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supporting families with cystic fibrosis

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Yanky Spira
Director
718-866-9000 ext. 101
Cell: 917-831-9951
yspira@cfsociety.org

Debbie Spira, MS CSP
Program Director
718-866-9000 ext. 102
dspira@cfsociety.org

Pessy Schlafrig
Medical Coordinator
718-866-9000 ext. 103
pessys@cfsociety.org

Aileen Vizel, RD CDN
Nutritionist
718-866-9000 ext. 104
nutrition1@cfsociety.org

Heshy Fischer
Executive Director
718-866-9000 ext. 105

Rabbi Dr. Ben-Zion Twerski, PhD
Psychologist

Dr. Dorothy Bisberg, MD
Pulmonologist

Yedidah Sachs-Yasgur, LCSW-R EMDR
Social Worker

Editor-in-Chief
Debbie Spira

Proofreaders
Aileen Vizel
Yanky Spira

Graphics by CZ Design
CZdesign1460@gmail.com/917-627-1460

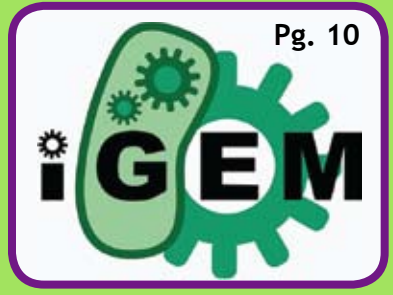
CF Society
4118-14th Avenue, Suite 11
Brooklyn, NY 11219
Phone/Fax: 718-866-9000
Email: cfsocietyorg@gmail.com
Website: www.cfsociety.org

TABLE OF CONTENTS

3 Editor's Note
5 Q & A
7 Guest Columnist
10 The Bottom Line
17 Navigating Nutrition
19 Short Story by M. Wiseman
21 Puzzle Plaza
24 Joke Junction
25 Comic Corner

OUR HEADLINES IN THE BOTTOM LINE

10 Fluorescent Bacteria Used to Create Cystic Fibrosis Bacteria Detector
10 Finding of New Protein Structure Could Benefit Cystic Fibrosis Research
11 Insightful Discovery Could Lead to Better Protection from Lung Infections
12 New Exciting Hope for Cystic Fibrosis Cure
13 Lung Exacerbations in Female Patients with CF Can Be Eased Using Hormone-Based Birth Control
13 In Treating and Diagnosing COPD and CF, New Imaging Algorithm Provides Significant Understanding
14 Exhilarating Expansion and Acceleration of Research, Care, and Patient Programs; CF Foundation Leads the Way
15 Medical Diagnostic Laboratories Provide New Prenatal Testing For Cystic Fibrosis
15 For Patients with Pulmonary Fibrosis, Two New Drug Options Offer Hope
16 65-Year-Old Inventor Develops Pills That Make Flatulence Smell Pleasant



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Editor's Note

Well, hullo!

Folks, do you ever wonder why you wake up in the morning and your legs look so skinny, despite having walked uphill, both ways, for 20 million miles, and then another 20 more? Sound familiar?

If you have CF, that's a common scenario.

Let me introduce you to Drs. Nicolaas E. Deutz and Marielle P. Engelon with their monumental study on protein and CF, titled "Why proteins are so important in Cystic Fibrosis." Protein? Cystic Fibrosis? Um, what's the connection? Get ready for some facts and figures that will get those thoughts zinging 'round your brain and help you become a healthier you.

Let's serve you up some fascinating truths about CF. To start with, you know how all CF doctors are consistently concerned with your child's BMI, right? That's because there is a **remarkable** correlation between a child's weight at 4 years of age to that child's height and lung function as an adult! Would you believe that the survival of a CF'er can depend on his nutritional status as a stubborn kid in kindergarten?

When it comes to chronic illnesses, the problem is that there is a hidden loss of muscle mass. Thus, with conditions like CF, 30-60% of patients present with muscle loss **even though they show a normal body weight**. Do you know what your muscle mass does for you? To answer this question, let's examine what happens with patients that have LOW muscle mass:

Let's serve you up some fascinating truths about CF.

- ↑ hospitalizations (per yr)
- ↑ duration of hospital stay
- ↓ lung function
- ↑ exacerbations
- ↓ quality of life
- ↑ bone loss
- ↓ muscle strength

In other words, as Drs. Deutz and Engelon put it, "PRESERVING MUSCLE MASS IS IMPORTANT IN CF!!" (their exclamation points, not mine.)

Fact: A person **must have** protein in order to build up muscle mass. But what happens if your child is pancreatic insufficient, or partially so? Exocrine pancreatic insufficiency (EPI) occurs in 90% of CF patients. Because EPI negatively affects digestion of fat and protein in the intestines (are you starting to see a glimmer of what's happening here?), protein recommendations will need to be raised depending on how significantly PI the patient is and how efficient the pancreatic enzymes are for the child.

Did you know that children with cystic fibrosis have about 55% digestion capacity for protein, and adults with CF are at approximately 50%? Is **your** child taking in enough protein for healthy living with CF- or not?

According to experts, recommended intake of protein is 1.5 g/kg (2.2 lbs) per day for chronic diseases like CF, and even more during conditions of high inflammation/ exacerbations. Typical growth and development is **absolutely** expected in children and teens with CF- when the proper nutrition and pancreatic enzyme replacement therapy (PERT) is received!

However, here's a startling fact: The doctors say that "pancreatic enzyme intake in CF normalizes protein digestion... after (a) **severe** delay - of 240 minutes! That's FOUR HOURS LATER!"... W-H-A-T? Then how on earth do people with CF gain the protein they need? Believe it or not, despite reduced protein digestion capacity,

Editor's Note

CF patients DO respond to **very high levels** of protein intake.

Still, here comes a tricky dichotemy. A child with CF needs the high protein intake to build muscle mass; however, doctors say it will likewise increase "colonic load of undigested, not absorbed proteins, peptides and amino acids." Hmm, that may not sound copacetic but don't worry, they propose a solution. Simply put, a child with CF should be getting the best quality proteins that can be digested with ease. Because it is the amino acids found in proteins that are necessary to stimulate muscle protein synthesis, that is precisely what CF'ers need to consume.

All right, people, let's tackle muscle loss in CF- so that lung function can increase, exacerbations can decline, muscle strength can improve, hospitalizations and durations of stay can become rare events, and quality of life can become something to crow about! Here's what they say to do:

- ☑ High protein intake
- ☑ Optimal quality of protein
- ☑ Proteins with high levels of essential amino acids
- ☑ Protein needs to be easily digestible
- ☑ Protein intake of 1.5 g/kg/2.2 lbs of body weight
- ☑ PERT with high enzyme activity for proteins
- ☑ Exercise (including weight-bearing exercise)
- ☑ Reduce inflammation

You think we're done? These researchers contend that a CF'er **must** be monitored for BMI, muscle and fat mass, and nutritional assessment, even when patients present with normal weight. In fact, they recommend that careful monitoring of all of the above must ALSO be done when body weight alters significantly and involuntarily, during/after exacerbations, and even when nutritional intervention is being applied!

By the way, recommended testing includes a DEXA scan, respiratory and muscle function testing (entailing use of a mouth pressure device, handgrip dynamometry, and quadriceps bench), PFTs (and assessing exhaled Nitric Oxide), measuring nutritional intake (taking proteins and amino acid mixtures to measure the direct effects, as well as after steady supplementation for several weeks), measurement of protein and amino acid metabolism (two catheters in the arm, infusing low level of non-radioactive isotopes and then drawing blood), and questionnaires (assessing mood, quality of life, usual food intake, and day-to-day physical activity).

So, are you flexing those biceps yet? (Remember to breathe as you do it; muscles need oxygen, not just amino acids!) If you would like to know more about this report, please email me for the link at dspira@cfsociety.org.

In other news, we now introduce a newly added feature called Your Voice, in which we highlight the artwork and writing that our readers have submitted. Enjoy that and our holiday bonus fun in both Puzzle Plaza and Comic Corner. And once again, we sincerely thank our kind sponsors and cartoonists who help make this publication complete! We've gotten a heap of great feedback here at the CFS Gazette; we can't wait to hear from you all.

Stay safe, stay healthy. Stay sane.

Debbie Spira

'Room service? Send up a larger room please.'

Ever since I can remember, my sputum cultures have grown pseudomonas and I have responded well to a course of oral antibiotics. Over the past six months, I have had a number of infections that have required IV antibiotics. My sputum cultures have grown MRSA and my pulmonary function tests have started a steep decline starting around the same time. Is there anything I can do to get a handle on the MRSA? Are the antibiotic therapies used for pseudomonas different than those used for MRSA?

-Name withheld to maintain privacy

Dr. Claire L. Keating Responds:

It has recently become known that MRSA infection in the lungs of CF patients results in more rapid lung function decline. The antibiotics used to treat MRSA are different than those used to treat Pseudomonas, so the physician should be giving targeted therapies against both MRSA and Pseudomonas when you get oral or IV antibiotics. While there are no specific eradication protocols for when MRSA appears in sputum cultures, many physicians do try to eradicate MRSA with intensive antibiotic and other topical therapies to nails and skin. You should discuss this with your physician. Of course, aggressive airway clearance also is critical in slowing the decline in lung function - this cannot be underestimated.

