In the coming months, Dental Implantology Update will feature a host of topics centered on evidence-based dentistry, with a review of fundamental concepts at each pass as a primer for the dental-implant practitioner. The relevance and place of evidence-based principles in health care today remains somewhat debated, with reproach on behalf of practitioners who feel their years of patient experience may, at times, be outweighed and overshadowed by policy measures imposed by those who rely solely on statistics. Others feel that as the cost of health care continues to rise, practitioners should be reigned in to using specific diagnostic and treatment options that have been proven successful only after rigorous study. Whatever its place in the larger scheme of the health care cost crisis, the use of evidence in dentistry remains fixed in the availability of data that serve to inform on practice guidelines and seek to answer specific clinical questions based on sound research principles.

Core Concepts: The Evidence-Based Dental Practice, Part I

By Arun Garg, DMD, and Ghislaine Guez, MD, MBA

Evidence-based Dentistry

In 2007, the American Dental Association founded the Center for Evidence-based Dentistry to help dentists “integrate clinically relevant scientific evidence at the point of care.” What does this mean to the dental-implant provider? In today’s fast-paced, patient-centered environment, models of practice, tools of the trade, even longstanding medical recommendations change daily. Guidelines also change as research on specific conditions progresses and as new technology renders existing methods obsolete. The busy implant specialist, managing the day-to-day needs of a practice, cannot access, let alone fully retain, this breadth of new data. Applying it appropriately to patient care is an added hurdle. What has grown out of the paradigm shift away from paternalistic and instinct-driven health care is a new focus on the critical evaluation of specific treatments, diagnostic tools, and methodologies through evidence of their use in practice and the application of these data to the appro-
appropriate patient set. It would be impossible to read, critically evaluate, and apply information from the thousands of new articles relevant to dental implantology that appear on a weekly, if not daily, basis. Thus, institutions like the ADA have founded, and maintain, a dedicated organization that focuses on helping practitioners achieve these goals in a reasonable manner.

The official ADA definition of evidence-based medicine is as follows:

Evidence-based dentistry (EBD) is an approach to oral health care that requires the judicious integration of systematic assessments of clinically relevant scientific evidence, relating to the patient’s oral and medical condition and history, with the dentist’s clinical expertise and the patient’s treatment needs and preferences.

In a frequently cited article entitled “Evidence-based Medicine, What It Is and What It Isn’t,” authors Sackett, Rosenberg, Gray, Haynes, and Richardson define evidence-based practice as “the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of the individual patient. It means integrating individual clinical expertise with the best available external clinical evidence from systematic research.”

Both of these definitions underscore the relevance of the individual provider’s absolute involvement in the management of the patient. Evidence-based practice, according to Sackett, is not “cookbook” practice or a formula-based approach; rather, it requires specific skills that allow practitioners to know which studies and guidelines apply to their patients and which do not. The most important first step is an appropriate clinical question.

The Clinical Question

Formulating the correct clinical question is an important process toward accessing the right data for a particular patient. Consider a brief case. A 52-year-old, obese female comes to the office for an initial visit for implant evaluation. In providing her history, she reports type 2 diabetes mellitus, controlled with insulin. She also reports a family history of heart disease and two hospitalizations within the last year, one for pneumonia and one for diabetic ketoacidosis, which is how she was first diagnosed with the disease. She confesses that she rarely checks her blood sugars at home. She is seeking evaluation for implant placement after referral from her dentist and, on exam, you note several teeth that would benefit from extraction and eventual implant placement. A clinical question, in this case, would not be “What does this patient need for successful and safe extraction?” Rather, a question more suitable for an evidence-based answer would be: “In a 52-year-old female with diabetes, does tight glycemic control improve post-extraction healing?”

