Millions of Smokers May Have Undiagnosed Lung Disease

More than half of long-term smokers who pass lung-function tests have respiratory-related impairments

Many long-term smokers and ex-smokers are considered disease free because they passed lung-function tests. However, more than half of them have respiratory-related impairments when more closely evaluated with lung imaging, walking and quality-of-life tests. Many of these people likely have the earliest stages of chronic obstructive pulmonary disease (COPD), the third leading cause of death in the United States.

According to James D. Crapo, MD, professor of medicine at National Jewish Health, the impact of chronic smoking on the lungs and the individual is substantially underestimated when using lung function tests alone. Dr. Crapo is senior author of the study published recently in *JAMA Internal Medicine*. In the study, researchers evaluated 8,872 people ages 45 to 80 years.

**BETTER HEALTH STARTS AFTER THE Last Cigarette**

After the last cigarette, the road to better health starts within minutes and continues for years. Here are the changes your body experiences along that journey.

**20 MINUTES**
- Blood pressure decreases
- Pulse rate drops
- Body temperature of hands and feet increases

**8 HOURS**
- Carbon monoxide level in blood drops to normal
- Oxygen level in blood increases to normal (if no lung disease)

**24 HOURS**
- Chance of a heart attack decreases

**48 HOURS**
- Nerve endings start regrowing
- Sense of smell and sense of taste improve

**2–12 WEEKS**
- Circulation improves
- Walking becomes easier
- Lung function improves

**4–36 WEEKS**
- Coughing, sinus congestion, tiredness and shortness of breath decrease

**1 YEAR**
- Risk of coronary heart disease decreases to half that of smokers

**5 YEARS**
- From five to 15 years after quitting, stroke risk is the same as people who never smoked

**10 YEARS**
- Risk of cancer drops to half that of smokers
- Risk of ulcer decreases

**15 YEARS**
- Risk of coronary heart disease is the same as people who have never smoked
- Risk of death is the same as people who have never smoked

*DISCLAIMER: If you have other health conditions, your results may differ*

You can download and print this infographic and others at [njhealth.org/practicetools](http://njhealth.org/practicetools)
To schedule a lung cancer screening CT for your patient

Contact the National Jewish Health lung cancer screening coordinator at 877.713.5066. Lung cancer screening CT is now covered by private insurance, Medicare and Colorado Medicaid for high-risk patients. To learn more about screening criteria, visit njhealth.org/lung-cancer-screening-program.

Beta-blockers and COPD

Chronic obstructive pulmonary disease (COPD) patients often have comorbid cardiovascular disease. Beta blockers, however, are significantly under-prescribed in COPD patients due to the concern that they may trigger bronchoconstriction and worsening of lung function.

National Jewish Health physician James D. Crapo, MD, worked with researchers from around the country to analyze data on use of beta-blockers in patients from the COPDGene cohort. The COPDGene study enrolled 10,300 current and former smokers aged 45-80 years. Of the full group of COPDGene participants, 3,464 had Stage 2-4 COPD based on GOLD criteria (Global Initiative for Chronic Obstructive Lung Disease) and were included in the research on the effect of beta blockers on COPD.

Beta blocker use was associated with a significantly lower rate of total and severe exacerbations during an average 2.1 years of follow-up. In study participants with GOLD stage 3 and 4 COPD and on home oxygen, use of beta blockers was also associated with similar reductions in the rate of total and severe COPD exacerbations. Subjects with severe COPD who are on home oxygen are a subgroup that has been considered to be at especially high risk for complications from beta blocker use.

While Dr. Crapo and the research team found that the use of beta blockers by study subjects with COPD is associated with a significant reduction in exacerbations, the use of other cardiac medications was not associated with a reduction in exacerbation risk.

Reference:
Pediatric and Adult Clinical Interests

Recurrent Infections: Is It Caused by Immune Deficiency?

Erwin W. Gelfand, MD, chairman, Department of Pediatrics, and professor of pediatrics, National Jewish Health

All children and many adults suffer from infections, often recurrent, and the concern is whether this susceptibility represents an immune disorder. Immune system disorders are uncommon, but nonetheless, suspicion may be warranted given certain cues. Prior to the liberal availability or use of antibiotics, immunodeficiency disorders presented with severe, often overwhelming infections including lobar pneumonia, osteomyelitis, meningitis, a need for repeated hospitalization and intravenous antibiotics. Today, the clinical presentation may be more subtle, as with the early introduction of effective antibiotics, bacterial infections often do not progress to a serious outcome.

So, what are the cues? Today more than 300 genetic defects within the immune system have been identified, and with the increased application of molecular genetics, more are discovered regularly. The focus here is on primary immunodeficiency diseases, where secondary causes are eliminated. There are many secondary causes of immunodeficiency, including HIV disease, malignancy, new biologic agents (e.g., Rituxan®, anti-tumor necrosis factor [TNF]), immunosuppressive drugs, chemotherapeutic agents, skin or mucosal barrier defects and even nutritional causes. Primary immunodeficiency diseases can have an onset at any age. With the availability of molecular genetics, it is not unusual today to identify a genetically-determined primary immunodeficiency in adulthood, even in the fifth or sixth

Approach to Assessing Immune Deficiency

When assessing a patient for possible immune deficiency, consider the following:

- Number of infections
- Severity of infections
- Type of infections
- Location of infections
- Need for antibiotics
- Need for hospitalization
- Failure to thrive
- School or work attendance and performance
- Is there a family history of immune disorders?
- Are the parents related? (e.g., first cousin marriages increase likelihood of a recessive condition)
- History of atopic disease (children with allergies often present with recurrent rhinositis, even pneumonia in asthmatics)
- In adults, fatigue rather than significant infection may be a presenting feature

The immune disorder clinics at National Jewish Health can help you determine the need for further evaluation, diagnosis and treatment.