Dr. Claire L. Keating, M.D.

I am 19 years old and I have CF. My lung function is still in the normal range and I have not had too many exacerbations. But I am suffering from digestive issues. I am taking my digestive enzymes and my stools are not overly greasy. Still, no matter what I eat, I cannot gain weight. Are there any new therapies that can help me?

-Name withheld to maintain privacy

Dr. Claire L. Keating Responds:

There are many reasons why a person with CF has difficulty gaining weight and it's important to work closely with your doctor and CF dietician on this. We do know that the higher the body mass index (and thus a better nutritional status), the healthier the person. Things to consider in your situation are: Are you taking enough enzymes with meals? Are you eating enough high fat high calorie foods and meeting your calorie needs every day? Are there any other issues going on like acid reflux, food intolerances, or excessive bloating or constipation? There are several interventions/ changes that your providers can suggest, such as a close examination of your daily diet (you may not eat as much as you think), adding an antacid, changing enzyme brands, adding nutritional supplements daily, or in more advanced cases, consideration of a feeding tube for overnight nutritional supplementation.

Dr. Claire L. Keating, M.D.

Claire L. Keating, MD is the Associate Director of the Gunnar Esiason Adult Cystic Fibrosis and Lung Program since 2009. She has done epidemiologic research in adult-diagnosis cystic fibrosis and has presented posters and published several abstracts and a paper. She is currently serving as PI on two pharmaceutical trials in cystic fibrosis and is a sub-investigator on several other clinical trials in pulmonary diseases.

Disclaimer: The answers relayed to our readers should not be solely relied upon when making treatment decisions. All health issues should be directly addressed to the patient's provider.

Is there a correlation between milk products and increased mucous? My 17-year old daughter with CF feels more congested after eating or drinking dairy. I was wondering if it is a real symptom or imagined?

-Name withheld to maintain privacy

Aileen Vizel Responds:

Thank you for taking the time to ask your important question. No, you are not imagining this! It has been medical-

ly proven that because of the way that dairy products such as cheeses, milk, ice cream, sour cream, and the like are broken down in the body, excess mucous production can result. To decrease this effect, avoid dairy products as much as possible! Another step that you can take is to increase foods in the diet that are known to decrease mucous production, such as garlic, onions, mustard, watercress, horseradish, parsley, celery, pickles, lemons, and anti-inflammatory oils (fish oil, nut-based oils).

Good luck!

Aileen Vizel, RD, CDN

My daughter is 4 years old, and at her age it's not easy getting her treatments done!! How do other children do it? I would really appreciate some helpful tips- thank you.

-Name withheld to maintain privacy

Debbie Spira Responds:

You ask an **excellent** question, one that many fellow parents have posed. The key phrase here is 'positive association'; meaning, turn CF into a positive experience for your daughter - and hence for you and the entire family. Let's say your daughter can't stand the vest. Why? She'd rather do anything but vesting. In fact, she'd prefer to stand on her head and swallow burning hot chili peppers while gargling pickle juice instead of donning her vest. Why? She can't stand the shaking. The coughing. How tired she gets. How boring it is. Knowing that all her friends are busy having fun while she's stuck in her room, under her parents' watchful gaze, nebulizing, vesting, coughing away. Do her a favor: Make chest therapy fun. Find out all the things your child loves to play with, loves to spend her time doing, and incorporate these favorites into treatment time. Not only will the positivity of that help nullify the perceived negativity of chest therapy, she'd have the added bonus of great deep breathing if she chooses fun activities like jump rope, trampoline, playing ball, jumping jacks, etc. while nebulizing. And keep a strict policy. She wants to play with the iPad? Sure! When vesting. She wants to read a book? Sure! When nebulizing. She wants to hear her favorite CD? Absolutely! When vesting **and** nebulizing. You can get in on the act too, y'know. Dress up like a clown and act her age, tickle her up- you'll have her giggling away (and surely taking those wonderful deep breaths) while delighting in your silliness. You can also try putting up a chart that she can plainly see and aim for a treat at the end of each week.

CF is hard enough. Let's make it FUN!

Debbie Spira, MS, CSP

To submit a question, email us at cfsocietyorg@gmail.com.

CYSTIC FIBROSIS FOUNDATION
ADDING TOMORROWS

28th Annual North American
Cystic Fibrosis CONFERENCE

OCTOBER 9-11, 2014 • GEORGIA WORLD CONGRESS CENTER • ATLANTA, GA

A REPORT FROM DR. DOROTHY S. BISBERG

Guest Columnist

At this year's North American Cystic Fibrosis Conference (NACFC) in Atlanta, Georgia, on the 25th Anniversary of the discovery of the CF gene, the CF Foundation made a promise to the entire CF Community: There will be a medication to treat the basic defect in CF for every single patient with the disease.

Come explore what was discussed:

The new class of medications are based on the patient's genetic mutations. Mutations (or changes) in the CF gene lead to the production of an abnormal or absent CFTR protein (Cystic Fibrosis Trans Membrane Conductance Regulator). CFTR is a chloride ion channel at the surface of the cell, a passageway for chloride to get in and out. The mutation also affects the sodium transport so that there is less salt (sodium chloride) outside the cell and more inside of the cell. Water follows salt, thus causing thick sticky secretions in the airways and the pancreatic duct. Obstruction of the airway leads to recurrent pulmonary infection and scarring. Obstruction of the pancreatic duct blocks the release of the enzymes needed for digestion.

There are over 1900 mutations in the CF gene that can lead to disease. These mutations are grouped into 5 different classes, depending upon how the formation of CFTR is affected. 87% of the patients in the U.S. carry at least one Delta F508 (47% carry both). This mutation is identified as a Class II defect where there is a problem in the processing of the CFTR protein which takes place in the cell. In the case of Delta F508, there is a problem in the folding of the protein. By the end of the year the CF Foundation is expecting approval by the FDA for a new combination treatment for those 47% of patients who carry 2 Delta F508 mutations. These two medications area Ivacaftor, a potentiator, and Lumacaftor, a corrector.

Ivacaftor, better known as Kalydeco, was developed first and is currently being used by 4% of CF patients (age 6 years and above) who carry the G551D mutation (a Class III gating mutation). Ivacaftor keeps CFTR open longer and thus increases the flow of chloride ions. Ivacaftor has also been shown to restore CFTR function. Studies have demonstrated a normalization of the sweat test and a significant improvement in lung function, as well as a dramatic decrease in the number of hospitalizations and pulmonary exacerbations. Patients taking Ivacaftor have also shown improvements in the GI tract. These improvements include weight gain, increased BMI and normal bowel PH. Initial studies were conducted in patients 6 years old and above. Several additional studies showed that Ivacaftor was found to be both safe and efficacious in 2 to 5 years old with the G551D mutation. Also, Ivacaftor was studied in 39 additional patients with other gating mutations. Except for one (G970R), results were similar to the 6551D studies and Ivacaftor is now recommended for all patients with these mutations (9 altogether).

The CF Foundation made a promise to the entire CF Community: There will be a medication to treat the basic defect in CF for every single patient with the disease.

Use of Lumacaftor along with Ivacaftor has been reported in two worldwide Phase 3 studies in over 1000 patients, 12 years of age and older, who carry two Delta F508 mutations. Results demonstrate 5% improvement in FEV1, a 40% reduction in pulmonary exacerbations, a 60% decrease in hospitalizations, and an increase in BMI.

It is estimated that by 2015, 60% of CF patients will be receiving treatment to correct the basic defect of CF. Acknowledging that new treatments have been adding to the treatment burden of multiple CF medications, such as those delivered via nebulizer, Ivacaftor and Lumacaftor should be an easier addition to the CF treatment regimen, considering they are both pills.