Finding the Data

Once the question is clear, accessing the literature requires knowledge of appropriate search databases like PubMed/MEDLINE and Cochrane Reviews. PubMed is a database of over 20 million citations from biomedical literature; it is a free resource put forth by the U.S. National Library of Medicine at the National Institutes of Health and can be accessed at www.pubmed.gov. Some basics on the use of major databases — vocabulary matters; users should understand the difference what Boolean operators AND, OR, and NOT do when putting together search topics. AND (all capital letters is in search basics on the use of major databases like PubMed/MEDLINE and Cochrane Reviews. PubMed is a database of over 20 million citations from biomedical literature; it is a free resource put forth by the U.S. National Library of Medicine at the National Institutes of Health and can be accessed at www.pubmed.gov. Some basics on the use of major databases — vocabulary matters; users should understand the difference what Boolean operators AND, OR, and NOT do when putting together search topics. AND (all capital letters is intended) will offer search results for two categories only when mentioned together — as an intersecting unit. For example, when searching for outcomes data on implants in dia-
betic patients, searching “diabetes AND dental implant” will not draw up articles on nanostructure and osseointegration of a titanium implant (unless it is in a diabetic patient). However, OR will provide results for either term. Another important note about vocabulary: MeSH stands for medical subheadings, and it can be useful to investigate different categories of topics that fall under the same root word. For example, if too many reports are generated with a search using the world “dental implants,” use of the more specific “dental implants, single-tooth” may narrow the field.

**Types of Studies**

There are seven basic types of studies, listed in Table 1. Each type of study is unique in quality and character and offers a different focus to the practicing provider who may or may not draw conclusions based on that particular study.

The clinical usefulness of the results of any particular study will depend on the reliability of the data, the conclusions that can be drawn from the results, and the applicability of the study type to the particular patient population being evaluated.

Part II of this feature will discuss blinding, reliability, critical appraisal of study design, and the basics of biostatistics.

### References

1. ADA Center for Evidence-Based Dentistry. About Us. Accessed online at www.ebd.ada.org.

**Case: Intermittent Jaw Pain**

**By Arun Garg, DMD, and Ghislaine Guez, MD, MBA**

A 74-year-old female with a past medical history notable for ulcerative colitis, heart disease (posterior myocardial infarction at age 64), and depression, and a dental history significant for edentulousness and chronic denture use, presents to a dental-implant specialist for evaluation. She complains that her dentures do not fit her properly, of late, and that she has noted some soreness in her jaw associated with denture use and when she chews. The soreness is most prominent on the left, though occasionally pain will radiate toward the right. She first noted the discomfort several months ago.

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### Table 1: Elements of the Clinical Question

<table>
<thead>
<tr>
<th>Elements of the Clinical Question</th>
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<tbody>
<tr>
<td><strong>P</strong> patient problem</td>
<td></td>
</tr>
<tr>
<td><strong>I</strong> intervention or exposure</td>
<td></td>
</tr>
<tr>
<td><strong>C</strong> comparison (if any) - comparison is not always required; often times the comparison is simply “than not”</td>
<td></td>
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<tr>
<td><strong>O</strong> outcome(s) - this may be a decreased number of adverse events, improved survival, patient wellbeing, or decreased cost (time course may be relevant here)</td>
<td></td>
</tr>
</tbody>
</table>

### Table 2: Types of Study Design, listed in terms of hierarchical value and dependence

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Brief Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meta Analysis</td>
<td>Considers existing literature and synthesizes data into a larger population estimate by statistically integrating the results</td>
</tr>
<tr>
<td>Systematic Review</td>
<td>Survey of the literature on a topic and inclusive review of pertinent controlled trials</td>
</tr>
<tr>
<td>Randomized Controlled Trial</td>
<td>Comparison of two or more treatment groups</td>
</tr>
<tr>
<td>Cohort Studies</td>
<td>Longitudinal evaluation of a group of people who do not yet have a particular disease</td>
</tr>
<tr>
<td>Case Control Studies</td>
<td>Outcome known, generally a retrospective analysis of patients with a specific disease process versus matched counterparts without the disease; often used for epidemiological data</td>
</tr>
<tr>
<td>Case Series</td>
<td>Observational evaluation of a patient, disease, or event; generally a single occurrence or a set of unique occurrences within a population</td>
</tr>
<tr>
<td>Animal Model Research</td>
<td>Non-human study of disease processes or treatment modalities; may have applicable principles or pave the way for human research</td>
</tr>
</tbody>
</table>
ago, though she was able to successfully ignore it with no loss of function until about 10 days ago, when the pain became so unbearable that she presented to her dentist and her physician seeking relief. Upon further prompting, she also reveals a history of low-grade fevers and night sweats for the past several months, occasional headaches, and at least a 15-pound weight loss over the course of one year, which was unintentional. The patient has a history of smoking, though she quit 30 years ago. The patient’s symptoms have prompted a more detailed work-up by her primary care physician, which is ongoing. However, the patient reports that her physician informed her that she does not have any bacteria growing in her blood, but that she is anemic. The patient’s dentist confirmed that her dentures were ill fitting and that she looked chronically ill, with pallor and weight loss. The patient’s physician advised her to hold off on any invasive dental procedures until after the work-up was completed and a diagnosis was obtained; however, the patient felt so frustrated by the discomfort that she sought the opinion of a second dental expert.

