



VIRGINIA • PEDIATRICS

American Academy of Pediatrics • Virginia Chapter



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VA-AAP Legislative Update

Aimee Seibert, Chapter Lobbyist

February 2, 2016

We are officially a third of the way through the 2016 Virginia legislative session. Legislation is moving quickly and there is no shortage of health care bills this year! The VA AAP is following these bills closely and ensuring children's health is at the forefront. We had a great White Coats on Call Day at the end of January. Thank you to everyone who came out!



Here's a look into some of the bills we're working on this year:

Independent Practice Nurse Practitioners

In 2012, the physician community and the nurse practitioners agreed upon a new model for care that was team-based and led by a physician. This is a collaborative model that we



believe provides the best patient care while allowing everyone to practice to the fullest extent of their education and training. Despite this compromise, the nurse practitioners are again pushing for independent practice. The VA AAP, along with the entire physician community, opposes this effort. Allowing nurse practitioners to practice independently would mean Virginia believes they have the same training and education as physicians and that is inaccurate. We are actively working with them to find a compromise

that ensures patients receive the highest quality of care.

Prescription Monitoring Program

The VA AAP stands with the Medical Society of Virginia and shares a concern for the meteoric rise in prescription drug misuse. We recognize the importance of the Prescription Monitoring Program to the care we provide our patients. We support legislation that requires a

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President's • MESSAGE

Barbara Kahler, MD, FAAP
President Virginia Chapter
American Academy of Pediatrics

Well, we are back to the time of year where snow and ice visit Virginia. I hope everyone survived "Jonas" intact. January also brings us to the time of year when National AAP and local officers begin the resolution process in preparation for The Annual Leadership Forum, also known as the ALF.

The ALF meets in March for four days in Chicago. (Let's hope for no snow there!)

We have just completed the District approval and will be headed to Chicago in March. Virginia has several resolutions moving forward.

On to our grants; Telemedicine is in progress with practices starting to use the equipment provided. HPV is scheduled to have its Learning Coalition in February, as well as the Bright Futures grant. So they are moving along nicely.

Thank you for your great ideas and support! *Barbara Kahler*



DATES TO Remember

CLINICAL CHALLENGES IN PEDIATRIC PRIMARY CARE 2016

April 9, 2016- 8 a.m.- 3 p.m.

*"Are We Drugging Our Children?
Rational Psychopharmacology
for the Child Under Six"*

Speaker: Bela Sood, MD

Lewis Ginter Botanical Garden
1800 Lakeside Avenue
Richmond, VA.

Contact: Sherry Black 804/228-5971 or
visit
www.virginiapediatrics.org

36TH MCLEMORE BIRDSONG PEDIATRIC CONFERENCE

May 13 – 15, 2016

Omni Homestead Resort,
Hot Springs, Virginia

For more information and registration go
to www.cmevillage.com

2016 PEDIATRIC CONFERENCES

VA-AAP ART & BUSINESS OF PEDIATRICS CONFERENCE

April 15 & 16, 2016

The Westin Richmond
6631 W. Broad Street
Richmond, Virginia

The FIRST DAY will focus on Pediatric Medicine. By lectures and question and answer periods, participants will learn to identify new tools they can take back to their practices and implement for improving medical care of infants, children, and teenagers. The SECOND DAY will focus on the Business of Pediatrics. Participants will gain an up to date understanding of the State of Pediatrics as it relates to the American Academy of Pediatrics, as well as the role of the...

The ALF process is detailed below:

- 1) An AAP member determines that there is an issue that needs to get to the Board of Directors. That member can contact the Chapter officers to help with format.
- 2) This document goes to the Chapter Board. They approve or disapprove the resolution, and pass it on to the Chapter FMC representative. They then edit the resolution.
- 3) The resolution goes before the District officers for approval.
- 4) The resolutions are assigned a reference committee for the discussion at the ALF.
- 5) At the ALF, there is discussion about the resolutions in their respective reference committees.
- 6) The main body of the ALF votes on the resolution.
- 7) The body votes on the Top 10 resolution.
- 8) These are then sent to the Board for consideration.
- 9) The Boards actions are published.

...Academy in our practice lives. Self-efficacy and understanding the position they hold as a person, a physician, and as a leader, will help participants improve the quality of care they give to their patients.

Better coding for 2016-2017!

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2016 PEDS AT THE BEACH CONFERENCE

July 15 – 17, 2016

**Wyndham Virginia Beach
Oceanfront Hotel**
Virginia Beach, VA

Register at:

www.vcuhealth.org/cme/register

Coaching Public Schools to Collect Student Weight Status Data Results in Local Health Innovation

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Despite reported stability in childhood obesity rates (Ogden, Carroll, Kit, and Flegal, 2014), obesity remains a critical health issue for children worldwide. While many states require student height and weight surveillance in public schools, not all states collect these data. Virginia does not currently require public schools to collect height and weight data and calculate student body mass index (BMI), though many Virginia schools do so voluntarily. Having local level childhood weight status data collected using a rigorous and consistent protocol enables regional and statewide reporting. Having these data stimulates innovative health action community, including homes, schools, churches and community organizations. The aim of this study, conducted by Eastern Virginia Medical School (EVMS) faculty, was to develop a community health youth weight status assessment protocol that was simple, efficient and scientifically accurate to encourage local school districts to conduct weight status measurements annually.

Participating school districts included large cities and small rural areas: Norfolk, Portsmouth, Franklin, Northampton County and Accomack County. EVMS faculty developed the protocol; stimulated weight status measurements annually within the schools; provided coaching; analyzed de-identified data; and reported data outcomes back to the school districts.

Protocol elements began with scheduling all measurements consistently in the Fall. Grade levels measured included kindergarten and grades 3, 5, 7 and 10. Instrumentation was provided by an electronic measurement system, BioMeasure Youth Measuring System, with its corresponding BioMeasure Youth Software, from Glenview Health Systems (BioMeasure Youth Measuring System, 2015). This system was selected for its speed and improved measurement accuracy. Students stand on the scale and have their weight measured simultaneously with their height, and both measurements are sent to a pre-populated database which automatically calculates body mass index (BMI). Average measurement time is 3 seconds per child.

Staffing requirements included assistance from a school district's information technology (IT) department to pre-load student name, school, grade, gender, and birthdate into a school-owned computer that had been loaded with the BioMeasure Youth Software. The IT manager daily backed-up the data on an external hard drive and safely secured the computer and hard drive in a locked area. Another school employee, usually the school health coordinator, was named the Measurement Project Manager. This person worked in concert with district principals to arrange a measurement date and place, and assign a school point person to make arrangements and assist within the school. The Project manager also trained someone in each school to assemble and calibrate the equipment, to properly guide children onto the scale, and another person to operate the computer, retrieving student names and double-checking for correctly recorded measurements. The Project Manager also insured a proper parent consent and child assent process and procured a private measurement space with a nearby place for students to line up, remove shoes and heavy clothing, and receive instruction. Classroom teachers provided a student roster which helped with young children who could not clearly articulate their name. Teachers also helped younger children with removing and putting back on shoes and heavy jackets.