Lumacaftor and Ivacaftor have also been tried in heterozygotes (one Delta F508 mutation), an additional 30% of the CF population. This treatment does not demonstrate any improvement in pulmonary function or change in the number of exacerbations. However, there was a decline in sweat chloride. The next step will be studying another drug VX661. This drug has been studied in patients with G551D/Delta F508 mutations occurring together and pro-

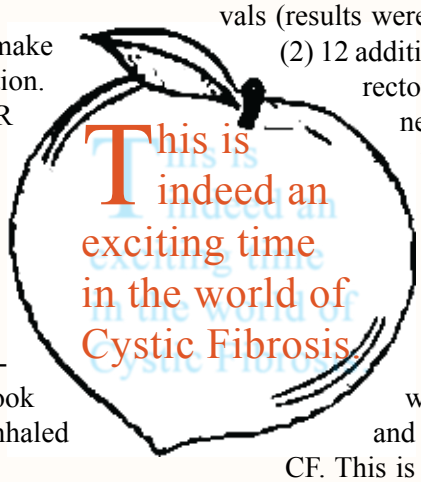
The Six Class Mutations:

Class	Defect
NORMAL	Normal CFTR protein function
CLASS I	*Defective protein synthesis*: Nonsense or frameshift mutations are associated with a complete lack of CFTR protein at the apical membrane (e.g. G542X, 394delTT and 1717-1G>A)
CLASS II	*Abnormal protein folding, processing, and trafficking*: Misfolded functional CFTR protein is largely degraded intracellularly, thus there is a complete lack of CFTR protein at the apical membrane (e.g. F508del and N1303K)
CLASS III	*Defective regulation, reduced gating*: Mutations prevent channel activation by inhibiting binding and hydrolysis of ATP at one of the two nucleotide-binding domains; therefore, the CFTR protein on the apical surface is non-functional (e.g. G551D)
CLASS IV	*Decreased conductance*: Abnormal anion conductance results in impaired protein function (e.g. R117H and R347P)
CLASS V	*Reduced abundance*: Abnormal splicing, promoter mutations or inefficient trafficking results in a reduced number of normally functioning protein at the apical membrane (e.g. A455E and 3849+10kbC>T)
CLASS VI	*Decreased stability or altered regulation of separate ion channels:* Mutations that cause inherent lability of the CFTR protein or alter regulation of other ion channels

Source: www.intechopen.cin.biijs.acute-pancreatitis/pancreatitis-in-cystic-fibrosis-and-cftr-related-disorder.

vides an additional 5% improvement to that seen when taking only Ivacaftor.

Class I mutations (nonsense mutations) make up another 12% of the CF gene population. With these mutations, production of CFTR is stopped and the protein is never made. Phase 3 studies of Atalauren, a "read through" agent, showed that patients receiving the drug had lower decline in lung function and a lower rate of pulmonary exacerbations compared to placebo, but not if the patient is on inhaled aminoglycosides (Tobi). The next study will look at patients who are not taking these inhaled medications.



Other efforts to correct the basic defect include: (1) The UK Gene therapy trial - Using a liposome- based gene delivery system by nebulizer, 12 doses at monthly intervals (results were not yet available for the NACFC) and (2) 12 additional companies are working on new correctors and potentiators. For Delta F508, the next generation of CFTR correctors will target different parts of CFTR to further stabilize folding and dramatically increase the amount of CFTR trafficked to the cell surface.

In summary, the message of the CF Foundation to the CF community is that we will restore "robust" CFTR activity and thus" robust" life for all individuals with CF. This is indeed an exciting time in the world of Cystic Fibrosis.

Dr. Dorothy Bisberg, M.D. is the director of the Division of Pediatric Pulmonology and the Cystic Fibrosis Center at St. Barnabas Medical Center in New Jersey.

THE BOTTOM LINE

Bringing you recent breaking news and updates pertaining to patients with debilitating lung diseases

On New Discoveries

Fluorescent Bacteria Used to Create Cystic Fibrosis Bacteria Detector

A group of undergraduate researchers from Dundee University are the proud recipients of 3 prizes from a conference in Boston, Massachusetts for their breakthrough work on harnessing a fluorescent bacteria to detect a potentially dangerous lung infection in cystic fibrosis (CF) patients. "The Lung Ranger," an early warning system for CF patients, was the team's entry for the International Genetically Engineered Machine (iGEM) competition, and was presented at the national Cystic Fibrosis Trust conference in Manchester.

The Lung Ranger is a user-friendly, hand-held medical device that can be used either by a doctor or a patient. The device uses the E. coli bacteria strain normally found in the colon for healthy digestion to detect the presence of either Pseudomonas aeruginosa or Burkholderia cenocepacia by emitting a detectable fluorescence. The fluorescent light now only allows for the detection of the bacteria types — both of which are quite dangerous to CF patients — but also allows doctors to measure severity of the bacterial infection as well.

Despite the fact that the Lung Ranger is still in the "proof of principle" stage of its development, the Dundee team has much to be proud of, as they have already been approached by some of the most prominent representatives in the industry who are interested in seeing how the project progresses and whether or not it can be commercialized into a viable device for treating cystic fibrosis.

Please see source: http://cysticfibrosis-newstoday.com/2014/11/10/cf-device-the-lung-ranger-from-dundee-university-wins-3-awards/

THE BOTTOM LINE

A group of undergraduate researchers from Dundee University were awarded triply at a Boston, Massachusetts conference for their breakthrough work of harnessing fluorescent bacteria to detect, and judge the severity of, potentially dangerous lung infections

They created "The Lung Ranger," an early warning system for CF patients and a user-friendly, hand-held medical device that can be wielded by patient and doctor alike; the device uses E. coli bacteria to detect the presence of both P. aeruginosa and B. cepacia by emitting a detectable fluorescence

Though still in the "proof of principle" stage of its development, they have already been approached by some of the most prominent representatives in the industry eager to see how the project progresses

On New Discoveries

Finding of New Protein Structure Could Benefit Cystic Fibrosis Research

In a recent study, published in the online issue of Nature, the authors determined the structure of an ABC transporter protein with a sub nanometer resolution for the first time. The new findings have implications in the continued study of Cystic Fibrosis.

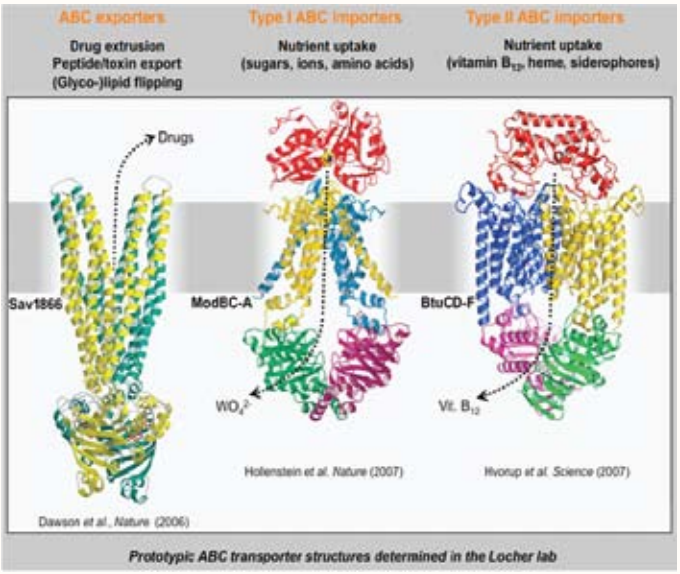
Cystic Fibrosis (CF) is a life-threatening disease caused by mutations in the CFTR gene (cystic fibrosis transmembrane conductance regulator gene). CFTR is an ABC gene — it belongs to the ABC transporters' family, but unlike ABC transporters that work as effluxes, CFTR regulates opening and closing of chloride and sodium ions' channels. Thus, in the absence of CFTR functional protein, thick mucus accumulates, leaving CF patients more susceptible to infections.

In this new study, researchers at the Institute for Biochemistry at the Goethe University and colleagues at the University of California in San Francisco were able to determine for the first time the structure of an ABC transporter at a sub-nanometer (less than a nanometer, with a nanometer being equal to 10-9 metros) resolution. The finding was achieved with a new single electron camera, together with new imaging techniques and with specific antibody fragments.

Professor Robert Tampé from the Institute for Biochemistry at the Goethe University and one of the study's corresponding authors noted, "On the one hand, ABC transporters cause diseases such as cystic fibrosis, while, on the other hand, they are responsible for the immune system recognizing infected cells or cancer cells. Over a period of five years, we have successfully implemented a number of innovative, methodological developments…"

Because ABC transporters are so pivotal in whether or not

THE BOTTOM LINE



Prototypic ABC transporter structures determined in the Locher lab

disease develops or is repelled by the body, this new insight into the structure of ABC transporter protein may lead to the development of next-generation therapeutics that can offer improved outcomes for slowing the progression of Cystic Fibrosis.

Please see source: http://cysticfibrosisnewstoday.com/2014/11/06/discovery-new-protein-structure-benefit-cystic-fibrosis-research/

THE BOTTOM LINE

A recent study helped researchers determine the structure of an ABC transporter protein with a sub nanometer resolution for the first time

CFTR regulates opening and closing of chloride and sodium ions' channels and is an ABC gene, belonging to the ABC transporters' family; ABC transporters cause medical conditions such as CF, yet also are responsible for the immune system recognizing infected cells

This new insight into the structure of ABC transporter protein may lead to the development of next-generation therapeutics that can offer improved outcomes for slowing the progression of CF

On New Discoveries

Insightful Discovery Could Lead to Better Protection from Lung Infections

A new study from Karolinska Institute, published in the American Journal of Respiratory and Critical Care Medicine, describes a new mechanism of antibacterial defense in the lung. This defense mechanism is mediated by Interleukin-26, an important finding for chronic lung infections.

Chronic lung diseases are a major medical condition throughout the world that is being exacerbated by pollution, smoking, and infections. In fact, the lung is a frequent target of infections, representing a significant risk for patients with chronic lung diseases such as COPD, severe asthma, and CF. However, the mechanisms that normally protect the lungs of a healthy person that may be impaired in chronic lung disease patients are still not well understood.