**Work-up**

The patient’s presentation is complex and requires a clear plan of action in order to tease out ambiguities. This case highlights the broad list of differentials that must be considered in an elderly patient with jaw pain, elegantly described in an article in the *Journal of the American Dental Association* in 1995. Given the variety and scope of the patient’s complaints, a road map of potential conditions would be useful at this point. Generally, a broad approach can be used to compile a list of differential diagnoses under categorical subheadings, as in Table 1. For this patient’s complaint, a broad differential should also incorporate her past medical history, as well as her physical exam findings.

**Cardiovascular Disease**

Angina is generally classified as stable, unstable, and variant. Stable angina is always associated with cardiovascular disease, and is generally easy to recognize — substernal chest pain, worse with activity, relieved by rest or nitroglycerine. Significant narrowing of the cardiac arteries by atherosclerotic plaque causes stable angina, though variation can occur in terms of timing and duration, depending on local factors at the level of the endothelium. Unstable angina is angina that occurs while at rest (or minimal exertion), is new in quality or character, or is crescendo in nature (prolonged, worsening, and severe). It can be difficult to differentiate unstable angina from other conditions, at times, due to patient variability and the changing nature of the symptoms. Variant angina is also called Prinzmetal’s angina, and it is caused by temporary vasospasm of the cardiac arteries. Cardiac pain or pressure can initiate, and be experienced in a variety of places beyond the chest and certainly does not need to include the chest to be cardiac in nature. Pain that radiates to the left shoulder and down the left arm is common, as is pain to the jaw and lower face, especially on

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**Table 1:** Broad categories of disease with specific differential diagnoses: TMJD; RA

<table>
<thead>
<tr>
<th>Cardiovascular</th>
<th>Dental</th>
<th>Endocrine</th>
<th>Infectious</th>
<th>Neoplastic</th>
</tr>
</thead>
<tbody>
<tr>
<td>angina (referred pain from cardiovascular ischemia)</td>
<td>Local trauma</td>
<td>Paget’s disease</td>
<td>Herpetic lesions (postherpetic neuralgia)</td>
<td>Metastatic Lesion</td>
</tr>
<tr>
<td></td>
<td>Bruxism</td>
<td>Subacute thyroiditis</td>
<td></td>
<td>Primary malignancy</td>
</tr>
<tr>
<td></td>
<td>Abscess</td>
<td>Poor denture fit</td>
<td></td>
<td>Lymphoma or leukemia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Muskuloskeletal</th>
<th>Neurologic</th>
<th>Psychological</th>
<th>Rheumatologic</th>
<th>Toxic/Metabolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMJD</td>
<td>Trigeminal neuralgia</td>
<td>Depression</td>
<td>Giant cell arteritis (temporal arteritis)</td>
<td>Reaction to cosmetic filler</td>
</tr>
<tr>
<td>Osteonecrosis</td>
<td></td>
<td>Generalized anxiety disorder</td>
<td></td>
<td>Biphasphonate use</td>
</tr>
<tr>
<td>Pathologic fracture</td>
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*Dental Implantology Update™* March 2011
the left side. Left jaw pain as the sole experiential component of pain can be exclusively cardiac in nature and, therefore, must remain on the differential, and further work-up is advised. Diagnostic tools to rule out angina as the cause of this patient’s jaw pain would include an electrocardiogram and, possibly, echocardiogram, stress test, and/or cardiac catheterization. Given her prior history of myocardial infarction, thorough differentiation between the previous cardiac episode and the current presentation is essential. Specific questions like “is this pain similar to the pain you had when you had your heart attack” are optimal in patients with underlying cardiovascular disease.