Time out of class was handled efficiently in elementary schools. Classrooms were called to the measurement area by public address system, and at 3 seconds per child measurement time, an entire classroom was measured within 12 to 15 minutes for an average class size of 25 students. Middle and high school scheduling was more challenging and less efficient than elementary schools. The project manager and IT team (often a local volunteer) usually arranged the measurement and waiting areas in a gymnasium and measured students as they came to physical education class. Sometimes this required the staff being on site at one middle or high school for an entire day. Schools that allowed students out of academic classes had more efficient measurement times, but principals were reluctant to release students from academic classes.

When all measurements were achieved, the IT manager provided EVMS de-identified data for analysis. EVMS faculty created reports for each school district and presented these reports to each district Superintendent. Most Superintendents, or the EVMS faculty member, reported the data to their School Board, placing the data in the public domain. Often Superintendents and School Board members asked for suggestions for reducing child weight status. EVMS faculty members provided information on school-based interventions and also explained ways that other community groups (homes, after school programs, faith communities, and other child-focused organizations) could share responsibility for healthy-weight children collectively.

One challenge to this weight-status measurement program included the instrumentation, which was heavy, sensitive to movement, noise and light, expensive, and had a life-span of about 5 years. Since the instrumentation was pivotal to the measurement initiative's efficiency, efforts were made to find an improved system. So far none has been found. In addition, smaller school districts were easier to schedule and provide uniform protocol implementation than larger districts. Both Norfolk and Portsmouth's Public Health Department participated in the project. Norfolk Public Health Department provides school nursing services for the district. While they found the data useful, they found the process time and resource-intensive. These barriers may be unique to the school-public health association.

Having these data publicly available stimulated community action. In response to the data collection initiative, Accomack County Public Schools instituted a faculty and staff wellness program on the theory that healthier faculty and staff were in a better position to assist students improve their health. Northampton County Public Schools instituted a school health newsletter and a faculty, staff and student health committee to provide advice on innovations to improve student weight status. Data from this initiative has also been used in grant proposals, which has resulted in several new funding streams to participating communities.

This work was supported in part by Eastern Virginia Medical School and Children's Hospital of The King's Daughters.

References

BioMeasure Youth Measuring System. Retrieved from www.biomeasure.net

Ogden CL, Carroll MD, Kit BK, and Flegal KM. (2014). Prevalence of childhood and adult obesity in the United States, 2011-2012. *JAMA*, 311(8), 806-814. <http://doi.org/10.1001/jama.2014.732>

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The Developing Intestinal Microbiome in Infants: Shaping Future Health

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The human microbiome is the genetic contents of all microbial life living in or on our body, with microbial cells far outnumbering human cells. The human intestine contains at least 1014 bacteria, with estimates of 1000 to 1200 bacterial species, in addition to other microorganisms, that exist in symbiosis with their host. This complex commu-

crobiome which rapidly develops during this time, reaching a relative stability by a few years of life that generally lasts into adulthood. Hence this early period may be critical for shaping future health. Indeed, even prior to birth, factors have been identified that may affect the early microbiome development including perinatal antibiotics. During

to infants who are born full term. Here at the Inova Translational Medicine Institute, we are conducting a longitudinal microbiome study of babies born prematurely and in the neonatal intensive care unit (NICU). We are following then into early childhood to examine why and how perturbations in microbiome development occur, and as-

sociations with early childhood health outcomes such as obesity and allergies.

Currently, many of the studies associating microbiome disturbances and disease are correlative rather than causative. However, there are an increasing number of longitudinal studies examining microbiome changes prior to disease develop-



nity of microorganisms has vital functions for their host, including development and maturation of the immune system, competitive exclusion of pathogens taking residence in the gut community, synthesis of vitamins, fermentation of dietary carbohydrates, and metabolism of bile and host hormones. Conversely, imbalance, or dysbiosis, of the microbiome has been associated with a wide range of diseases, including gastrointestinal conditions such as necrotizing enterocolitis, inflammatory bowel disease and irritable bowel syndrome, metabolic conditions including obesity, atopic conditions such as asthma and allergies and autoimmune disease.

The first few months and years of a child's life are essential in shaping the intestinal mi-

crobiome which rapidly develops during this time, reaching a relative stability by a few years of life that generally lasts into adulthood. Hence this early period may be critical for shaping future health. Indeed, even prior to birth, factors have been identified that may affect the early microbiome development including perinatal antibiotics. During

the dynamic development of the intestinal microbiome in the first few months of life, which helps program the immune system, many factors, some modifiable, have been associated with differential establishment and colonization of the infant gut microbiome; these include vaginal versus cesarean section delivery, breast feeding versus formula feeding, antibiotic exposure and early nutrition.

ment which will hopefully give better insight into how perturbations of the microbiome cause disease, with relation to immune function and interaction with the human genome. This knowledge is essential to enable future possible microbiome manipulation and prevention of disease. Until this time, caregivers can implement general strategies to try and optimize "normal" microbiome development, including encouraging use of breast milk and judicious use of antibiotics.

For further information regarding our study "Neonatal Intestinal Microbiome: Impact on Infant and Early Childhood Health and Disease," please contact study coordinator Elisabeth Klein and Inova Translational Medicine Institute (ITMI) at 703-776-8199.

VIRGINIA•PEDIATRICS

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Pediatric Specialists of Virginia: A Timely Contribution to the Care of Children

Leon Moores, MD
Chief Executive Officer

Pediatric Specialists of Virginia

*Professor of Neurosurgery Virginia Commonwealth University School of Medicine and
Professor of Surgery and Pediatrics, Uniformed Services University School of Medicine*

Pediatric Specialists
of Virginia



Pediatric Specialists of Virginia (PSV) represents a unique and collaborative approach to organizing pediatric specialty services in a manner to better address the needs of both children and families in Northern Virginia as well as referring pediatricians, family practitioners and other consulting specialties. PSV was created by Children's National Health System (CNHS) and INOVA in September, 2013 as a not-for-profit medical group practice.

vices in eight locations throughout Northern Virginia and nearby communities.

Pediatric Specialists of Virginia is designed as a physician-led organization where focus on achieving an optimal patient-centered care experience guides key decisions. From the start, the governing committee overseeing PSV with representation from both CNHS and INOVA included physician leadership that was expanded in 2014 and 2015 by

selecting a physician executive as its head and bringing on two full-time PSV physicians as members. Beyond that, physician chiefs were chosen to head up key work for the medical group. Those leaders of strategy, experience, quality, medical informatics,

research, and education serve with the Chief Medical and Surgical officers, the CEO and the COO as the full leadership team guiding PSV's development and forming its culture. For example, some of their decisions to date have led to more broadly publicizing the research in which many PSV physicians participate, and endorsing a move toward full transparency in posting patient reviews and ratings.

In 2015 became the first year that PSV was first recognized as a 501(c)(3) charitable organization. This designation enables PSV to better address the needs of a wide variety of patients and families, many of whom face hardships exacerbated by the stress

of caring for a child with a serious injury or chronic illness. PSV is able to accept donations that can be turned into additional temporary support for those families with urgent needs. Furthermore, as PSV's philanthropic funds increase, additional support for education and emotional support services can be provided to address needs that are not met by insurance plan reimbursement. Pediatric Specialists of Virginia does accept most insurance health plans including Virginia Medicaid in its clinics and ambulatory surgery center.

