Rosacea Linked to Higher Risks of Parkinson’s and Alzheimer’s Diseases

New studies have now shown potential links between rosacea and increased risk of the nervous system disorders Parkinson’s and Alzheimer’s diseases, in addition to a growing number of other medical conditions.1,2

In the new findings, a research team led by Dr. Alexander Egeberg at the University of Copenhagen analyzed data from the Danish national health registry, which collects the medical history of all Danish citizens. The studies tracked the entire population of Denmark over 18 years of age – more than 5.4 million people.

After isolating the subset of the population that had been diagnosed with rosacea, the researchers analyzed whether there was an increased likelihood rosacea patients have other medical conditions by comparing the percentage of rosacea patients diagnosed with a particular condition with the percentage of diagnoses of this particular condition in the general population.

The scientific investigators found that all individuals with rosacea had a 1.71 times greater risk of developing Parkinson’s disease than those without rosacea, and those with ocular rosacea had a 2.03 times greater risk of developing the disorder. In addition, the average onset of Parkinson’s symptoms occurred approximately 2.4 years earlier in rosacea patients than in those without the skin disorder.

The researchers also found that patients with rosacea had a 7 percent increased risk of dementia and a 25 percent increased risk of Alzheimer’s.

New eye studies are helping researchers better understand ocular rosacea. See back page.

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New Research on Comorbidities Extends Scientific Knowledge

The surge of scientific studies linking rosacea and a wide variety of other medical disorders, called comorbidities, may have been inspired by similar findings about another skin disorder, according to Dr. Sewon Kang, chairman of dermatology at Johns Hopkins School of Medicine and a member of the NRS Medical Advisory Board.

“I believe the recent interest in exploring rosacea, comorbidities and systemic illnesses stems from earlier work in psoriasis,” he said. “Mounting evidence that psoriasis is not simply a skin disease but has systemic inflammation has piqued interest in exploring similar associations in other skin conditions like rosacea.”

In recent months, rosacea has been reported to be associated with an increased incidence of a growing number of other disorders, including potentially life-threatening systemic illnesses such as coronary artery disease, high blood pressure, high cholesterol, diabetes, stroke and even brain and thyroid cancers.

Comorbidity alone is simply the occurrence of two disorders or illnesses in the same person, at the same time or one after another, and does not necessarily mean that one causes the other. While such reports may cause unnecessary worry in some individuals who have or suspect they may have rosacea, they are...
Survey Shows Rosacea Patients Often Use More Than One Medical Therapy

As with other chronic disorders that may involve multiple symptoms, a new NRS survey of 1,534 rosacea patients has documented that more than one therapy is often used over the course of managing the condition.

Nearly 80 percent of respondents reported that they had been prescribed more than one medication for their rosacea. Twenty-five percent had been prescribed two medications over the course of treatment, while 22 percent had used three and 29 percent four or more.

Fifty-two percent said they had used more than one medication at the same time. Of those who switched medications, 58 percent said it was due to ineffectiveness; 18 percent said it was due to side effects; and 16 percent said the change was on advice from their physician.

“It’s common practice to prescribe separate therapies to treat different symptoms of rosacea,” said Dr. Richard Odom, professor of clinical dermatology at the University of California - San Francisco. “Just as the flu may be treated with one medicine to reduce fever and a separate medication to treat cough or congestion, dermatologists may often prescribe one therapy to reduce redness and another to treat rosacea’s papules and pustules.”

While finding the right combination of management options can require adjustments over time, the good news is that most patients have found a regimen that is effective for their individual cases, as most of those surveyed reported that they were satisfied or at least somewhat satisfied with their current medical therapy.

Tips for Rosacea Trigger-Free Living

You know how it is. You’re going about your daily life when bam! Your rosacea flares up. While it may not be possible to avoid everything that might trigger a sudden increase in signs and symptoms, here are some ways to keep flare-ups to a minimum.