In this study, the team from the Institute of Environmental Medicine, and the Department of Medicine, Solna, with colleagues at the Sahlgrenska Academy in Gothenburg discovered a new anti-bacterial mechanism in human lungs mediated by Interleukin-26 (a member of the large group of cytokines, the interleukins, with key roles in mediating the response of the immune system to infections). Exposing the respiratory track of healthy individuals to an endotoxin, a toxic substance bound to the bacterial cell wall, significantly induced Interleukin-26 expression on alveolar macrophages (a type of white blood cell found in the pulmonary alveolus). Macrophages release of Interleukin-26 triggered neutrophils, a short-lived and highly motile type of white blood cell, to mobilize towards bacteria and attack it.

Anders Lindén, Professor at the Institute of Environmental Medicine and study lead author, noted, "We have concluded that this mechanism is important for understanding antibacterial defense in the lungs of healthy individuals and how the immune defense system is activated when common respiratory infections or pneumonia occurs. In the long run, we hope that this knowledge will play an important role in helping us to understand how groups of patients with chronic lung diseases develop an increased sensitivity to bacterial infections, which could lead to the development of a new treatment for infections."

Please see source: http://cysticfibrosisnewstoday.com/2014/10/23/lung-infection-protection-cystic-fibrosis-patients-developed-new-discovery/

THE BOTTOM LINE

A new study describes a new mechanism of antibacterial defense in the lung that is mediated by Interleukin-26, an important finding for chronic lung infections

The trajectory of the antibacterial defense: respiratory track is exposed to endotoxin -> inducing Interleukin-26 upon alveolar macrophages -> macrophages trigger neutrophils that launch attacks on bacteria

Researchers say this mechanism is vital for understanding antibacterial defense in the lungs of healthy people and when common respiratory infections occur; this could lead to the development of a new treatment for lung infections

THE BOTTOM LINE

New Exciting Hope for Cystic Fibrosis Cure

Twenty-three years ago, a young pediatrician named Dr Anil Mehta took nasal cells from a healthy 5-year old child for research he was doing. He has been researching a new approach to reversing cystic fibrosis.

The doctor is now leading the research at the amazing microbiology center in Dundee University Medical School, where the nasal cells have hit their mark and delivered a consortium of Italian and French researchers a eureka moment. Dr. Mehta met his Italian opposite number who was working with a leading French scientist at a conference some four years ago. The Italian expert had found a drug that is used in a completely unrelated disease that cleared the debris that destroys the lung in a patient with cystic fibrosis. His approach amazed Dr Mehta because it was totally new to the field.

"The overactive enzyme TG2 acts like an out-of-control spot welder, binding together every protein it comes into contact with," said Dr. Mehta. "My colleagues showed they had a medicine capable of bringing that welder under control." By administering Cysteamine, a drug long used to treat Cystinosis in children, combated overactive TG2 and reversed inflammation.

But this wasn't enough. Dr Mehta's team already had a totally different drug, based on nasal cells, which had reversed the environment in the cystic fibrosis cell present as they regenerated that tissue. Another overactive enzyme, protein kinase CK2, is found in cystic fibrosis patient cell biopsies. This enzyme also leads to inflammation and was inhibited through the use of EGCG, which is an approved over-the-counter tonic derived from green tea. "These drugs are already licensed, and being off-patent means the cost of developing a drug therapy should not be prohibitive," noted Dr. Mehta.

They next approached a doctor in Naples who applied the two drugs together, Cysteamine and epigallocatechin gallate (EGCG), to 10 humans, nine of whom no longer displayed the hallmarks of the disease after only two months of therapy. A large-scale clinical trial investigating the combination treatment in an international cystic fibrosis population is in planning stages.

"The results suggest that it might be possible to arrest the disease," said Dr. Mehta. "Obviously we are still at an early stage, but if these results are replicated in a placebo controlled clinical trial, then I believe it could be a potential game-changer."

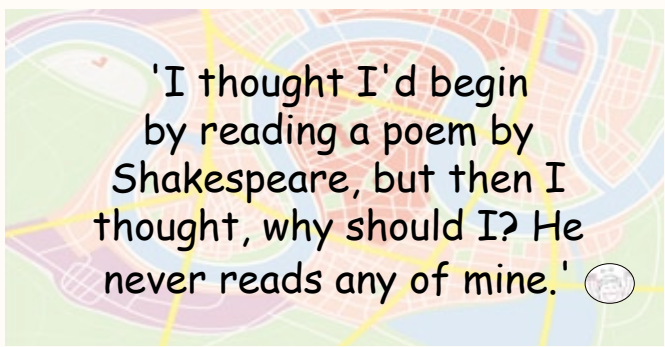
Please see source: http://blogs.channel4.com/snowblog/eureka-moment-offers-hope-cystic-fibrosis-cure/24757 and http://cysticfibrosisnewstoday.com/2014/11/12/new-combination-therapy-may-treat-90-cf-patients/

THE BOTTOM LINE

Dr Anil Mehta, now leading the research at the microbiology center in Dundee University Medical School, has successfully made use of healthy nasal cells to blaze a new frontier in finding the cure for CF

His research team is combining his drug, based on nasal cells, which had reversed the environment in the cystic fibrosis cell present as the tissue regenerated, with a drug that clears the debris destroying the lungs in a CF patient

Having successfully tested the combined drugs in a small clinical trial, a large-scale clinical trial for cystic fibrosis participants throughout the world is in planning stages



THE BOTTOM LINE

Lung Exacerbations in Female Patients with CF Can Be Eased Using Hormone-Based Birth Control

A new case study on the effect of female hormones in pulmonary exacerbations in cystic fibrosis patients, published in the journal BMC Pulmonary Medicine by Dr. Adelaida Lamas, supports previous evidence associating female hormones in the development of recurrent infectious pulmonary exacerbations and the deterioration of lung function in a woman with CF. The new findings suggest that hormone-based birth control for women with CF could offer a therapeutic value for avoiding lung function issues.

The disease affects both genders, but there is a gender-based dichotomy relative to disease severity, with women having a survival disadvantage and weaker lung function. The origin of this gender difference and susceptibility is not well understood, but in previous studies, female hormones have been implicated in the development of pulmonary exacerbations (PE).

In this study, Dr. Lamas along with colleagues analyzed the clinical case of a 20 year-old female patient diagnosed with CF with severe recurrent PE. These severe recurrent PEs were always associated with the menstrual cycle, have been occurring since her first menstrual cycle, and come in combination with lung function deterioration despite being subjected to various treatments with intravenous antibiotics. As part of the study, the patient was implanted subcutaneously with 68 mg of etonogestrel (Implanon®), Organon Espanola S.A., a hormone-releasing birth control implant that prevents pregnancy for 3 years and contains a progestin hormone called etonogestrel. The researchers observed that after the insertion of the etonogestrel implant, the patient did not have pulmonary exacerbations, and pulmonary function was recovered.

Overall, this study shows and correlates with former studies that female hormones are crucial players in the development of PE and in the deterioration of lung function in female patients with CF. Notably, the study highlights that hormonal control through contraceptive methods may be considered as a possible treatment for this pathological condition.

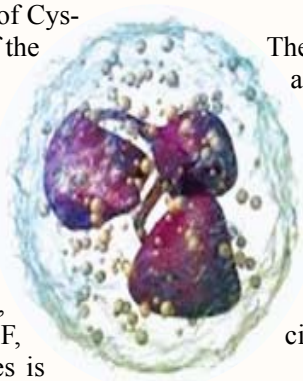
Please see source: http://cysticfibrosisnewstoday.com/2014/10/27/hormone-based-birth-control-could-ease-cystic-fibrosis-lung-exacerbations-in-female-patients/

THE BOTTOM LINE

- A new case study on the effect of female hormones in pulmonary exacerbations in CF patients supports previous evidence associating female hormones in the development of recurrent infectious pulmonary exacerbations and the deterioration of lung function in a woman with CF
- A 20 year-old female patient with CF presenting with severe recurrent pulmonary exacerbations associated with her menstrual cycles was given a hormone-releasing birth control implant that prevents pregnancy for 3 years and contains a progestin hormone called etonogestrel
- This study highlights that hormonal control through contraceptive methods may be considered as a possible treatment for recurrent debilitating pulmonary exacerbations in female patients

In Treating and Diagnosing COPD and CF, New Imaging Algorithm Provides Significant Understanding

A recent study, by Dr. Sara Zarei and colleagues at San Diego State University, presents a new algorithm that improves recorded imaging results of the lungs of Cystic Fibrosis patients, by providing information of the infection site at a microscopic level.



Chronic Obstructive Pulmonary Disease (COPD) and Cystic Fibrosis (CF) induces chronic lung inflammation, causing airflow limitation and the scarring of lung tissues. The inflammatory response in the airways leads to the recruitment of large amount of neutrophils, among other potentially harmful responses. In CF, the scarring induced by inflammatory cytokines is primarily due to the contact between the lung lining and the mucus biofilm, with both factors resulting in damaging to the lungs of a CF patient.