With all of these developments, PSV is poised to demonstrate how its model of organization and care offers a "best in class" response to the challenges of population management and partnering with primary care physicians. Primary care pediatricians and family practitioners have a responsibility to care for the needs of children throughout the year in an organized and proactive manner for preventable illness. PSV can complement that care model by partnering with primary care practitioners for the care of children with chronic and serious injuries, conditions and health problems. We also partner with families to care for children over the course of their childhood, trying to diagnose and treat difficult health problems in the best manner possible while we work to prevent or reduce harmful and costly acute episodes of care. PSV has begun to explore through pilot programs how such partnerships with primary care practices could work for specific specialties such as gastroenterology and endocrinology. As we learn from these initial partnering endeavors, other initiatives will be developed to include more specialties and primary care groups.

Pediatric Specialists of Virginia has special clinician-only contact lines for urgent referrals or consultations (703-PSV-1234 or PSVDocs@PSVCare.org). If you'd like further information about PSV, please visit our website at PSVCare.org.



The leaders of the two systems believed that forming such a group could benefit the children of Northern Virginia by having a wide spectrum of pediatric medical and surgical specialties available as part of a single enterprise for quicker and more coordinated consultations to better address the multiple and complicated health problems presented by these children and their families. Moreover, PSV would represent a single-source referral option that could become a better partner for primary care practices needing specialized resources to augment the care of their patients. From that startup with five specialties, PSV has rapidly grown in two years to encompass sixteen specialties with 89 full or part-time clinicians providing ser-

Pharmacogenomics

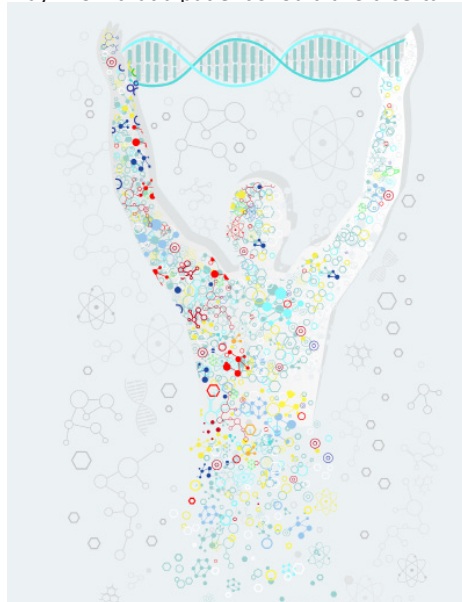
Benjamin D. Solomon, MD

Chief, Division of Medical Genomics

Inova Translational Medicine Institute

Inova Children's Hospital

Pharmacogenomics (sometimes called pharmacogenetics) combines the sciences of pharmacology and genomics. The goal of pharmacogenomics is to learn whether patients have specific genetic changes that affect how their body processes or metabolizes certain medications. By being aware of the presence of these genetic changes, clinicians may know that a patient should avoid certain



medications because of the potential for adverse drug reactions, or if the dosage of other medications should be adjusted because of differences in drug metabolism. In practice, pharmacogenomic testing currently usually involves targeted DNA testing, which may be done through a buccal swab or a blood test. Pharmacogenomics has a central role in the recent emphasis on personalized or precision medicine.¹

With the increased interest in genetics and genomics and personalized medicine, the field of pharmacogenomics is growing rapidly, and many groups are implementing pharmacogenomics in a variety of ways, including in both pediatric and adult medicine. This can be challenging for a number of reasons. One major challenge is that most physicians are not highly trained in this complex and quickly evolving field, especially in terms of actual clinical practice. With this in mind (though realizing this brief description does not begin to scratch the surface!), I have prepared a

list of current, key points about pharmacogenomics relevant to the practitioner who may encounter pharmacogenomics clinically:

1. All pharmacogenomic information is not created equally! Thousands of individual genetic variants have been described as possibly being associated with responses to many different (but certainly not all) medications. There is very strong evidence for some of these associations, but for many, the evidence is not nearly as robust. This can be difficult for clinicians and patients: pharmacogenomic testing panels may include a combination of many variants reportedly associated with numerous medications, but the level of evidence may be variable. One resource that helps rank the evidence and which otherwise serves as a clearinghouse for pharmacogenomic-related information is the "PharmGKB" (<https://www.pharmgkb.org/>), which arose from a Stanford-based project in this area. A link on their website provides a list of ranked variants: <https://www.pharmgkb.org/search/clinicalAnnotationList.action?levelOfEvidence=top>, then click on "Download a list of all clinical variants."

Conversely, one can also search the website for medications with pharmacogenomic implications.

2. Just as there are different levels of evidence, there are clinical guidelines for the interpretation of some (but again, not all) pharmacogenomic variants. The Clinical Pharmacogenetics Implementation Consortium (CPIC)² presents peer-reviewed, published guidelines, which are made available through the PharmGKB as well as in journal format. Clinicians with an interest in this field are eligible to join CPIC. There are also other active pharmacogenomic societies in other parts of the world, such as the Dutch Pharmacogenetics Working Group (DPWG).³ As with other fields of medicine, the guidelines continue to grow and evolve with scientific and medical progress.

3. There may be different pharmacogenomic tests that make sense in different clinical situations. For a healthy person, where the goal is predictive healthcare, the scope may be very narrow – one might select a small group

of "top tier" variants with the most understood pharmacogenomic implications. In another type of situation, a patient may need a medication where it is well known that some people have genetic variants that influence medication response. In this case, doctors may order a pharmacogenomic test related to just that medication prior to treatment. In practice, one of the challenges is that this depends on the clinician knowing they need to order the test in that situation, and involves waiting for the result to come back before prescribing accordingly. A third situation might involve a person who is already on multiple medications that do not appear to be working as expected. In this case, a panel related to those medications (if available) might be ordered. However, returning to the first point above, there needs to be caution, as there may be commercial panels available that appear applicable but which are based on lower levels of evidence.

4. As mentioned, pharmacogenomic information is based on changes in a person's DNA – this means that this information is applicable throughout a person's life whenever they might encounter a relevant medication. However, these genetic changes are only one piece of the puzzle. Other factors contribute to how well drugs work, including the age (and size) of the patient, medical conditions the patient has, other medications a person is taking, and many other environmental and lifestyle factors.

5. Although this field is admittedly intimidating, clinicians should not feel that they need to "go it alone!" In addition to some of the resources above, clinicians are encouraged to discuss pharmacogenomics, including specific results, with their friendly neighborhood geneticist, genetic counselor, pharmacologist, or other expert in the field.

References

1. Collins FS, Varmus H. A new initiative on precision medicine. *The New England Journal of Medicine*. Feb 26 2015;372(9):793-795.
2. Relling MV, Klein TE. CPIC: Clinical Pharmacogenetics Implementation Consortium of the Pharmacogenomics Research Network. *Clinical pharmacology and therapeutics*. Mar 2011;89(3):464-467.
3. Swen JJ, Nijenhuis M, de Boer A, et al. Pharmacogenetics: from bench to byte—an update of guidelines. *Clinical pharmacology and therapeutics*. May 2011;89(5):662-673.