Know your triggers. Once you have uncovered the lifestyle and environmental factors that contribute to your flare-ups, you have a much better chance of controlling your condition. The NRS provides a diary to help identify and avoid those factors that affect your individual case.

Stay cool. Heat is one of the primary triggers for many rosacea patients. If you feel yourself begin to overheat in warmer weather or while exercising, calm the redness and burning by applying cool compresses to your face or misting yourself with a spray bottle filled with cool water. Flushing can often be controlled by chewing on ice chips.

Avoid stress. Don’t try to do too much in a day, and schedule specific downtime when you can relax and regroup. Consider meditating, and allow yourself time off from your daily roles to do something fun.

Use sunscreen and avoid wind. Sun exposure is the most frequently cited factor that aggravates rosacea. Be sure to use sunscreen daily with an SPF of 30 or higher. Stay in shaded areas, or wear a broad-brimmed hat. On windy days, a scarf can help protect your face.

Take your meds. Remember to use your medication as prescribed by your doctor to help maintain long-term remission of your signs and symptoms.

Comorbidities

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important to physicians for a variety of reasons, including correct diagnosis as well as identifying appropriate therapies, said Dr. Anna Chien, assistant professor of dermatology and co-director of the Cutaneous Translational Research Program at Johns Hopkins.

“Doctors have to be aware of a multitude of individual health issues and concerns for each of their patients, and any known associations between rosacea and other disorders can be helpful indicators when investigating a patient’s overall well-being,” she said. “Also, it’s important for patients to remember that though some diseases reported to be associated with rosacea may occur very rarely, these discoveries are important in furthering understanding of rosacea’s pathogenesis and potential therapy options.”

The term “comorbidity” was coined in 1970, when a report in the Journal of Chronic Diseases noted that the presence of two disorders can affect the time of detection, prognosis, selection of therapy and the outcome of the original disease, according to Dr. Alvan Feinstein, former Yale professor of medicine and epidemiology and member of the NRS Expert Committee on the Classification and Staging of Rosacea, which established the first classification system for the disorder in 2002.

For medical scientists, comorbidity may provide pointers to the patterns and causes of diseases. A recent report noted that comorbidity raises the question of whether there is an underlying common cause and what impact the two disorders may have on clinical care. Intuitively, the authors said, diseases may be expected to cluster if they share a common pattern of influences. Other possible explanations may be that one disease directly causes the other, that risk factors for the individual diseases may make them more likely to appear together, or simple chance.

Clinically, awareness of comorbidity may help health care providers assess the burden of disease — the impact of the disorders taken in context with the individual’s life situation — for the benefit of patients as well as health service planning.

“Information about the appearance of rosacea with other disorders provides important clues in tracking down its causes and treatments,” Dr Chien said. “It is exciting that ongoing research on rosacea has uncovered associations that allow it to be more clearly understood and may suggest meaningful research pathways in the future.”
disease in particular, compared to those who didn’t have rosacea. Women with rosacea showed a greater increased risk of Alzheimer’s disease than men with the disorder (28 percent vs. 16 percent). Rosacea patients over 60 years old had a 20 percent greater risk of Alzheimer’s disease, while younger age groups showed no significant increased risk.

The basis for a connection between rosacea and neurodegenerative disorders like Parkinson’s and Alzheimer’s is unknown, though matrix metalloproteinases (MMPs) and antimicrobial peptides (AMPs) may play a role. These proteins are present in all animals and play a role in the innate immune system and other cellular functions. Increased levels of MMPs and AMPs have been implicated in several inflammatory diseases, and have been studied as a potential cause of inflammation in rosacea.

Recent recognition of the involvement of the nervous system in rosacea, including symptoms such as burning and stinging, painful skin, facial flushing, migraine and other symptoms, also supports these findings, the researchers said. They further noted that a previous study had found increased MMP activity in the tear fluid of patients with ocular rosacea.

