- FDA reviews the animal data to be sure the proposed human study is acceptably safe, and follows the subsequent development
- In early clinical development, FDA’s primary concern is the safety of the human study subjects
- As development proceeds, FDA often advises firms on the design of clinical trials, but generally does not require firms to follow its advice unless there is a safety concern
- FDA advice often centers on assurance that safety is adequately monitored and assessed, and that adequate data is generated to support the selected dose / frequency of dosing and to establish that the drug has meaningful beneficial effects
- When the firm believes it has adequate data to support approval, it submits a New Drug Application (NDA) for FDA to review
- After approval, FDA continues to evaluate safety information

**Understanding the Risks**
- FDA recognizes that at the time of approval, it is likely that not all of the risks of a drug are known
- FDA requires an adequate “safety database” prior to approval, so that it has a reasonable understanding of the risks
  - number of patients exposed to the drug in clinical trials
  - duration of exposure
  - appropriate observation and testing of study subjects
- Often, balancing the known risks of a drug with the established benefit is a challenge
- FDA requires firms to continue to monitor safety once a drug has been approved

**The Efficacy Requirement**
- The Law says that a marketing application will be rejected if there is “a lack of substantial evidence that the drug will have the effect it purports or is represented to have ... in the proposed labeling.”
- Question: So why doesn’t the FDA approve any drug, as long as the claims about the benefits of the drug are “honest”?  
  Answer: The effect must be clinically meaningful.
  - Not in the FD&C Act, but established by a Supreme Court case (Warner-Lambert v Heckler, 1986)

**Summary**
- Much of drug development occurs prior to FDA involvement
- FDA becomes involved when human studies begin
- FDA will generally allow research to proceed, unless there is a concern for the safety of the study subjects
- FDA interacts with firms during the course of drug development in order to provide its best advice on how to obtain the data that will ultimately be necessary for drug approval (safety and efficacy).
- FDA assumes that all drugs have risks and therefore requires demonstration of a meaningful beneficial effect
- FDA requires adequate assessment of safety before approval and continues to monitor the safety of drugs after introduction into the market

**“Feels, Functions, or Survives”**
- All drugs have safety risks (some are known at the time of approval, and some may be unknown). Therefore, the only reason that a patient would want to take a drug would be if the drug:
  - prolonged life
  - resulted in some type of benefit that the patient can detect  
    (improvement in symptoms, improvement in functional capacity)
  - decreased the chances of developing a condition or disease complication that is itself apparent to the patient and is undesirable (e.g. stroke)
- Therefore, the clinical trials must establish one of these benefits.
- It is not enough to show that the drug impacts a lab value or other measure that the patient can’t feel,
notes

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US Food and Drug Administration—
Patient-focused Drug Development Program