Reconstituted Infant Formula Fluoridation: A Review of the Literature

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Abstract

Purpose: To conduct a review of the current literature regarding the fluoride content of reconstituted infant formulas and the recommendations made by the appropriate authorities concerning the optimum fluoride delivery to infants and their associated risks of dental caries or dental fluorosis. **Evidence Review:** An electronic database search using the terms "fluoride," "infant formula," "fluorosis," "fluoride supplement," "breast-feeding," "reconstituted infant formula," and "systemic fluoride" was conducted. **Findings and Discussion:** The optimal level of water fluoridation is 0.7 ppm¹, as determined by multiple national organizations and federal departments. Different types of infant formula have differing levels of fluoridation, most notably that powdered formulas reconstituted with optimally fluoridated water have the potential to be over the recommended fluoride concentration. The current literature does not show a definitive link between infant formulas with above-optimal fluoride levels and dental fluorosis. However, it is recommended that parents be informed of the risks of dental fluorosis, and those who are concerned should consider using fluoride-free water to reconstitute powdered infant formula. **Conclusions and Relevance:** More studies are needed using the current fluoride concentration ceiling in order to determine the amount of fluoride delivered to infants under six months of age using reconstituted formula.

Background

During the 20th century, public water fluoridation has been argued as having both systemic and topical anti-caries effects on the dentition and skeletal structure of children. Due to the lack of primary tooth eruption in the first five to six months of life, there are no topical effects to study related to infant formula fluoridation. The Environmental Protection Agency (EPA) and the Department of Health and Human Services (DHHS) recommend the optimal level of public water fluoridation of 0.7 ppm. However, human breast milk is much lower in fluoride content (0.019 ppm), regardless of the level of community water fluorida-

tion.² Therefore, infants who are solely breastfed receive an insignificant amount of systemic fluoride. The American Academy of Pediatric Dentistry (AAPD) does not recommend fluoride supplementation to children under six months of age regardless of water fluoride concentration,^{3,4} and the American Academy of Pediatrics (AAP) recommends exclusive breastfeeding for the first six months of life.⁵ It can be assumed that based on these recommendations, the current best practice is denies infants less than six months of age access to any appreciable fluoride. But when comparing the breastfeeding recommendations of the AAP (which result in very limited fluoride exposure) to the higher fluoride concentrations of different types of infant formula, parents are left pondering the best level of systemic fluoride exposure for their infants.

There are, however, deleterious effects of high systemic fluoride levels during development of the dentition. The most common side effect of high systemic fluoride during early childhood is enamel fluorosis primarily of the permanent dentition. The exact mechanism in which high fluoride levels interfere with tooth formation is not known, but it is understood to alter enamel prism formation. Constantly exposing ameloblasts to fluoride during the multiple developmental stages can cause severe fluorotic changes in the final enamel structure.⁶ Calcification of the permanent maxillary central incisors begins around 3-4 months of age,⁷ and is completed at 4-5 years of age. It is during this time of tooth formation that the child is sensitive to raised systemic levels of fluoride, and the susceptibility of maxillary incisors to fluorosis diminishes after the age of five.^{8,9} Fluorosis is seen as unaesthetic opacities in the enamel, ranging from white spots to yellow and brown. In rare cases of severe fluorosis, the tooth structure, hardness, and overall strength are all adversely affected.

A 2002 national survey of children in the United States aged 12-15 years shows eight percent as having mild fluorosis and five percent having moderate fluorosis.¹⁰ It

should be noted that from a public health perspective, mild fluorosis is not associated negatively with oral health-related quality of life.¹¹ Thus, it can be asserted that the public health community as a whole views mild fluorosis as an acceptable result of widespread water fluoridation, as the anti-caries effects outweigh the esthetic concerns.

It has been generally accepted in medical literature that a total daily fluoride intake between 0.05-0.07 mg/kg is optimal.¹² In practice, however, the amount of fluoride delivered can vary widely considering the range of liquid intake among infants in different climates and cultures.¹³ The Institute of Medicine established a tolerable upper intake level of 0.7 mg F per day for infants less than six months of age.¹⁴ This upper level can be surpassed due to intake of fluoride from infant formula, especially powders reconstituted with optimally fluoridated water.¹⁵

Evidence Review

Articles included in this review focus on the fluoride contents of infant formula, and the effects of fluoride on the diet of children under three years of age, and most specifically those under six months. In addition, studies that make recommendations on the adequate level of infant formula fluoridation and the ideal total fluoride intake of children are also included. The author conducted a PubMed search with the keywords "fluoride," "infant formula," "fluorosis," "fluoride supplement," "breastfeeding," "reconstituted infant formula," and "systemic fluoride." The publications included consist of review articles, guideline statements, clinical trials, and observational studies. Preference was given to guidelines from national and international health organizations, meta-analysis articles, and primary experimental studies. An initial database search yielded 1,210 results. Duplicate records, inaccessible manuscripts, case-reports, and studies using a fluoride concentration of greater than 1.2 ppm were excluded. A total of 31 relevant articles were included in this litera-



ture review.

Findings and Discussion

The amount of fluoride in infant formulas is much higher than that of breast milk. Premixed/ready-to-feed infant formula has been shown to have fluoride concentrations of 0.09–0.17 ppm (milk-based) and 0.19–0.38 ppm (soy-based),¹⁵ which are both well below the upper limit set by the EPA and DHHS. There are two different types of concentrated infant formula (liquid and powder), and each has its own fluoride levels. The variability of the water used in reconstituting powder formula also plays an important role in the final concentration of fluoride. Several studies have found powdered infant formulas have a final fluoride concentration of 0.83–1.07 ppm.^{17,18,19} Using optimally fluoridated water (which at the time of these studies ranged from 0.7–1.2 ppm) or ground water with naturally high levels of fluoride to reconstitute infant formulas can elevate the fluoride concentrations above the current recommended levels, and thus raise concerns regarding the increased risk of fluorosis.^{20,21}

In a longitudinal study in conjunction with the Iowa Fluoride Study, Marshall concluded in 2004 that the fluoride concentration in the water used to reconstitute infant formula is a major determinant of primary tooth fluorosis.²² He found a significant increase in the incidence of fluorosis occurs in children where infant formula is reconstituted using fluoridated drinking water. In another study including patients with fluorosis of both primary and permanent dentitions, there is a significantly greater cumulative fluoride intake from reconstituted powder infant formula than any other source between the ages of 3–9 months.⁹

The current AAPD policy regarding reconstituted infant formula states that using optimally fluoridated water is acceptable, although parents concerned about the risks of fluorosis can be advised to use fluoride-free water sources. This recommendation supports an assertion by Levy in 1995 that from a public health perspective, mild fluorosis is not a problem and thus general recommendations to avoid reconstituting concentrated infant formula with fluoridated water are not warranted.^{11,23} As Fomon pointed out in 2000, it is important to consider the environment and water source for each particular family, in that parents should be aware of the fluoride concentration of their

ground water.²⁴ In nonfluoridated areas, infants who are fed formula for greater than six months show an increased prevalence of fluorosis when compared to infants being solely breast-fed. No difference in the prevalence of fluorosis has been seen in areas of optimal water fluoridation.^{25,26}

Conclusions and Relevance

The AAP recommends very limited fluoride exposure to children less than six months of age (a diet of solely breast milk), while the AAPD does not advise against feeding infants formula which may contain more than the optimal concentration of fluoride unless the parent is concerned about fluorosis. It is clear that more research is needed to determine the optimal systemic fluoride levels for infants when taking into account their diet and water fluoride levels.²⁷ Longitudinal studies must be conducted to compare the topical and systemic risks and benefits of fluoride exposure in order to deliver a more coherent message to parents and caregivers.^{28,29,30} Without definitive studies regarding the systemic benefits of fluoride in the first six months of life, no convincing recommendations can be made.