The researchers pointed out that although the study suggests a potential connection between these disorders, it does not necessarily mean that a causal relationship exists, and noted that because of the homogeneity of the Danish population, the results may not be extrapolated to other ethnicities.
New Ocular Rosacea Studies Help Define Disease Process

Two recent small studies on ocular rosacea yielded new findings that help in understanding its manifestations as well as the disease process.

Researchers at Kirikkale University in Turkey found that despite a high incidence of dry eye in individuals with rosacea, corneal and conjunctival sensitivity were not significantly different from those of the eyes of individuals without the disorder. This is the first time to their knowledge that such a study has been conducted.

The sensitivity of the cornea and the conjunctiva — the mucous membrane that covers the front of the eye and lines the insides of the eyelids — was measured in 55 people with rosacea and 37 healthy individuals with a device that mechanically stimulates the ocular surface with a nylon filament. The investigators also compared sensitivity with other standard ophthalmology examination results.

They noted that while the incidence of dry eye in people with rosacea is higher than normal, it was not associated with changes in ocular sensitivity, even though subjective symptoms were reported as slightly higher by rosacea patients responding to a questionnaire that assessed ocular irritation. The researchers suggested that ocular rosacea may result in an increased number of nerves involved in pain transmission. They further noted that subjective symptoms may not correlate with the objective dry eye test results.

In addition, no correlation was found between sensitivity results and results of other standard ophthalmology examination measurements. The sensitivity findings may have implications for individuals undergoing cataract or LASIK surgery, they noted.

In another study at Ege University in Turkey, researchers found that 15 ocular rosacea patients had a low value for corneal hysteresis — a measurement of the cornea’s ability to regain its shape when pressure is applied — which has been linked to a greater risk of progression in patients with glaucoma.

While glaucoma frequency in ocular rosacea patients was not previously investigated, the higher incidence of steroid use in rosacea and ocular rosacea patients might cause a tendency toward glaucoma, the investigators said, and a low value for corneal hysteresis may mean a faster rate of visual field loss in individuals with glaucoma.

Though results of small studies often appear obscure, they provide important information that helps physicians and researchers understand the biological and chemical underpinnings of a disease and how it may affect patients in a variety of circumstances.
DO YOU SEE YOU
OR DO YOU SEE ROSACEA?

Ask your doctor about prescription treatment options

If you have bumps and blemishes of rosacea, they may be all you see when you look in the mirror. But it doesn’t have to be that way. There are treatments available, such as prescription ORACEA® (doxycycline, USP) 40 mg Capsules (OR-RAY-SHA). ORACEA Capsules help treat the bumps and blemishes of rosacea in adult patients. It’s a once-daily capsule that works from within to target and relieve inflammatory lesions of rosacea.

Ask your doctor about ORACEA Capsules, the #1 prescription rosacea brand among dermatologists,† and see if it’s right for you.

Important Safety Information

Indication: ORACEA® (doxycycline, USP) 40 mg Capsules are indicated for the treatment of only inflammatory lesions (papules and pustules) of rosacea in adult patients. ORACEA Capsules do not lessen the facial redness caused by rosacea.

Adverse Events: In controlled clinical studies, the most commonly reported adverse events (>2%) in patients treated with ORACEA Capsules were nasopharyngitis, sinusitis, diarrhea, hypertension and aspartate aminotransferase increase. Warnings/Precautions: ORACEA Capsules should not be used to treat or prevent infections. ORACEA Capsules should not be taken by patients who have a known hypersensitivity to doxycycline or other tetracyclines. ORACEA Capsules should not be taken during pregnancy, by nursing mothers, or during tooth development (up to the age of 8 years). Although photosensitivity was not observed in clinical trials, ORACEA Capsules patients should minimize or avoid exposure to natural or artificial sunlight. The efficacy of ORACEA Capsules treatment beyond 16 weeks and safety beyond 9 months have not been established.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see Brief Summary of the full Prescribing Information on the next page.