There are clinical tests for the global measurement of airflow obstruction and restriction such as spirometry. This offers indicators such as the forced expiratory volume (FEV) that measures the first second of forceful breath, and forced vital capacity (FVC), which measures the volume of air that can be powerfully blown out after a full inspiration movement. However, these tests do not provide detailed information about the specific site of mucus obstruction.

Additional information can be obtained by the repeated

THE BOTTOM LINE

imaging of the lungs of CF patients, which is normally done by chest x-ray and Computed Tomography (CT). Due to radiation exposure, Magnetic Resonance Imaging (MRI) is more recently being used to obtain imagery of the lung. However, despite the clarity and precision of MRI images, they do not give information on smaller airways at the microscopic level.

In this study, the working hypothesis indicated that accumulation of mucus is the primary cause of damage to the lung. The study was to supply the clinicians with an algorithm that enables following the site and progression of mucus in the lungs of CF patients using imaging tools. Thus, the new approach will help doctors visualize the effect of mucus progression on lung function and associate it with the current stage of the disease. The models will allow doctors to quantitatively follow CF patients' responses to various therapies and prescribe the adequate treatment, and may play a crucial role in future Cystic Fibrosis treatments.

Please see source: http://cysticfibrosisnewstoday.com/2014/11/05/new-imaging-algorithm-offers-key-insights-into-cystic-fibrosis-diagnosis-treatment/

THE BOTTOM LINE

A recent study presents a new algorithm that improves recorded imaging results of the lungs of CF patients, by providing information of the infection site at a microscopic level

X-rays, CT scans, and MRIs are typically used to detect lung inflammation, mucus production, and active lung infections

Researchers have developed an algorithm that enables visualizing and following the effect of mucus progression on lung function using the standard imaging tools available

On the CFF

Exhilarating Expansion and Acceleration of Research, Care, and Patient Programs; CF Foundation Leads the Way

The Cystic Fibrosis Foundation (CFF) announced an unprecedented acceleration and expansion of its research, care and patient programs for the CF community. This action is possible as a result of the sale of the Foundation's royalty rights to CF treatments developed by Vertex Pharmaceuticals Inc. The Foundation received $3.3 billion from the sale to Royalty Pharma.

"This is a transformational moment for the Foundation and the entire CF community," said Robert J. Beall, Ph.D., president and CEO of the Cystic Fibrosis Foundation. "These new resources will allow us to supercharge our efforts to help all people with CF live long, healthy and fulfilling lives today and work to find a cure. We could not have taken this exciting step forward without the steadfast commitment and decades of hard work of many volunteers and donors, researchers and health care professionals, together with people with CF and their families."

The sale is the most recent and significant example of the Foundation's successful venture philanthropy model, through which the organization provides upfront funding for pharmaceutical companies to help reduce the financial risk of developing drugs to treat CF. Funds from any royalties the Foundation receives are reinvested to accelerate further drug discovery and advance its mission to find a cure.

In addition to increasing its research funding for innovative strategies to target the genetic cause of CF, the Foundation plans to strengthen the specialized care and support that people with CF and their families receive at more than 120 Foundation-accredited care centers across the country. The Foundation will also expand its resources to help people with CF and their families afford costly medications and manage health care coverage and insurance.

Beall continued, "We still need the support of donors and volunteers to realize our goals. We plan to invest these funds in the wisest way possible: to help people with CF live healthier lives today and have more tomorrows."

Please see source: http://www.cff.org/aboutCFFoundation/NewsEvents/2014NewsArchive/11-19-Expansion-of-Research-and-Programs.cfm

THE BOTTOM LINE

The CF Foundation sold their royalty rights to CF treatments, developed by Vertex Pharmaceuticals, to Royalty Pharma for $3.3 billion

As a result, the CFF has announced enormous gains in expansion and acceleration of their research, care, and patient programs; funds are reinvested to advance its mission for a cure

This follows their successful venture philanthropy model, whereby CFF provides upfront funding for pharmaceutical companies to help reduce the financial risk of developing drugs to treat CF

THE BOTTOM LINE

Medical Diagnostic Laboratories Provide New Prenatal Testing For Cystic Fibrosis

A novel Cystic Fibrosis testing technology that features next-generation DNA sequencing platforms has been launched by Medical Diagnostic Laboratories. MDL specializes in complex, state-of-the-art, automated DNA-based molecular analyses.

The MDL Cystic Fibrosis Core Test is a CFTR gene sequence exam that is non-invasive and can be done using specimens from mouthwash samples, cervico-vaginal swabs, or blood samples from pregnant women. It uses breakthrough technology to provide a series of CF testing through high-accuracy genetic testing, and is able to screen the 23 major mutations recommended by the ACOG and the ACMG for the disease.

Since the discovery of the cystic fibrosis transmembrane conductance regulator (CFTR) gene in 1989, more than 1,800 different mutations have been discovered by scientists. Therefore, the test not only analyzes the disease's 23 major mutations, but also the 9 that are recommended by the U.S. Food and Drug Administration for determining the efficiency of Ivacaftor (Kalydeco).

The MDL also provides Cystic Fibrosis Site Specific Analysis screens for identified CF mutations between family members, since CF is a genetically inherited disease that affects the respiratory, gastrointestinal, and reproductive function.

The National Institute of Health (NIH), the American College of Medical Genetics (ACMG), and the American College of Obstetricians and Gynecologists (ACOG) advise that all pregnant women should receive CF carrier screening, which has already been included in the national newborn screening panels.

Early detection is crucial in the treatment of cystic fibrosis, and therefore, every year, millions of babies undergo newborn screening for the diagnosis of genetic, metabolic, and endocrine disorders, as well as hearing impairment.

Please see source: http://cysticfibrosisnewstoday.com/2014/10/24/mdl-provides-new-prenatal-cystic-fibrosis-testing/

THE BOTTOM LINE

- MDL has launched a novel Cystic Fibrosis testing technology for pregnant women that features next-generation DNA sequencing platforms
- The MDL Cystic Fibrosis Core Test is a CFTR gene sequence exam that is non-invasive and can be done using specimens from mouthwash samples, cervico-vaginal swabs, or blood samples from pregnant women; the test is able to screen the 23 major mutations, plus the 9 recommended by the FDA
- The MDL also provides Cystic Fibrosis Site Specific Analysis screens for identified CF mutations between family members

'I'm so ugly. My father carries around the picture of the kid who came with his wallet.'

Q: Why can't a blonde dial 911?

A: She can't find the eleven.

For Patients with Pulmonary Fibrosis, Two New Drug Options Offer Hope

Where there was once nothing … finally, something for patients suffering with a devastating lung disease. Not one, but two new drugs give hope to those running out of breath … and time.

Idiopathic Pulmonary Fibrosis is an aggressive and deadly disease that causes scarring in the lungs. But two new drugs – pirfenidone and nintedanib – work at the molecular level to slow the fibrotic process and progression of the disease.

University of Chicago Medicine pulmonologist Dr. Imre Noth says, "Both drugs roughly improved the rate of decline about 50 percent. What that means is, for patients who you would have expected to deteriorate over one or two years, may take two or four. Somebody who was going to take four to eight years anyway, is now going to take eight to 16."

THE BOTTOM LINE

The two drugs are extremely expensive – a one-year supply runs $94,000 to $96,000. But the drug companies say they will help those who can't afford to pay – they have assistance programs available. And for more support, contact the Pulmonary Fibrosis Foundation, which funded research on these breakthrough drugs.

Please see source: http://wgntv.com/2014/11/05/two-new-drug-options-give-hope-to-those-suffering-pulmonary-fibrosis/

THE BOTTOM LINE

- Two new drugs have been developed for patients with Pulmonary Fibrosis- Pirfenidone and Nintedanib
- Both drugs work at the molecular level to slow the fibrotic process and progression of the disease, promising hope for a longer, healthier life
- Though prohibitively expensive, drug companies offer assistance programs to help to those who can't afford the price tag; alternatively, the Pulmonary Fibrosis Foundation can also be appealed to

On Hilarious Inventions

65-Year-Old Inventor Develops Pills That Make Flatulence Smell Pleasant

Christian Poincheval, a Frenchman has developed a range of pills aimed at making people's flatulence smell sweeter - of chocolate or of roses - which he says will make the perfect holiday present.

The 65-year-old artist and inventor says his pills are aimed at easing indigestion and are made of 100% natural ingredients such as fennel, seaweed and blueberries. The pills are sold on the internet on pilulepet.com and have been approved by health authorities, according to the inventor who is based in the village of Gesvres in western France.

For this year's festive season he has added a new product that alters the rude smell of flatulence to the scent of chocolate. They retail at €9.99 euros ($12.27) for a jar of 60 and bring benefits such as "the reduction of gas and bloating." Other products listed on the site, which features pictures of the bearded Mr Poincheval posing as an imp, include rose-perfumed fart pills and tablets to reduce the pong of canine flatulence.

Mr. Poincheval said he came up with the idea for the pills one evening when he was enjoying a hearty meal with some friends. He said their flatulence was so awful, they "nearly suffocated. Something had to be done."