The studies cited in this review were conducted at the previous upper limit of artificial water fluoridation of 1–1.2 ppm. Recent revisions in the fluoridation recommendations by the United States Department of Health and Human Services and the Environmental Protection Agency lowered the maximum concentration to 0.7 ppm. The updated limit is less than half the allowable fluoride concentration in drinking water of 1.5 ppm³¹ according to the World Health Organization (WHO), and less than the WHO's current recommendation for artificial fluoridation of 1 ppm. Once additional studies are conducted implementing the new guidelines of optimally fluoridated drinking water in the United States in conjunction with more information regarding systemic fluoride consumption in infants via formula, updated recommendations can be made to parents concerned with infant exposure to fluoride.

Acknowledgments

The authors wish to thank Judy Reinhartz, Ph.D. and Dennis Reinhartz, Ph.D. for their support.

References:

1. U.S. Public Health Service Recommendation for Fluoride Concentration in Drinking Water for the Prevention of Dental Caries. Public Health Reports. July–August 2015; Vol. 130, pp 1–14.
2. Spak, C.J. et al. Fluoride in human milk. *Acta Paediatr Scand* 72:

- 699–701, 1983.
3. AAPD. Guideline on Fluoride Therapy. Reference Manual. v36, no6, pp 14–15. 2014.
4. AAPD. Policy on use of fluoride. Reference Manual, Vol. 36, No. 6, 43–44, 2014.
5. AAP. Breastfeeding and the Use of Human Milk. *Pediatrics*. v115, no2, Feb. 1, 2005, pp 496–506.
6. Bronckers, ALJ et al. The Impact of Fluoride on Ameloblasts and the Mechanisms of Enamel Fluorosis. *J Dent Res* 88(10): 877–893, 2009.
7. Logan WHG, Kronfeld R: Development of the human jaws and surrounding structures from birth to the age of fifteen years. *JADA* 20:379–427, 1933.
8. Evans RW, Stamm JW. An epidemiologic estimate of the critical period during which human maxillary central incisors are most susceptible to fluorosis. *J Public Health Dent* 1991;51:251–9.
9. Mascarenhas, AK. Risk factors for dental fluorosis: A review of the recent literature. *Pediatr Dent* 22:269–277, 2000.
10. Beltran-Aguilar ED et al. Surveillance for dental caries, dental sealants, tooth retention, edentulism, and enamel fluorosis – United States, 1988–1994 and 1999–2002. *MMWR* 2005;54(3):1–43.
11. Levy, SM et al. Associations between fluorosis of permanent incisors and fluoride intake from infant formula, other dietary sources and dentifrice during early childhood. *JADA* 2010;141(10):1190–1201.
12. Burt BA. The changing patterns of systemic fluoride intake. *J Dent Res*. 1992;71:1228–1237.
13. Cressey, Peter. Dietary fluoride intake for fully formula-fed infants in New Zealand: impact of formula and water fluoride. *Journal of Public Health Dentistry* 70(2010)285–291.
14. U.S. Institute of Medicine, Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, And Fluoride*. Washington: National Academy Press; 1997.
15. Hujuel PP et al. Infant formula and enamel fluorosis: A systematic review. *JADA* 2009;140(7):841–854.
16. Zohoori FV et al. Impact of water fluoride concentration on the fluoride content of infant foods and drinks requiring preparation with liquids before feeding. *Community Dent Oral Epidemiol* 2012; 40: 432–440.
17. McKnight-Hanes, M. Carole et al. Fluoride content of infant formulas: soy-based formulas as a potential factor in dental fluorosis. *Pediatr Dent*: Sept. 1998, Vol. 10, No. 3, 189–194.
18. Maguire A et al. Fluoride content of ready-to-feed (RTF) infant food and drinks in the UK. *Community Dent Oral Epidemiol* 2012;40:26–36.
19. Berg, Joel et al. Evidence-based clinical recommendations regarding fluoride intake from reconstituted infant formula and enamel fluorosis. *JADA* 2011;142(1):79–87.
20. Van Winkle S et al. Water and formula fluoride concentrations: significance for infants fed formula. *Pediatr Dent* 17:305–10, 1995.
21. Pendrys DG, Katz RV. Risk factors for enamel fluorosis in optimally fluoridated children born after the US manufacturers' decision to reduce the fluoride concentration of infant formula. *Am J Epidemiol* 1998;148:967–74.
22. Marshall, Teresa A. et al. Associations between intakes of fluoride from beverages during infancy and dental fluorosis of primary teeth. *Journal of the American College of Nutrition*, Vol. 23, No. 2, 108–116 (2004).
23. Levy SM et al. Infants' fluoride intake from drinking water alone, and from water added to formula, beverages, and food. *J Dent Res* 74(7): 1399–1407, July 1995.
24. Fomon, Samuel. Fluoride intake and prevalence of dental fluorosis: Trends in fluoride intake with special attention to infants. *J Public Health Dent* 2000;60(3):131–9.
25. Do, Loc et al. Association between infant formula feeding and dental fluorosis and caries in Australian children. *J Public Health Dent* 2012;72:112–121.
26. Buzalaf, M.A.R.B et al. Risk of fluorosis associated with infant formulas prepared with bottled water. *J Dent Child*. 2004;71:110–113.
27. Koletzko, Berthold. Global standard for the composition of infant formula: recommendation of an ESPGHAN coordinated international expert group. *J Pediatr Gastroenterol Nutr*, Vol. 41, No. 5, November 2005, 584–599.
28. Burt, Brian A. et al. The case for eliminating the use of dietary fluoride supplements for young children. *J Public Health Dent* 1999;59(4):269–74.
29. Hellwig, E., Lennon, A.M. Systemic versus topical fluoride. *Caries Res* 2004;38:258–262.
30. Limeback, Hardy. A re-examination of the pre-eruptive and post-eruptive mechanism of the anti-caries effects of fluoride: is there any anti-caries benefit from swallowing fluoride. *Community Dent Oral Epidemiol* 1999;27:62–71.
31. World Health Organization. Guidelines for Drinking-water Quality. 2008

Medication-Related Osteonecrosis of the Jaw: Incidences Among Children and Adolescents

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Abstract

Background. Bisphosphonate therapy in adults has been linked to increased risk for osteonecrosis of the jaw. The purpose of this review was to determine if children and adolescents are at a higher risk for developing osteonecrosis of the jaw after taking bisphosphonates. **Methods.** A detailed literature search was undertaken in order to identify studies focusing on the incidence of bisphosphonate-related osteonecrosis of the jaw in children and adolescents. The search strategy included the following keywords in multiple combinations: children, adolescents, bisphosphonates, osteonecrosis, BRONJ, and jaw. **Results.** It appears that the pediatric population may not be at high risk for developing MRONJ. There have been no reported credible cases of MRONJ in children or adolescents. **Conclusions.** There is not enough evidence to determine if there is a direct relationship between antiresorptive/antiangiogenic therapy and medication-related osteonecrosis of the jaw in children and adolescents. More prospective studies are needed.