*30 mg immediate release & 10 mg delayed release beads
†According to data from Symphony Health Solutions, Pharmaceutical Audit Suite, January 2015–December 2015.

Learn more at Oracea.com or by calling 1-800-806-6883

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BRIEF SUMMARY
This summary contains important information about ORACEA (Or-RAY-sha) Capsules. It is not meant to take the place of your doctor’s instructions. Read this information carefully before you start taking ORACEA Capsules. Ask your doctor or pharmacist if you do not understand any of this information or if you want to know more about ORACEA Capsules. For full Prescribing Information and Patient Information please see the package insert.

WHAT IS ORACEA CAPSULES?
ORACEA Capsules is a tetracycline class medicine. ORACEA Capsules is a prescription medicine to treat only the pimples or bumps (papules and pustules) caused by a condition called rosacea. ORACEA Capsules does not lessen redness caused by rosacea. ORACEA Capsules should not be used for the treatment or prevention of infections. It is not known if ORACEA Capsules is effective for use for longer than 16 weeks, safe for use longer than 9 months, or safe and effective in children. ORACEA Capsules should not be used in infants and children less than 8 years of age because it may cause stained teeth in infants and children.

WHO SHOULD NOT TAKE ORACEA CAPSULES?
Do not take ORACEA Capsules if you are allergic to doxycycline or other medicines in the tetracycline class. Ask your doctor or pharmacist for a list of these medicines if you are not sure.

WHAT SHOULD I TELL MY DOCTOR BEFORE TAKING ORACEA CAPSULES?
Before you take ORACEA Capsules tell your doctor if you:

- have kidney problems.
- have liver problems.
- have diarrhea or watery stools.
- have vision problems.
- have had surgery on your stomach (gastric surgery).
- have or had a yeast or fungal infection in your mouth or vagina.
- have any other medical condition.
- are pregnant or planning to become pregnant. ORACEA Capsules may harm your unborn baby. Taking ORACEA Capsules while you are pregnant may cause serious side effects on the growth of bone and teeth of your baby. Stop taking ORACEA Capsules and call your doctor right away if you become pregnant while taking ORACEA Capsules.
- are breastfeeding or plan to breastfeed. ORACEA Capsules can pass into your breast milk and may harm your baby. Talk to your doctor about the best way to feed your baby if you take ORACEA Capsules. You and your doctor should decide if you will take ORACEA Capsules or breastfeed. You should not do both.

You should not take ORACEA Capsules if you are male with a female sexual partner who plans to become pregnant at any time while you are being treated with ORACEA Capsules.

Tell your doctor about all of the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. ORACEA Capsules and other medicines can affect each other causing serious side effects.

Especially tell your doctor if you take:

- birth control pills. ORACEA Capsules may reduce the effectiveness of birth control pills. Talk to your doctor about what types of birth control you can use to prevent pregnancy while taking ORACEA Capsules.
- a blood thinner medicine
- a penicillin (antibacterial medicine).
- proton pump inhibitors or antacids that contain aluminum, calcium, or magnesium.
- products containing iron or bismuth subsalicylate.
- a medicine taken by mouth that contains isotreminoin or acitretin.
- a medicine to treat seizures, such as carbamazepine or phenytoin.

Ask your doctor or pharmacist for a full list of your medicines, if you are not sure. Know the medicines you take. Keep a list of your medicines and show it to your doctor and pharmacist when you get a new medicine.