So he began researching natural ingredients that would reduce flatulence and after months of experimentation came up with the recipe for his pills. He has been selling the pills since 2006 and says he sells several hundred a month.

"I have all sorts of customers," he said. "Some buy them because they have problems with flatulence and some buy them as a joke to send to their friends."

Please see source: http://www.telegraph.co.uk/news/worldnews/europe/france/11253203/Frenchman-develops-pills-to-make-flatulence-smell-of-roses.html

THE BOTTOM LINE

- A Frenchman named Christian Poincheval has developed a range of pills aimed at making people's flatulence smell sweeter
- Following a disastrous dinner with friends, he began researching natural ingredients that would reduce flatulence, and after months of experimentation, came up with the recipe for his pills
- The pills are touted as bringing benefits such as "the reduction of gas and bloating"; products include chocolate- and rose-perfumed flatulence pills

'Just because nobody complains, doesn't mean all parachutes are perfect.'

"I needed a password eight characters long, so I picked Snow White and the Seven Dwarves."

Navigating Nutrition

Change, Shmange! Who Needs It?

As you all know, CF can be so complicated, take up so much of your time to manage, and wreak havoc on your emotional and psychological health. When you open up this magazine and see a nutrition article about taking care of your body by exercising and eating healthy foods… you think to yourself, don't I already have enough to deal with? Why should I care enough to focus on this aspect of my disease management when I already have so many other things vying for my attention? Maybe I should just skip this article and move on to airway clearance techniques or inspirational stories about how people are making the most of their lives!

Well, you have a point... or do you?

Change is rough, and we usually tend to avoid it at all costs, in all areas of life. That is why I have decided to write this article! Motivation to stay on top of your nutritional needs is the first step toward change. Many of the ideas that you will read in this column may take time to "digest" (haha) but with the right amount of motivation, you may just be able to make the changes that you feel are necessary.

Medical research has been done comparing the weight of CF patients with their overall health, and whadaya-know?! Those patients with poor nutrition and weight gain had more problems on a day-to-day basis, as well as decreased longevity. There seems to be a direct correlation between the weight and nutritional status of someone with CF and how well they do, both short- and long-term. There are many reasons for this, one of which is that malnutrition damages the immune system, rendering it impossible to fight off infection (which we know is all too common in CF). Conversely, a few extra pounds, or "meat on the bones", can help boost the immune system and increase comfort- and ultimately, longevity.

Navigating Nutrition

Medical research has been done comparing the weight of CF patients with their overall health, and whadayaknow?! Those patients with poor nutrition and weight gain had more problems on a day-to-day basis, as well as decreased longevity.

So, now that we understand the importance of good nutrition, the next time you pick up this magazine and read about BMI, nutritional supplements, and/or herbal supplementation, do not fear change. Do not think that something else may better suit your needs. Think about those inspirational articles where people with CF accomplish the unimaginable, and then realize that if your treatment plan includes exercise and nutrition, you too may one day be able to write one of those stories... about yourself.

Aileen Vizel, RD CDN

Aileen can be contacted via telephone at 718-866-9000 ext. 104, or via email at nutrition1@cfsociety.org.

COMING UP NEXT MONTH

Are you in your "normal range" of weight?
- *What you need to know*
- *And what to do if you're not!*

'She said she was approaching forty and... I couldn't help wondering from what direction.'

Doctor: "You'll live to be 60!"

Patient: "I AM 60!"

Doctor: "See! What did I tell you?"

Tried to take a photograph of some fog.

Mist.

THE PERFECT SNOW DAY

The first snowstorm of the season is always a magical time. The world outside is fresh and crisp, sounds subdued by a gentle fluff. When David woke up that December morning to find the bottom half of his bedroom window obscured in feathery flakes, he knew it was going to be the most perfect day.

"Mom!" he shouted out, carelessly tossing his covers off the side of his bed. He bounced out of bed and rattled downstairs. His mother Sarah was sitting by the kitchen table nursing a coffee and scrolling through her emails.

"Good morning David!" she said, patting the seat next to her, "you're up early. Did you have a look outside?"

David's face split open in a grin and he nodded eagerly. "Do you think there'll be school today?"

"I really don't think so. The main streets haven't been cleared yet and the snow is still falling. I think it'll be a snow day."

David cackled. He ran to the phone in the hallway and called his good friend Josh. Josh, of course, was up as well, and they quickly made plans to meet up at the corner of Main and Peach St – the top of the biggest hill in town – with sleds and shovels and all the sorts of paraphernalia a boy could ever need on a snow day.

"MOOOOM!! I'M GOING OUT!" David screamed in excitement, hopping on his left foot as he shoved his right foot into a stubborn snow boot.

Sarah poked her head around the doorway and frowned. "Not like that you're not, Mister. Go put on another pair of pants over those PJs-"

"Okay."

"- and a sweatshirt and another pair of warm socks please."

"OK! Fine!"

"While you're dressing I'm going to look for your snow pants."

"Oh Mom! Come ON! I don't need stupid snow pants."

"Oh, yes you do."

"No Mom, no snow pants, please, OK? I'll be fine. I'm not a little kid anymore, I don't need stupid snow pants."

"I-" Sarah sighed as David dashed upstairs before she could get another word in edgewise.

Two and a half minutes later and David was already clunking back down the stairs, a bit stiffly, with a second pair of sweatpants pulled up to his bony waist, pulling a sweatshirt down over his chest as he sped along.

Sarah stood in the hallway, waving the despised snow pants at him. "Please David, I don't want you to get sick."

"I'm not going to get sick, Mom- I'll wear my hat and gloves and everything."

"David, you know what happens when you get sick… do you want to do IVs again?" She once again held the snow pants out to David. David folded his arms tight.

"Ma, I'll look like an idiot. None of the other boys are going to be wearing that stuff. It's not cool. I'll be FINE." David opened the closet door and rummaged through the bin at the back for his ski gloves.

Sarah walked over to him and put on his hat, yanking down the sides firmly over his ears. She rested her chin on the top his head and looked him in the

Short Stories by M. Wiseman

eyes through the hallway mirror. Her brow creased.

"Don't worry Mom," said David, "I'm just going sledding, I'm not going ice fishing or climbing Mt. Everest or nothing."

"Oh David, I'm your Mom, it's my job to worry," said Sarah. She sighed.

David was growing up so fast, and the truth is, as much as she wanted to, was it fair to force him to do something that made him so uncomfortable?

Could she bar him from leaving the house today? Yes. Could she keep him inside until the weather was balmy and spring had come? Technically, yes. She could, by physical force. He was a skinny little 10-year old with cystic fibrosis. Stubborn he might be, but she could pin him down and drag him upstairs if she really felt it necessary.

But where would that leave them? Would it be worth a half-hour fight and threats of being grounded all winter to get those snow pants on? Even if he did go, miserable, head down, and stuffed up like a snowman, wrapped in oodles of scarves, what would be the point? He was getting older, and she couldn't force him to do as she said forever. One day, G-d willing soon, he would tower over her and he'd have to make up his own mind.

Could she bar him from leaving the house today? Yes. Could she keep him inside until the weather was balmy and spring had come? Technically, yes. She could, by physical force. He was a skinny little 10-year old with cystic fibrosis.

Sarah took a deep breath. "I'm leaving these right here." She hung the pants over the stair railing. "I'm asking you to listen to me, because I have your best interests in mind. I want you to be well enough to play in the snow all winter long, not stuck at home sick and miserable like you were last year. But if you won't do it to protect yourself, do it for me so I won't be worried all day long."

She walked out and sat back down at the kitchen table, shoulders drawn and tensed, hands wrapped very tightly around her coffee mug. After a few moments, she heard the front door slam. Still she waited, listening to snow crunching underfoot, the garage door squeaking slowly open, then grinding shut, and footsteps getting further away. Finally, she stood and made her way back to the hallway.

The snow pants were gone.