The physicians in these clinics (Drs. Erwin Gelfand, Jordan Abbott, Pia Hauk and Sanny Chan) have decades of experience treating children and adults and can assist you via consultation or arranging an evaluation for a patient.
National Jewish Health physicians Barry Make, MD, and Russell Bowler, MD, and their colleagues recently summarized the most common and significant variables associated with case-finding or missed cases of COPD in primary care. Although spirometry is the diagnostic gold standard for clinically significant COPD, the researchers found that a brief, easy-to-use, self-administered questionnaire may be a more practical method for identifying patients with clinically significant COPD who are in need of follow-up and diagnostic spirometry testing.

Study authors conducted an extensive literature search of PubMed and EMBASE to identify articles describing case-finding and epidemiological research to detect or characterize new cases of COPD.

In both the epidemiological and screening studies, factors that appear to be strongly associated with COPD were older age, BMI, smoking history and symptoms such as cough, wheeze and dyspnea. Other lines of research suggest that factors such as prenatal maternal smoking, low birth weight, postnatal tobacco exposure and childhood respiratory infections may predispose individuals to COPD. Factors not included in the screening studies and not statistically significant in the epidemiological studies reviewed included income, fatigue/tiredness, cardiac co-morbidity and taking breathing medications or antibiotics.

The literature review described in this research lays the groundwork for a multi-method screening approach for identifying undiagnosed, clinically-significant COPD in a primary care setting. The findings from this study are being used in further work to develop a simple questionnaire able to identify undiagnosed, high-risk COPD patients in primary care. Such a questionnaire, combined with values from a peak flow meter, may further refine the patient population for whom spirometry is needed.

Reference:
Pediatric and Adult Clinical Interests

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decade of life. Primary immunodeficiencies are more common in males than females, as many genes controlling immune function reside on the X chromosome.

Lack of one or more components of the immune system results in an immune disorder. Our ability to fight infection resides in different immune compartments, which together orchestrate an effective and defensive immune response. The innate immune arm comprises components that don’t need prior experience and include the complement system, neutrophils and other granulocytes, and natural killer (NK) cells. The adaptive immune system, that arm enhanced by prior experience, naturally through exposure or following vaccination, is comprised of T lymphocytes and B lymphocytes.

Defects in a specific component or compartment often manifest with infection due to specific organisms. Thus, neutrophil defects (low absolute number or function) often present with recurrent staphylococcal infection, whereas T lymphocyte defects are seen in patients with recurrent viral, fungal or opportunistic infection (e.g. Pneumocystis jiroveci). Defects in B lymphocyte function (as a result of low or absent numbers or functional abnormalities) resulting in low immunoglobulin levels, particularly IgG, lead to recurrent infections with encapsulated bacteria (S. pneumonia, H. influenza, N. meningitides). Similarly, some of the complement deficiencies present with infection due to encapsulated organisms.

Complement defects in the classical or alternative pathway are not common. Late component defects (C5-9) may present with meningitis, whereas early component defects (C1q, r, s, C4, C2) may present with a lupus-like illness. C2 deficiency is the most common complement component defect and may present with upper respiratory tract infections. In some patients, recurrent bacterial sepsis and infections at other sites are seen. The rare C3 deficiency presents with recurrent infections due to encapsulated organisms.

Other Common Primary Immunodeficiency Diseases

With the increasing awareness and diagnosis of immune deficiency disorders, many names have been assigned based on specific genetic defects. Disorders of B lymphocyte function and immunoglobulin production (hypogammaglobulinemia) are the most common and include selective IgA deficiency, X-linked agammaglobulinemia characterized by the absence of B lymphocytes and common variable immunodeficiency disease (CVID), a heterogeneous group of diseases marked by low immunoglobulin levels, failure of normal antibody production and both significant or low-grade infection.

Primary disorders of the T lymphocyte system are much rarer compared to the secondary deficiency arising from HIV infection and include severe combined immunodeficiency disease or SCID, now also recognized to comprise a number of different genetic disorders. Many of these patients have low absolute lymphocyte numbers, although this is not universal. Since 2012, newborn screening for SCID has been carried out by the State of Colorado with evaluations of suspected babies at National Jewish Health. Other disorders seen are DiGeorge syndrome, characterized by congenital heart defects, hypocalcemia and variable T lymphocyte function, and a large spectrum of molecular/genetic defects.

The most common disorder of the neutrophil system is a low absolute number either resulting from a genetic defect or secondary to a drug or viral infection. Among the neutrophil functional defects, chronic granulomatous disease, X-linked or autosomal recessive, is the most common.

Laboratory Assessment of Immune Deficiency

Laboratory testing has become increasingly sophisticated, including molecular/genetic assessments. If initial screening tests suggest concern for an underlying immune disorder, then referral to a specialist with expertise may be indicated to reduce costs and focus the evaluation.

Tests for immune deficiency usually include:

- Complete blood count (in addition to other parameters, provides absolute neutrophil and absolute lymphocyte numbers)
- Quantitative serum immunoglobulins (IgG, IgA, IgM)

Of note:

- A complete blood count and quantitative immunoglobulins are usually sufficient to diagnose >90 percent of patients with a primary immunodeficiency.
- Most patients diagnosed clinically with sinusitis really only have rhinitis.
- The most common cause of recurrent otitis media and rhinosinusitis is underlying allergy.
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