**Oral/Dental Pain**

Patients can construe any number of oral and dental problems as jaw pain. This includes, and is not limited to, bruxism, caries, abscess, ill-fitting dentures, and local trauma. Bruxism may be considered in this general category, though it can also fall under the umbrella category of temporomandibular joint disorders as well. Evidence demonstrates that when enough force is applied to the temporomandibular joint in the process of prolonged tooth-clenching, jaw muscle soreness ensues. For most individuals, a tooth-ache is localizable and associated with clear evidence of disease — an abscess or caries, for example. In the segment of the population with chronic periodontitis, again pain is generally accompanied by a clear source of invasive infection, such as an abscess, beyond what is occurring at the level of the gingiva, which is not typically associated with pain.

Ill-fitting dentures often cause wearers significant discomfort and embarrassment. For this reason, the American Dental Association recently issued a list of evidence-based guidelines for the care and maintenance of complete dentures, something absent despite a. Fifteen care points are suggested; the last one speaks most to this patient’s needs: “Patients who wear dentures should be checked annually by the dentist, prosthodontist, or dental professional for maintenance of optimum denture fit and function, for evaluation for oral lesions and bone loss, and for assessment of oral-health status.”

**Endocrine Disorders**

Among endocrine-related disorders associated with jaw pain, Paget’s disease of bone (also called osteitis deformans) is most commonly implicated. The disease is characteristic for increased bone metabolism and turnover, with elevated rates of bone remodeling. Rather than making affected bone stronger, Paget-diseased bone is disorganized and susceptible to fracture and structural deformity. The etiology of the disease remains poorly elucidated, with evidence of genetic and infectious (viral) predisposing factors, though no definitive cause exists to date. Though it is the second most common bone disorder after osteoporosis, little research exists on the use of implants in patients with Paget disease of bone. It is a disease of overexpressed and overactive osteoclasts. Authors Favus and Vokes write:

> The characteristic feature of Paget disease is increased bone resorption accompanied by accelerated bone formation. An initial osteolytic phase involves prominent bone resorptions and marked hypervascularization. … The second phase is a period of very active bone formation and resorption that replaces normal lamellar bone with haphazard (woven) bone. … In the final sclerotic phase, bone resorption declines progressively and leads to a hard, dense, less vascular pagetic or mosaic bone, which represents the so-called burnt out phase of Paget disease. All three phases may be present at the same time at different skeletal sites.

The presenting feature for most patients with Paget’s disease is bony pain, the result of active lytic lesions, fracture, hypervascularity, or bowing. Long bones are commonly affected, as is the pelvis; skull involvement may indicate more advanced disease, and generally causes headaches and increased cranial size. Patients with this disease have been known to complain of having to increase hat size. If the maxilla or mandible is affected, there could be corresponding separation of teeth and malocclusion that results with growth of the underlying bone. Distortion of facial structure results in advanced disease (leonine facies or mandibular prognathism). Loss of teeth also has been reported. Diagnosis is made by review of radiographic and laboratory findings. Radiographs of the skull will show characteristic “cotton wool” spots, the result of disorganized areas of bone with sclerosis.

A second endocrine condition known to cause neck and jaw pain is subacute thyroiditis; of the three subacute thyroiditis conditions, it is the granulomatous (or de Quervain) thyroiditis that is associated with pain, and this pain has been known to radiate to the neck and jaw. Subacute thyroiditis generally resolves on its own without treatment (though appropriate management of thyrotoxicosis is essential); this painful subtype tends to occur in patients who also have a history of recent viral illness (high fevers, myalgias, neck pain). Symptoms consistent with transient hyperthyroidism will likely be present — palpitations, anxiety, heat intolerance, weakness and fatigue, and gastrointestinal hypermotility. Diagnosis requires low levels of thyroid stimulating hormone (TSH) and elevated T3 and T4 (thyroid hormone). ESR (erythrocyte sedimentation rate) will also be very elevated. On physician exam, many patients with subacute thyroiditis will have tenderness to palpation at the neck.

**Infectious Processes**

In searching for the underlying cause of intermittent jaw pain in a pa-
tient who presents to the dental-implant practitioner, infectious etiologies must not be overlooked. Common infectious processes that present with pain are herpes zoster, osteomyelitis (rare without prior radiation exposure or immune compromise), and abscess (discussed above).