WHAT ARE THE POSSIBLE SIDE EFFECTS OF ORACEA CAPSULES?
ORACEA Capsules may cause serious side effects, including:

- Harm to an unborn baby. See “What should I tell my doctor before taking ORACEA Capsules?”
- Permanent teeth discoloration. ORACEA Capsules may permanently turn a baby or child's teeth yellow-grey-brown during tooth development. ORACEA Capsules should not be used during tooth development. Tooth development happens in the last half of pregnancy, and from birth to 8 years of age. See “What should I tell my doctor before taking ORACEA Capsules?”
- Intestine infection (pseudomembranous colitis). Pseudomembranous colitis can happen with most antibiotics, including ORACEA Capsules. Call your doctor right away if you get diarrhea or bloody stools.
- Immune system reactions including a lupus-like syndrome, hepatitis, and inflammation of blood or lymph vessels (vasculitis). Stop taking ORACEA Capsules and tell your doctor right away if you get joint pain, fever, rash or body weakness.
- Discoloration (hyperpigmentation). ORACEA Capsules can cause darkening of your skin, scars, teeth, gums, nails, and whites of your eyes.
- Benign intracranial hypertension, also called pseudotumor cerebri. This is a condition where there is high pressure in the fluid around the brain. The swelling may lead to vision changes and permanent vision loss. Stop taking ORACEA Capsules and tell your doctor right away if you have blurred vision, vision loss, or unusual headaches.

The most common side effects of ORACEA Capsules include: soreness in the nose and throat, diarrhea, sinus infection, stomach (abdominal) bloating or pain, fungus infection, high blood pressure (hypertension), flu-like symptoms, and change in certain blood tests.

Tell your doctor if you have any side effect that bothers you or does not go away. These are not all the possible side effects of ORACEA Capsules. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to GALDERMA LABORATORIES, L.P. at 1-866-735-4137.

HOW SHOULD I TAKE ORACEA CAPSULES?
• Take ORACEA Capsules exactly as prescribed by your doctor. Taking more than your prescribed dose may increase your chance of side effects, including the chance that bacteria will become resistant to ORACEA Capsules.
• Take ORACEA Capsules 1 time a day in the morning on an empty stomach.
• You should take ORACEA Capsules at least one hour before or two hours after a meal.
• Take ORACEA Capsules with enough fluid to completely swallow the capsule and to lower your risk of getting irritation or ulcer in your esophagus. Your esophagus is the tube that connects your mouth to your stomach.
• If you took too much ORACEA Capsules, call your doctor right away.
• Your doctor may do blood tests during treatment with ORACEA Capsules to check for side effects.

WHAT SHOULD I AVOID WHILE TAKING ORACEA CAPSULES?
• Avoid sunlight or artificial sunlight, such as a tanning booth or sunlamp. You could get severe sunburn. Use sunscreen and wear clothes that cover your skin while out in sunlight.

HOW SHOULD I STORE ORACEA CAPSULES?
• Store ORACEA Capsules at room temperature between 59°F to 86°F (15°C to 30°C).
• Keep ORACEA Capsules in a tightly closed container.
• Keep ORACEA Capsules inside container and out of light.
• Keep ORACEA and all medicine out of the reach of children.

GENERAL INFORMATION ABOUT ORACEA CAPSULES
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not take ORACEA Capsules for a condition for which it was not prescribed. Do not give ORACEA Capsules to other people, even if they have the same symptoms you have. It may harm them.

This Brief Summary summarizes the most important information about ORACEA Capsules. If you would like more information, talk with your doctor. You can also ask your doctor or pharmacist for information that is written for health professionals.

WHAT ARE THE INGREDIENTS IN ORACEA CAPSULES?
Active ingredient: doxycycline. Inactive ingredients: hypromellose, iron oxide red, iron oxide yellow, methacrylic acid copolymer, polyethylene glycol, Polysorbate 80, sugar spheres, talc, titanium dioxide, and triethyl citrate.

WHERE SHOULD I GO FOR MORE INFORMATION ABOUT ORACEA CAPSULES?
• Talk to your doctor or pharmacist
• Go to www.oracea.com or call 1-866-735-4137

GALDERMA LABORATORIES, L.P., Fort Worth, Texas 76177 USA
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