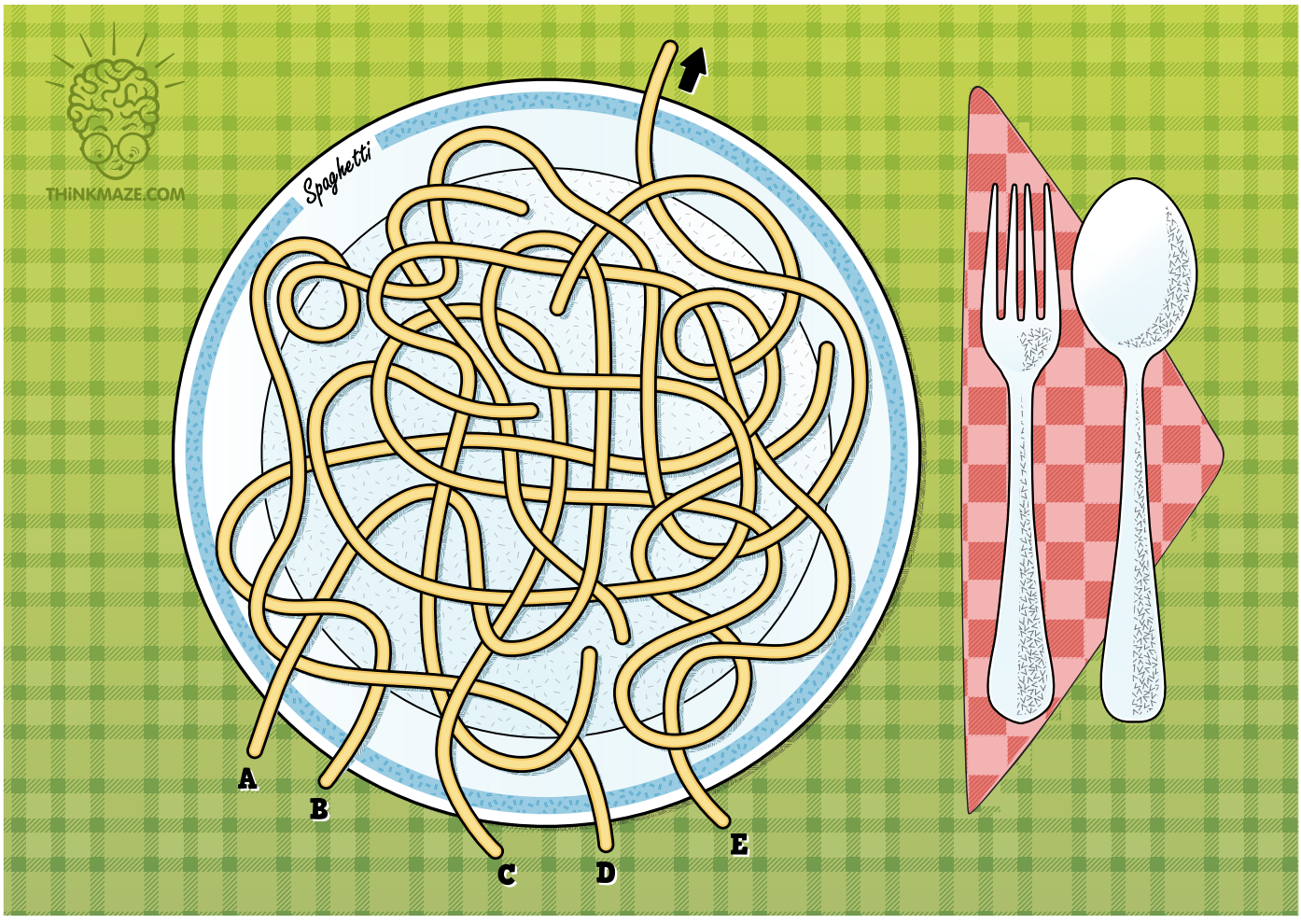
Her smile caught halfway between a sob and a laugh.

And down by Main and Peach Street- my dear readers, believe me you- David was decidedly NOT the only 10-year old forced into snow pants.

PUZZLE PLAZA BONUS!!

THE SPAGHETTI THAT RAN AWAY

Can you find the strand of spaghetti that is slithering off this plate? We challenge you to a 10 second race. (Answer on pg.22)



CRYPTOGRAM

You've been given a sentence in which one set of letters was substituted for another. The words are in their correct order with spaces in between each word. For example, THE GREEN SCARF might be written as GLI SJIIK TZOJN, I being used for E, J being used for R etc. In this Cryptogram, we've filled in a few correct letters in orange to help our beginners. Helpful Hints: You can break the code by watching for the frequency of certain letters. Keep in mind that the words THE and AND occur very often in our language. Embrace the challenge and good luck! (Answer on pg. 23)

DAH' L GE DFCMED GJ JAFN DNAGIEKC. GE IED GJ JAFN DNEOKC!

MURPHY'S LAW

Your finished puzzle will yield a common fact of life. Unscramble the Murphy's Law-themed words and then transfer the letters to the corresponding squares at the bottom using their identical numbers. (Answers on pg. 23)

NHSETCAPNEAP
2 57 77 35 43 45 27 63 40

CECDENCOINI
58 25 47 39 73 4

KCLU
7

TALIINEEBV
23 33 11 19 52

TYINESD
12 32 22 53

TAFE
10 75 51

MAKRA
14

TUUNEFRONTA
18 62 34 60 30 66 15

VESGADDINTAA
17 44 70 41 67 78

SETSIARD
46 61 5 71 68 55

EACBELD
13 50 20

RILCUIOSDU
36 74 65 9 37

ROUTELB
31 48 42 29 21 3

CARZY
69 16

LEATIBCEPRD
54 59 49 1 64 28

GEFFA
72 8

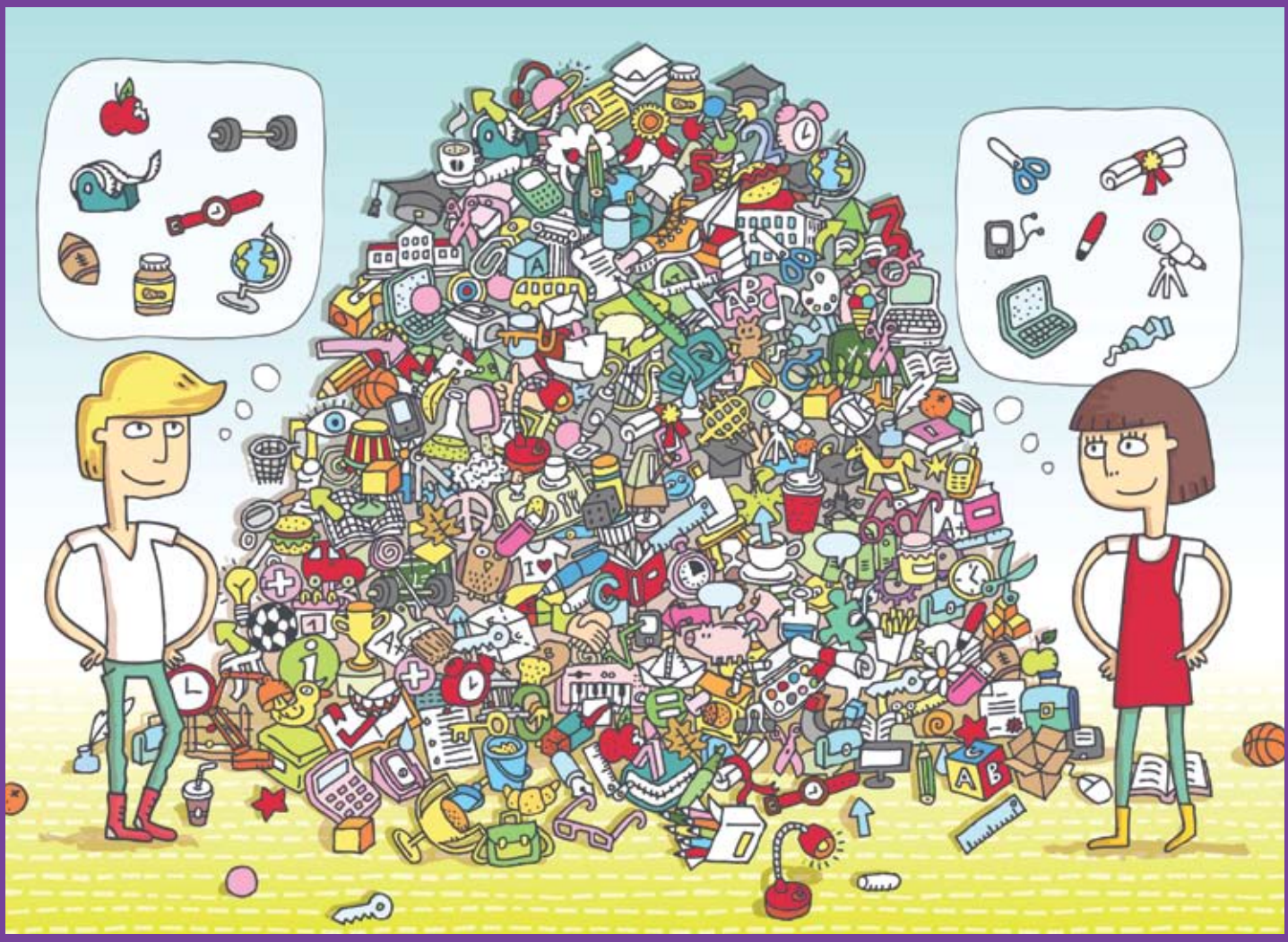
TOVGINRAAAG
24 76 26 38 56 6

1	2	3	4	2	5	6	7	8	9	10	11	2	12	13	14	15	16	17	18	19	20	21	22	23	24
W																									
25	26	2	27	2	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	W	43	44	45		
46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	62	67	2	68	69	56	70	71
62	72	11	2	73	74	75	76	77	78	11																		

Answer to The Spaghetti That Ran Away: D

WADE THROUGH THE JUNK

Danny and Debra have lost their most favorite objects. Their friend Dennis is also missing the following objects: basketball hoop, bus, blue arrow, french fries, owl, lightbulb and rocking horse. Can you find all 21 objects that these friends are missing? (Answer on pg.26)



Answer to Cryptogram:

Don't be pushed by your problems. Be led by your dreams!