Varicella-zoster virus (VZV) is the reactivation of varicella (chickenpox) infection along the course of the dorsal nerve root. After initial exposure, usually in childhood, the host processes the infection, but the virus remains latent until a systemic change allows for reactivation. Unless systemic reactivation occurs (which is rare and generally not seen outside of an immunocompromised host), VZV lesions erupt in a dermatomal distribution, with characteristic herpes blisters that occur and mature in unison. VZV is exquisitely painful and, oftentimes, the pain precedes the visual lesions. It is most commonly a disease of the elderly, though it can occur in younger patients. Involvement of the trigeminal nerve root can cause pain of the face and jaw. That this patient’s symptoms have persisted for months without any clear evidence of lesions up to this point makes this diagnosis less likely. Persistent neuralgia following herpes is known as postherpes zoster neuralgia, and also presents with tremendous pain and patient suffering. Generally, pain is described as sharp or burning, rather than soreness. Patients often report pain on light touch.

**Neoplasm**

The possibility of neoplasm in an elderly patient with constitutional symptoms and features of malignancy (fevers, weight loss, night sweats) cannot be understated. The malignancy could be a primary intracranial process or a metastatic lesion from some other source; hematologic and lymph tumors also cannot be excluded. Several cancers metastasize to bone, which could explain this patient’s jaw pain. Lung, breast, and prostate cancers, and various carcinomas of the head and neck, tend to go to the bone when they metastasize. Certainly, the proximity of head and neck cancers to the skull makes it essential to perform a detailed and thorough examination looking for evidence of malignancy, including assessment of cervical and clavicular lymphadenopathy. Suspicion of metastasis generally prompts imaging studies (computed tomography, magnetic resonance imaging, plain radiographs, positron emission tomography, or bone scan), and eventually requires tissue for confirmation and tumor differentiation and staging, which will affect treatment. Bony involvement in metastatic disease can occur via one of three mechanisms: direct extension, venous spread, and seeding of tumor emboli via circulation. This patient does have risk factors for lung and head and neck cancers (smoking history), and she is exhibiting constitutional signs and symptoms consistent with chronic illness (weight loss, fevers, anemia).

**Rheumatological Disease**

The patient’s case presentation is worrisome for temporal arteritis, also called giant cell arteritis (GCA). GCA is a vasculitic process that affects medium- and large-sized arteries in older individuals, whose pathophysiology remains unclear, though it is thought that dendritic cells initiate an inflammatory cascade that progresses to damaged vessel walls. Presenting features of this disease include headache, of new onset, and generally in the vicinity of the temporal arteries. Some patients report tenderness to palpation of the temporal artery, which may manifest as pain when brushing hair or grooming. Additionally, and striking in this patient’s case, jaw claudication is often present. Jaw claudication is the sensation of pain or cramping with use, as with chewing. This patient notes that she feels jaw pain when using her dentures, which may have nothing to do with the dentures at all, rather it may be a manifestation of insufficient blood flow to the jaw when chewing. The sidedness also points to this process; however, the fact that the patient’s headaches have persisted for months, and are not new onset, lowers GCA the list of differential diagnoses. Lab studies will demonstrate elevated C-reactive protein (CRP) and erythrocyte sedimentation rate, markers of an activated inflammatory response. Anemia may or may not be present, depending on the chronicity of the process. The most severe complication of GCA is visual loss, which is often permanent. Some patients with GCA experience other visual changes that forewarn of impending loss of vision, including diplopia. For definitive diagnosis, tissue biopsy is required — specifically a temporal artery biopsy. Treatment (high-dose corticosteroids) should be started before biopsy, and will not affect biopsy outcome; therefore, if GCA is highly suspected, immediate referral of the patient to the local emergency depart-
ment is warranted for further diagnostic evaluation.

Rheumatoid arthritis and osteoarthritis are two very different rheumatological entities with different etiologies and pathophysiologicals. Both affect the joints and cause joint pain or arthralgias. Joint inflammation is typical in RA, with the affected joint displaying signs of such — erythema, warmth, and swelling. Symptoms of stiffness and joint fullness tend to be worse in the morning, and improve with use. Prolonged inflammation can lead to structural changes of the joint, cartilage destruction, joint fusion, and secondary osteoarthritis. In RA, joint involvement is usually symmetric, and typically affects the hands and wrists, as well as other small and large joints. Rheumatoid arthritis can, and does, affect the temporomandibular joint in sufferers — causing a significant degree of pain.