Background

Bisphosphonates are a class of antiresorptive medications used to treat a variety of pathologic conditions including metastatic cancer affecting the bone, hypercalcemia of malignancy, primary hyperparathyroidism, osteoporosis, Paget's disease, and osteogenesis imperfecta.¹ Bisphosphonates inhibit osteoclasts through suppression of isoprenylation by inhibiting farnesyl diphosphate synthase in the cholesterol pathway.² Although the mechanism of action is complex, the overall effect is that they decrease osteoclast-mediated resorption of bone. This process leads to lower bone turnover and an increase in bone mineral density.³ Patients taking this class of drugs, usually experience a positive impact on the quality of their life, including a lower risk of fractures and less bone pain. However, for patients with advanced cancer involving the skeleton, bisphosphonates do not improve the overall survival rate.⁴

Bisphosphonates have a longer history of use in adults, but they were first used in children in the 1990's to treat osteogenesis imperfecta (OI).⁵ Since that time, their use in children has increased but still remains limited compared

to adults. In children, they are used mostly to treat OI and the majority of the clinical studies involving the use of intravenous pamidronate to treat it. Children and adolescents with OI have shown improvements in muscle force, vertebral bone mass and size, bone pain, fracture rate, and growth when treated with intravenous (IV) bisphosphonates.⁶

The first report in 2003, established a link between bisphosphonates and the development of bisphosphonate-related osteonecrosis of the jaws (BRONJ).⁷ Traditionally, the term BRONJ has been defined as a condition of exposed bone in the maxillofacial region that lasts for more than eight weeks in a patient with no history of radiation exposure and a history of taking oral or IV bisphosphonates.⁸ However, in 2014 the American Association of Oral and Maxillofacial Surgeons (AAOMS) recommended changing the nomenclature to medication-related osteonecrosis of the jaw (MRONJ) because of a number of osteonecrosis cases related to the jaw involved other antiresorptive and antiangiogenic medications.⁴ Symptoms of MRONJ include pain, mobility of teeth, inflammation of gingival tissues and risk of infection due to the exposed necrotic bone.⁹

Although the amount of bisphosphonates prescribed in the United States is down compared to their peak use in 2008, millions of adults are exposed to them annually, and their use has increased in children.¹⁰ The risk of developing MRONJ varies depending on what study is reviewed, and the majority of the data is based on adult populations.

Looking at the adult population, the risk of developing MRONJ for patients taking oral bisphosphonates ranges from 1:10,000 to 1:100,000 while the risk for those taking IV bisphosphonates ranges from 1:10 to 1:100.¹¹ The risk increases the longer the patient is on bisphosphonate therapy. Among cancer patients taking the bisphosphonate zoledronate, the incidence was 0.5% at year 1, 1.0% at year 2, and 1.3% at year 3.¹² For patients exposed to oral bisphosphonates, the incidence was reported at 0.1% at baseline and increased to 0.21% after 4 years of oral bisphosphonate use.¹³ MRONJ can also develop spontaneously,

without any history of bisphosphonate use, and this risk ranges from 0-1.9 per 10,000 patients.⁴

It is not completely understood why IV bisphosphonates are associated with a higher risk of MRONJ compared to oral medications, but several theories exist.¹⁴ The first is the bioavailability of the medication. With oral bisphosphonates, less than 1% of the drug is absorbed by the gastrointestinal tract, while more than 50% of the IV dose is bioavailable.¹⁵ Another explanation might be that IV bisphosphonates are used to treat more serious diseases such as malignant cancers and these patients will have other confounding factors such as use of corticosteroids.¹⁶ Finally, another theory is that IV bisphosphonates users receive more concentrated doses at shorter intervals compared to oral bisphosphonates users. Although there is a range, the cumulative dose of the bisphosphonate zoledronic acid, at which MRONJ has occurred is 62 mg (range 4-240) and for pamidronate, another bisphosphonate, is 3825 mg (range 630-8640).¹⁷ Patients increase their risk for MRONJ the longer they are on bisphosphonate therapy and the more concentrated the dose.

Dentoalveolar surgery puts the patients exposed to bisphosphonates at high risk for developing MRONJ.⁴ There is variation among studies but the current estimate for risk of MRONJ among patients taking oral bisphosphonates after tooth extraction is 0.5%.¹⁸ For cancer patients taking IV bisphosphonates, it ranges from a low of 1.6% to a high of 14.8%.^{19,20} The pathophysiology of MRONJ is not yet fully understood. The maxilla and mandible alveolar bone experience an increased bone turnover rate which helps promote oral bone healing. Bone remodeling rate is slowed by the bisphosphonate effect on the osteoclasts. Bisphosphonates also have angiogenesis-inhibition properties, and these two effects help explain why bone healing could be impaired.⁴

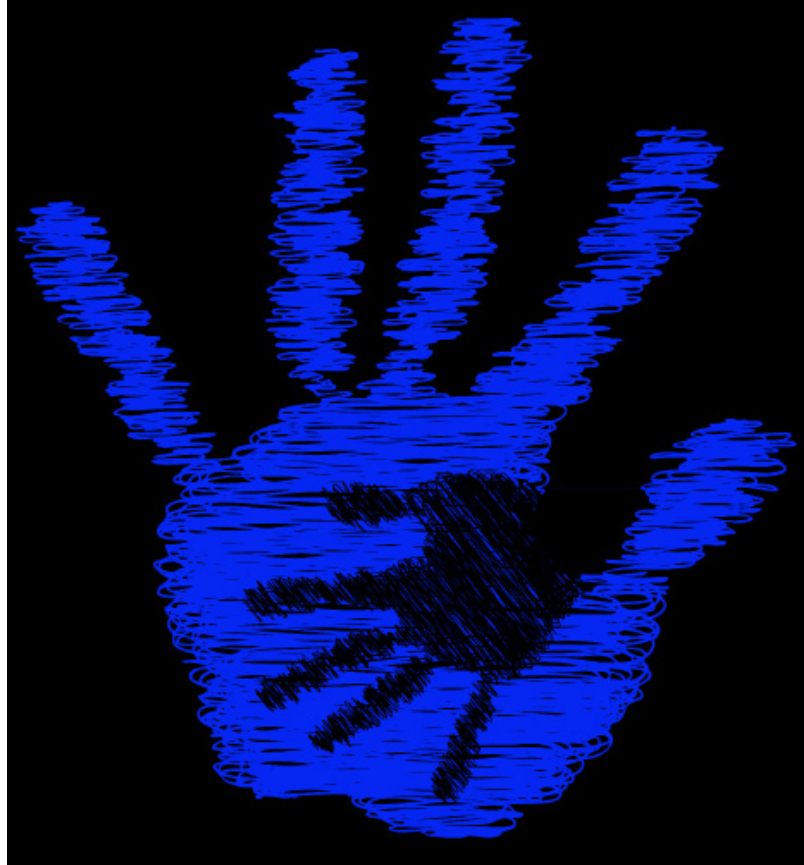
Prevention is the key to reducing the risk of MRONJ, and AAOMS recommends a multi-

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disciplinary approach to the treatment of patients on antiresorptive medications. This approach includes a dental consultation before

incidence of bisphosphonate-related osteonecrosis of the jaw in children and adolescents. The search strategy included the following



keywords in multiple combinations: children, adolescents, bisphosphonates, osteonecrosis, MRONJ, and jaw. Due to the paucity of results all relevant studies were included. Currently, there are only seven relevant retrospective studies addressing the risk of MRONJ in children and adolescents. Additional information such as expert opinion and adult studies were supplemented by re-

who received monthly IV doses of a bisphosphonate (disodium pamidronate) ranging for a minimum of 6 months of treatment time to 12.5 years. Thirty-eight oral surgical procedures were performed on 22 of the patients, and none of the 64 patients developed MRONJ.