Answer to Murphy's Law:

1. Happenstance 2. Coincidence 3. Luck 4. Inevitable 5. Destiny 6. Fate 7. Karma 8. Unfortunate 9. Disadvantage 10. Disaster 11. Debacle 12. Ridiculous 13. Trouble 14. Crazy 15. Predictable 16. Gaffe 17. Aggravation

SOLUTION:

"The chance of the bread falling with the buttered side down is equally proportionate to the cost of the carpet."

JOKE

JUNCTION

A taxi passenger taps the driver on the shoulder to ask him a question. The driver screams, loses control of the car, nearly hits a bus, goes up on the sidewalk, and stops centimeters from a shop window.

For a second, everything goes quiet in the cab, then the driver says, "Look mate, don't ever do that again. You scared the daylights out of me!"

The passenger apologizes and says, "I didn't realize that a little tap would scare you so much."

The driver replies, "Sorry, it's not really your fault. Today is my first day as a cab driver. I've been driving a funeral van for the last 25 years."

An old man is met by his attorney, and is told he is going to be audited. He rides to the IRS office with his attorney, and when he gets there, he begins to talk with the IRS agent.

"I bet $2,000 I can bite my own eye!" The IRS agent agrees to the bet, believing it an impossible task. The old man laughs, pulls out his glass eye, and bites it. The IRS agent is dumbfounded.

The old man bets $3,000 he can bite his other eye. The IRS agent knows there's no way possible to do this, so he once more agrees.

The old man cackles, pulls out his dentures, and bites his eye.

My therapist told me the way to achieve true inner peace is to finish what I start. So far I've finished two bags of M&Ms and a chocolate cake. I feel better already.

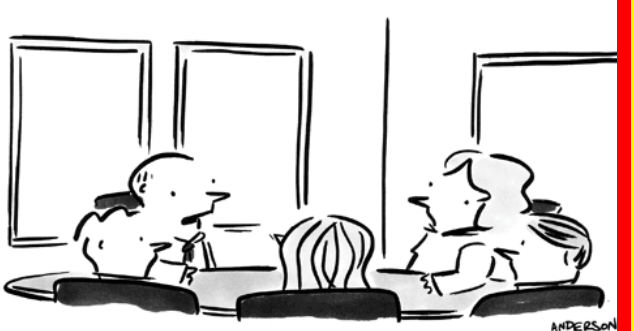
A few decades ago we had Johnny Cash, Bob Hope and Steve Jobs. Now we have no Cash, no Hope and no Jobs. Please don't let Bob Wise die.

My sister bet me a hundred dollars I couldn't build a car out of spaghetti. You should have seen the look on her face when I drove pasta.

The Doc diagnosed me with having a dual personality. Then he charges me 82 dollars for the visit. So I give him 41 bucks and say, 'Get the other 41 bucks from the other guy.'

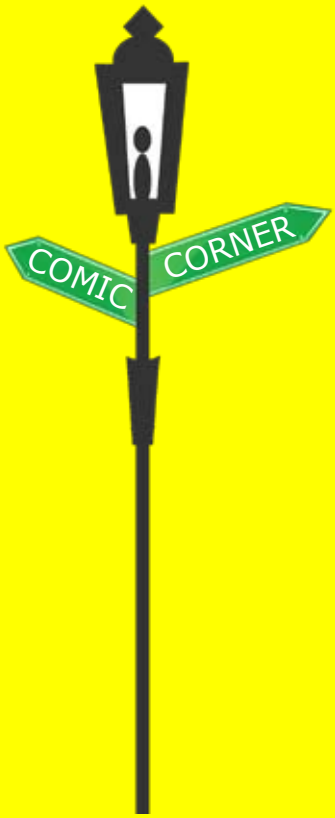
JUNCTION

JOKE

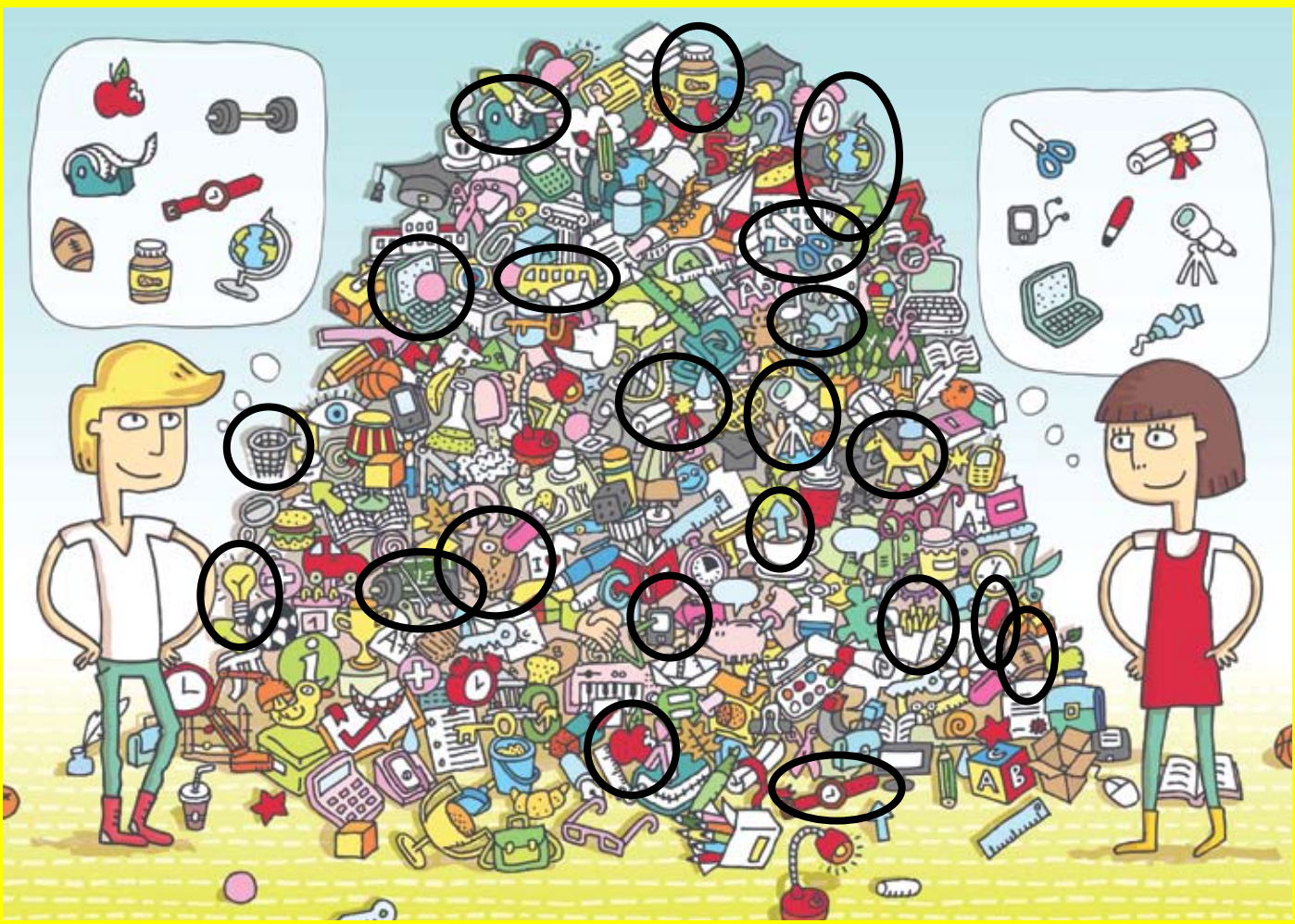


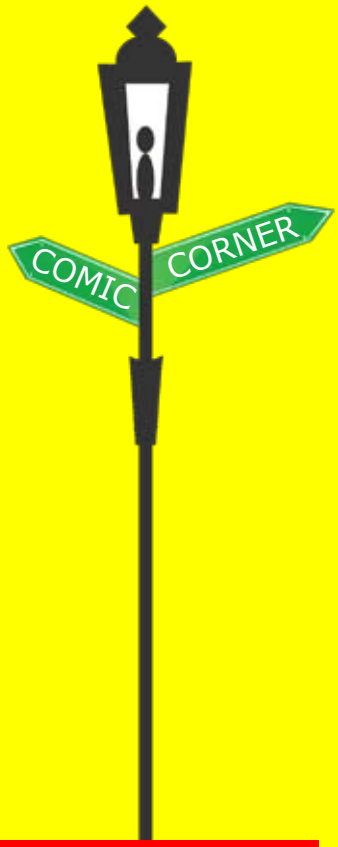
"OK, now that we all agree, let's all go back to our desks and discuss why this won't work."

"Let's see, Kevin, your favorite activity in school was recess. Have you ever considered becoming a congressman?"



Solution to Wade Through the Junk:





10 years old,
Uncle has CF

בס"ד