Osteoarthritis is a musculoskeletal disorder that results as a consequence of cartilage degradation, the classic “wear and tear” phenomenon. As much as 12% of the U.S. population is affected (between the ages of 25 to 74 years), and the number is growing as the population ages. In osteoarthritis, as cartilage wears down, osteophytes (bone spurs) form and areas of focal inflammation appear as a consequence of the destructive process. These changes are often well visualized radiographically and, thus, diagnosis often requires imaging (most commonly radiographs). Treatment mainstays are acetaminophen and nonsteroidal anti-inflammatories. Gastrointestinal prophylaxis is usually offered with chronic nonsteroidal anti-inflammatory medication. Symptom relief can also be offered by way of joint injections (cortisone or hyaluronic acid). Osteoarthritis of the temporomandibular joint does exist, though clinical features associated with it are seen less commonly; generally, the disease processes affecting that particular set of joints are lumped into the larger subheading “temporomandibular joint disorders,” and will be discussed in part II of this article.

This patient’s lab data, radiographic findings, and pathology reports, as well as a discussion on the definitive diagnosis will be offered in next month’s conclusion to the case. ■

References

FDA Approves Quadrivalent HPV vaccine for use in males ages 9-26 years

By Arun Garg, DMD, and Ghislaine Guez, MD, MBA

In December of 2010, four years after the approval of the quadrivalent HPV vaccine for girls and women ages 9-26 years, the FDA has approved its administration to, and use in, the opposite sex. Within the last year, two articles in Dental Implantology Update have featured data on the disturbing trend of the rising prevalence of oropharyngeal carcinomas associated with HPV infection. And while HPV-associated cancers of the head and neck are more responsive to chemotheraphy and radiation treatment than other forms of oropharyngeal cancers, there is almost always significant morbidity and mortality attached to its diagnosis.

Still, reviews are not universally favorable toward the implementation of vaccination protocols in males just yet. Long-term safety of this vaccine in males and females has not yet been adequately documented or even established. Additionally, the cost of vaccination remains high ($400 for a series inclusive of three shots), and the overall cost-effectiveness of vaccinating both sexes remains uncertain if the primary morbidity and mortality gains are in the prevention of cervical cancers, the most prevalent invasive neoplasms of the HPV-associated cancers, and the most costly disease burden among them. The authors of a new study documenting the efficacy
FDA expands HPV vaccination criteria. Will head- and neck-cancer incidence change?

of the vaccine in males suggest that in areas where vaccination of women remains low, immunity against virulent HPV strains 16 and 18 (strains associated with the development of invasive cancers) in the other sex would prove beneficial in terms of cost-effectiveness toward cervical-cancer reduction.\(^3\) There is also appreciable consideration toward vaccinating early, before high-risk groups diverge at the point of sexual maturity. HPV-associated head and neck cancers are found more frequently in homosexual males than in heterosexual males. Unless the collective group (all males) is immunized, there is no way to limit vaccination to the high-risk group. And sharing the vaccination burden among both sexes seems, at the end of the day, more egalitarian, given that both are responsible for its transmission.

It is unclear, at present, the number of boys and men who will seek out vaccination against HPV, or how those numbers will affect population rates of HPV-associated head and neck cancers. Nonetheless, making strides toward its eradication, from a public-health standpoint, is a step in the right direction. Regular vaccination in the United States among both sexes is a long way off; how the public responds to the expansion of vaccination criteria to males remains to be seen. Outcome data concerning vaccination rates in females has been lower than what was expected. ■

References

Call for Submissions
Dental Implantology Update is accepting publication submissions on a variety of topics including dental research, trends in implantology, novel procedures and technologies, and the link between medical and dental pathophysiology of disease. Submissions should not be more than 3,500 words. Photographs, radiographs, slides, and illustrations are welcome, provided they are approved for use by the owner of the image. Email Leslie Hamlin at leslie.hamlin@ahcmedia.com for more information.

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