Chahine et al ²³ (2008) contacted 278 pediatric patients who received at least one cycle of intravenous bisphosphonate (pamidronate) at the Shriners Hospital for Children in Montreal between 1992-2006. The range of pamidronate exposure was from one infusion to 11.2 years of regular infusions. Dental extractions had been performed on 113 patients during or after bisphosphonate therapy. None of the 278 patients had MRONJ, and there were no postoperative complications reported after dental extractions.

Brown et al ²⁴ (2008) clinically and radiographically evaluated 42 pediatric patients who were treated with IV bisphosphonates at the Royal Children's Hospital in Australia. Eleven patients had an invasive dental procedure including dental extractions and surgical exposure of permanent teeth, and MRONJ was not seen in any of them. Schwartz et al ²² (2008) reviewed the charts of 15 patients (2 yrs – 16 yrs) with OI who had dental extractions at the Montreal Children's Hospital dental clinic. A total of 60 teeth were extracted. A majority of the patients (65%) were undergoing active bisphosphonate treatment. In 23% of the patients the extractions took place after bisphosphonate therapy, while in 5% the status was unknown, and in 7% a placebo had been given. None of the patients developed MRONJ.

Only one study suggested MRONJ incidence in children. Moeini et al ²⁶ reported 12 patients (7 yrs – 21 yrs) diagnosed clinically with MRONJ in Esfahan City, Iran. However, there were other confounding factors including that all the patients were diagnosed with thalassemia major. This condition impairs the ability of hemoglobin to carry oxygen and may interfere with bone healing. It was also unclear why the patients were taking bisphosphonates and what their clinical definition of MRONJ was. Due to the inconsistencies, the article was not used as evidence for MRONJ in children or adolescents.

Discussion

The studies reviewed do not contain large numbers of participants. The Moeini et al. study was not as relevant due to the incon-

treatment begins.⁴ The dental consult includes a thorough oral evaluation and identification of any acute infections or sites of potential infections that could worsen once treatment starts. A more aggressive treatment plan should be considered if indicated, including extractions of non-restorable teeth and full coverage crowns instead of intracoronary restorations. Other preventative therapies such as antibiotic prophylaxis, chlorhexidine rinses, and temporary suspension of bisphosphonates should also be considered. If a patient develops MRONJ, the management goals include eliminating pain, controlling infection, minimizing the progression of the necrosis, and avoidance of other elective dental surgery. Surgical removal and recontouring of alveolar bone should be considered for areas of necrotic bone that become a constant source of irritation.⁴

Methods

A detailed literature search of PubMed, EBSCO, and Google Scholar databases was performed in order to identify studies related to the

viewing references from the included studies.

Results

Following an extensive literature search, seven studies were found that specifically looked at the incidence of MRONJ among children. Currently, there are no credible cases of MRONJ in children or adolescents. Bhatt et al ⁶ (2014) follow 99 children treated with intravenous bisphosphonates at the Children's Hospital at Westmead, Australia. Nineteen of these children have undergone oral surgical procedures, including fifty dental extractions, and no complications were identified.

Maines et al ²⁵ (2011) evaluated 102 patients (1.2 yrs – 24 yrs) who received IV neridronate infusions for OI for at least one year at the Pediatric Clinic of the University of Verona. MRONJ was not seen in any patients however; no patients underwent dental extractions. Malmgren et al ²¹ (2008) evaluated 64 patients (3 mo – 20.9 yrs) from the Swedish National Centre for children and adolescents with OI

... (cont.) Medication-Related Osteonecrosis of the Jaw: Incidences Among Children and Adolescents

sistencies in the study and the Maines et al. study was not as relevant because no dental treatment was rendered. However, after reviewing the remaining studies it appears that the pediatric population may not be at high risk for developing MRONJ. There have been no reported credible cases of MRONJ in children or adolescents. There are several reasons suggested for the low risk in children, which include a lack of comorbidities and low doses of bisphosphonates since most children are treated for OI and not cancer, and increased bone vascularity in childhood.^{25,9} Since the true incidence of MRONJ in children and adolescents is unknown, precautions and management guidelines have been adopted from those established for the adult population.²⁵ The guidelines for children are based on anecdotal evidence and multidisciplinary expert opinion because of the lack of high-quality data from clinical trials.²⁷ However, the pediatric skeleton is fundamentally different from the adult skeleton, making a comparison difficult.¹⁴

These guidelines might need to be modified after considering the low risk of developing MRONJ in children. Until further information is available, any necessary dental treatment should be completed before bisphosphonate treatment if possible, and patients must undergo continued dental evaluations in order to screen for MRONJ.²⁴ However, patients needing dental surgery after bisphosphonate therapy initiation should not be denied treatment because of the potential complications.²²

The long term risk of children developing MRONJ is not fully understood. The half-life of one IV dose of a nitrogen containing bisphosphonate is estimated between 1.5 years up to 10 years.^{28,29} This long half-life means that children could potentially be at risk for developing MRONJ well into adulthood. Other potential side effects of antiresorptive medication include oral ulcerations, delayed tooth eruption, and complications with orthodontic treatment.^{9,30,6}

Conclusions

There is not enough evidence to determine if there is a direct relationship between antiresorptive/antiangiogenic therapy and medication-related osteonecrosis of the jaw in children and adolescents. More prospective studies are needed to determine if there is a direct causal relationship. All of the treatment protocols for the prevention and management of MRONJ are adapted from the adult population treatment, which is not necessarily applicable to the pediatric population. Due to

the long skeletal half-life of the medications, it is currently unknown if pediatric patients who have undergone bisphosphonate therapy will be at risk for developing MRONJ as they mature. Until we learn more about this relationship, precautions should be taken when treating pediatric patients, but dental procedures should not be avoided when deemed necessary.