RICHARD M. KLEIN

Slides not available at time of printing.
Roundtables: Questions and Answers with the Experts
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PALLIATIVE AND HOSPICE CARE: MOLLY BOURNE, MD
LUNG TRANSPLANT SPECIALIST: ERROL L. BUSH, MD
FAMILIAL PF, GENETIC COUNSELING: ROBIN R. DETERDING, MD; JANET TALBERT, MS, CGC
ILD NURSE SPECIALISTS: KATHLEEN O. LINDELL, PHD, RN; SUSAN S. JACOBS, RN, MS
ADVOCACY: BRIAN Baird, MS, PHD; RICHARD M. KLEIN; EUGENE J. SULLIVAN, MD
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<thead>
<tr>
<th>Acronym</th>
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<tr>
<td>6MWD</td>
<td>six minute walk distance test</td>
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<td>ABG</td>
<td>arterial blood gas</td>
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<tr>
<td>ACCP</td>
<td>American College of Chest Physicians</td>
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<td>ADLs</td>
<td>activities of daily living</td>
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<td>acute interstitial pneumonia</td>
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<td>ALAT</td>
<td>Asociacion Latinoamericana de Torax</td>
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<tr>
<td>ARDS</td>
<td>acute respiratory distress syndrome</td>
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<tr>
<td>ATS</td>
<td>American Thoracic Society</td>
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<td>bronchoalveolar lavage</td>
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<td>biopsy</td>
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<td>CT</td>
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<td>demand positive airway pressure</td>
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<td>endotracheal tube</td>
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<td>Food and Drug Administration</td>
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<td>FEF</td>
<td>forced expiratory flow</td>
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<td>forced expiratory flow at maximum effort</td>
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<td>FEV</td>
<td>forced expiratory volume</td>
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<td>FEVI</td>
<td>forced expiratory volume in 1 second</td>
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<td>FIP</td>
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<td>FPF</td>
<td>familial pulmonary fibrosis</td>
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<tr>
<td>FRC</td>
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<td>forced vital capacity</td>
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<td>Acronym</td>
<td>Definition</td>
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<td>HEPA</td>
<td>high efficiency particulate air</td>
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<td>HIPAA</td>
<td>Health Insurance Portability and Accountability Act</td>
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<td>HP</td>
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<td>heart rate</td>
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<td>high resolution CT scan</td>
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<td>IADLs</td>
<td>instrumental activities of daily living</td>
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<td>inspiratory capacity</td>
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<td>intensive care unit</td>
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<td>IIP</td>
<td>idiopathic interstitial pneumonia</td>
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<td>ILD</td>
<td>interstitial lung disease</td>
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<td>inspiratory reserve volume</td>
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<td>Japanese Respiratory Society</td>
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<td>LIP</td>
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<td>liquid oxygen</td>
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<td>LPM</td>
<td>liters per minute oxygen or O₂ flow rate</td>
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<td>MDI</td>
<td>metered dose inhaler</td>
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<td>magnetic resonance imaging</td>
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<td>MVV</td>
<td>maximal voluntary ventilation</td>
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<td>NHLBI</td>
<td>National Heart, Lung, and Blood Institute</td>
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<td>National Institutes of Health</td>
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<td>NIV</td>
<td>non-invasive ventilator</td>
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<td>NSIP</td>
<td>non-specific interstitial pneumonitis</td>
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<tr>
<td>O₂</td>
<td>oxygen</td>
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<td>obstructive airway disease</td>
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<td>occupational lung disease</td>
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<td>obstructive sleep apnea</td>
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<tr>
<td>OTC</td>
<td>over the counter</td>
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<tr>
<td>P</td>
<td>partial pressure of oxygen in arterial blood</td>
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<td>PAP</td>
<td>positive airway pressure</td>
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<tr>
<td>PCO₂</td>
<td>partial pressure of carbon dioxide in arterial blood</td>
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<tr>
<td>PCP</td>
<td>primary care physician</td>
</tr>
<tr>
<td>PE</td>
<td>pulmonary embolism or pulmonary edema</td>
</tr>
<tr>
<td>PEEP</td>
<td>positive end expiratory pressure</td>
</tr>
<tr>
<td>PEF</td>
<td>peak expiratory flow rate</td>
</tr>
<tr>
<td>PEP</td>
<td>positive expiratory pressure</td>
</tr>
<tr>
<td>PF-CVD</td>
<td>pulmonary fibrosis associated with a collagen vascular disorder</td>
</tr>
<tr>
<td>PF</td>
<td>pulmonary fibrosis</td>
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<tr>
<td>PFT</td>
<td>pulmonary function test</td>
</tr>
<tr>
<td>PH</td>
<td>pulmonary hypertension</td>
</tr>
<tr>
<td>PLB</td>
<td>pursed lip breathing</td>
</tr>
<tr>
<td>PND</td>
<td>paroxysmal nocturnal dyspnea/post nasal drip</td>
</tr>
<tr>
<td>PO₂</td>
<td>oxygen tension in arterial blood</td>
</tr>
<tr>
<td>POLST</td>
<td>Physician Orders for Life-Sustaining Treatment</td>
</tr>
<tr>
<td>PPH</td>
<td>primary pulmonary hypertension</td>
</tr>
<tr>
<td>PPV</td>
<td>positive pressure ventilation</td>
</tr>
<tr>
<td>PR</td>
<td>pulmonary rehabilitation</td>
</tr>
<tr>
<td>PT</td>
<td>physical therapy</td>
</tr>
<tr>
<td>PTX</td>
<td>pneumothorax</td>
</tr>
<tr>
<td>PULM or PULMO</td>
<td>pulmonary</td>
</tr>
</tbody>
</table>
acronyms
acronym glossary

Q
QOL: quality of life

R
R/O: rule out
RA: rheumatoid arthritis
RAD: reactive airway disease
RB-ILD: respiratory bronchiolitis associated interstitial lung disease
RCT: randomized controlled trial
RDS: respiratory distress syndrome
RLD: restrictive lung disease
RLS: restless leg syndrome
RR: respiratory rate
RRT: Registered Respiratory Therapist
RT: Respiratory Therapist/respiratory therapy
RV: residual volume
Rx: treatment/therapy/prescription

S
SaO₂: arterial blood oxygen saturation
SOB: shortness of breath
SSDI: Social Security Disability Insurance
SSI: Supplemental Security Insurance

T
TLC: total lung capacity
TTO₂: transtracheal oxygen
TV: tidal volume
TX: transplant

U
UIP: usual interstitial pneumonia
URI: upper respiratory infection

V
VATS: video assisted thoracic surgery
VC: vital capacity
VCO₂: carbon dioxide production
VO₂: oxygen consumption
VQ SCAN: ventilation perfusion scan