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References

1. Ngan KK, Bowe J, Goodger N. The risk of bisphosphonate-related osteonecrosis of the jaw in children. A case report and literature review. *Dent Update* 2013;40:733-738.
2. Rodan GA. Bisphosphonates and primary hyperparathyroidism. *J Bone Miner Res* 2002;2:150-153.
3. Papaoulios SE. Bisphosphonates: how do they work? *Best Pract Res Clin Endocrinol Metab* 2008;22:831-847.
4. American Association of Oral and Maxillofacial Surgeons. Position Paper on Medication-Related Osteonecrosis of the Jaw – 2014 Update. Approved by the board of trustees 2014. Accessed online 2015.
5. Astrom E, Soderhall S. Beneficial effect of bisphosphonate during five years of treatment of severe osteogenesis imperfecta. *Acta Paediatr* 1998;87:64-68.
6. Bhatt RN, Hibbert SA, Munns CF. The use of bisphosphonates in children: review of the literature and guidelines for dental management. *Australian Dental Journal* 2014;59:9-19.
7. Marx RE. Pamidronate (Aredia) and zoledronate (Zometa) induced avascular necrosis of the jaws: a growing epidemic. *J Oral Maxillofac Surg* 2003;61:1115-1117.
8. Advisory Task Force on Bisphosphonate-Related Osteonecrosis of the Jaws, American Association of Oral and Maxillofacial Surgeons. American Association of Oral and Maxillofacial Surgeons position paper on bisphosphonate-related osteonecrosis of the jaws. *J Oral Maxillofac Surg* 2007;65:369-376.
9. Christou J, Johnson AR, Hodgson TA. Bisphosphonate-related osteonecrosis of the jaws and its relevance to children – a review. *International Journal of Paediatric Dentistry* 2013;23:330-337.
10. Wysowski DK, Greene P. Trends in osteoporosis treatment with oral and intravenous bisphosphonates in the United States, 2002-2012. *Bone* 2013;57(2):423-428.
11. Khosla S, Burr D, Cauley J, et al. Bisphosphonate-associated osteonecrosis of the jaw: report of a taskforce of the American Society for Bone and Mineral Research. *J Bone Miner Res* 2007;22:224-236.
12. Guarneri V, Miles D, Robert N, et al. Bevacizumab and osteonecrosis of the jaw: Incidence and association with bisphosphonate therapy in three large prospective trials in advanced breast cancer. *Breast Cancer Res Treat* 2010;122:181-188.
13. United States Food and Drug Administration. Avastin (bevacizumab) safety information. Available at: <http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm275758.htm>. Accessed Feb 1, 2014.

14. Hennedige AA, Jayasinghe J, Khajeh J, Macfarlane TV. Systematic review on the incidence of bisphosphonate related osteonecrosis of the jaw in children diagnosed with osteogenesis imperfecta. *J Oral Maxillofac Res* 2013;4:4 (e1).
15. Ezra A, Golomb G. Administration routes and delivery systems of bisphosphonates for the treatment of bone resorption. *Adv Drug Deliv Rev* 2000;42(3):175-195.
16. Marx RE, Sawatari Y, Fortin M, Broumand V. Bisphosphonate-induced exposed bone (osteonecrosis/osteopetrosis) of the jaws: risk factors, recognition, prevention, and treatment. *J Oral Maxillofac Surg* 2005;63(11):1567-1575.
17. Mavrokokki T, Cheng A, Stein B, Goss A. Nature and frequency of bisphosphonate-associated osteonecrosis of the jaws in Australia. *Journal of Oral and Maxillofacial Surgery* 2007;65:415-423.
18. Kunchur R, Need A, Hughes T, et al. Clinical investigation of C-terminal cross-linking telopeptide test in prevention and management of bisphosphonate-associated osteonecrosis of the jaws. *J Oral Maxillofac Surg* 2009;67:1167-1173.
19. Scoletta M, Arata V, Arduino PG, et al. Tooth extractions in intravenous bisphosphonate-treated patients: A refined protocol. *J Oral Maxillofac Surg* 2013;71:994-999.
20. Yamazaki T, Yamori M, Ishizaki T, et al. Increased incidence of osteonecrosis of the jaw after tooth extraction in patients treated with bisphosphonates: A cohort study. *Int J Oral Maxillofac Surg* 2012;41:1397-1403.
21. Malmgren B, Astrom E, Soderhall S. No osteonecrosis in jaws of young patients with osteogenesis imperfecta treated with bisphosphonates. *J Oral Pathol Med* 2008;37:196-200.
22. Schwartz S, Joseph C, Iera D, Vu DD. Bisphosphonates, osteonecrosis, osteogenesis imperfecta and dental extractions: A case series. *JADA* 2008;74:537-542.
23. Chahine C, Cheung MS, Head TW, Schwartz S, Glorieux FH, Rauch F. Tooth extraction socket healing in pediatric patients treated with intravenous pamidronate. *J Pediatr* 2008;153:719-720.
24. Brown JJ, Ramalingam L, Zacharint R. Bisphosphonate-associated osteonecrosis of the jaw: Does it occur in children? *Clinical Endocrinology* 2008;68:863-867.
25. Maines E, Monti E, Doro F, Morandi G, Cavarzere P, Antoniazzi F. Children and adolescents treated with neridronate for osteogenesis show no evidence of any osteonecrosis of the jaw. *J Bone Miner Metab* 2012;30:434-438.
26. Moeini M, Moeini M, Lotfzadeh N, Alavi M. Radiography finding in the jaws in children taking bisphosphonate. *Iranian Journal of Pediatric Hematology Oncology* 2013;3(3):114-118.
27. Khan AA, Sandor GK, Dore E, et al. Canadian consensus practice guidelines for bisphosphonate associated osteonecrosis of the jaw. *J Rheumatol* 2008;35:1391-1397.
28. Lin JH. Bisphosphonates: A review of their pharmacokinetic properties. *The Bone Journal* 1996;18(2):75-85.
29. Drake MT, Clarke BL, Khosla S. Bisphosphonates: Mechanism of action and role in clinical practice. *May Clin Proc* 2008;83(9):1032-1045.
30. Kamoun-Goldrat A, Ginisty D, Le Merrer M. Effects of bisphosphonates on tooth eruption in children with osteogenesis imperfecta. *Eur J Oral Sci* 2008;116:195-198.

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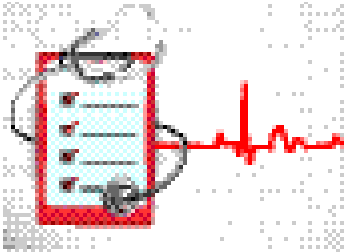
... VA-AAP Legislative Update

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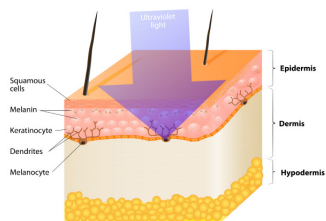


Virginia Chapter



check of the PMP for prescriptions longer than 14 days and allows office staff to check the PMP. There are numerous bills regarding this issue and we are working with the patrons to amend them so that we may offer our support.

TANNING PROCESS



Tanning

We once again supported legislation that would prohibit indoor tanning for minors under the age of 18. Unfortunately, the bill failed to report with a tied vote of 7-7. While we are disappointed it did not pass, this is significant progress and the closest the vote has ever been. We are hopeful that will be able to pass this legislation once and for all in the near future!



Smoking in Cars

Another bill we support every year is progressing through the legislature. HB1348, carried by Delegate Pillion, would prohibit smoking in cars when a child under the age of eight is present. The bill passed subcommittee with only one opposing vote! It will soon be heard in full committee and we are working hard to help it pass.



Raw Milk

We had an early victory this session with the defeat of HB 62 (Morris), which would allow the sale of raw milk. Dr. Sam Bartle testified against this bill and we were glad to see it tabled in subcommittee.



As you can see, the VA AAP is working hard this session to advocate for pediatric health. We will keep you updated as the 2016 legislative session continues!



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