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Editorial

Toward an Efficient Child Protective Strategy in Lebanon:

A Call for Pediatricians' True Child Advocacy

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OBJECTIVE:

The Control of Child Abuse and Neglect (CAN) is a sustained and tedious long term process that requires a synchronized, consensual and comprehensive teamwork approach. Since the regional 2005 United Nation Study on Violence (UNSV) conference in Cairo, the Child Right Convention (CRC) Geneva meeting in 2006 and the latter UNSV remarks in 2007, Lebanon has continued to join United Nation efforts in order to control CAN and VAC. Despite many obstacles, a multisectoral team was established within the Higher Council for Childhood, with a high level of common understanding of child rights. In this strategy, pediatricians in Lebanon have a prominent role, in terms of diagnostic skills, referral of cases, networking of professionals, as well as awareness and advocacy for the child rights and family protection.

INTRODUCTION:

This paper reviews the current approach and gaps encountered in the evaluation and control processes of CAN in Lebanon. The whole procedure itself is an integrated and multileveled approach that incorporates children's rights, professional evidence of maltreatment, relevant social factors and pre-identified intersectoral responsibilities for the control of VAC and CAN. Several obstacles hinder the implementation of the above process on a national level. In the Lebanese context, those are: absence of legislations that implement free child health care in Constitution, insufficient universal screening for child health problems and uneven access of children to health care facilities. This report also unveils the means in which the Lebanese strategy for child protection should be developed to comply with the United Nations Convention for the Rights of the Child, taking into consideration the needs and limitations of a developing, insecure and ill-resourced country like Lebanon.

THE BACKGROUND, SINCE THE UNSV STUDY ON VAC

In 2001, the United Nations General Assembly, following the recommendations from the CRC, requested the Secretary-General to conduct an in-depth study of the question of worldwide violence against children. In 2003, Professor Paulo Pinheiro, from Brazil, was appointed as expert to guide the study. In 2004, World Vision, Human Rights Watch, Save the Children, and the International Society for the Prevention of Child Abuse and Neglect were appointed as an advisory panel of representatives of selected non-governmental organizations and therefore convened to advise on the nature and conduct of the study.

The final report from that study was delivered to the UN General Assembly in the beginning of 2007. The study provided an "in-depth" summary of the extent and the burden of the problem, where children are exposed to violence in their homes, their communities and in the schools. Representatives from the Arab region participated in the report and provided relevant - yet insufficient - information about the Middle East & North Africa region (MENA) situation of children and the efforts undertaken in this regard.

THE RATIONALE OF THE LEBANESE SPECIFICITIES AND GAPS

Despite ongoing efforts by the Lebanese government and many Lebanese organizations to address the multiple social and professional obstacles hindering the child rights implementation in Lebanon, CAN remains a serious threat for both the child as a victim and for the professional team as well, in a still unhealthy Lebanese society. In Lebanon, legislations are still far from meeting the CRC requirements and there is no specific governmental budget allocated for the process of child protection, and rehabilitation and prevention of child maltreatment. In fact, children are submitted, in terms of civil rights, to inherited traditions and to the mercy of the different religious references prevailing in Lebanon. Add to above facts, the absence of independent structures for child rights monitoring (e.g. National Child Defender, or National Child Observatory) and absence of a National Child Helpline. A high percentage of maltreated children are still living in institutions (schools, communities, judicial environment, and orphanages) that are poorly oriented to CRC, CAN & VAC issues. In addition, there is scarcity of therapy programs for victims and virtually non for abusers. Furthermore, there is a wide discrepancy in the humanitarian and social situation of refugee children who live in Lebanon and their Lebanese and non-Lebanese peers. Furthermore, after the July 2006 war on Lebanon, children have been exposed to slaughter, physical and psychological maltreatment resulting from their displacement away from their home places and villages, as well as to premature internal reconciliation issues like socio-political turmoil, security and safety concern, economical uncertainty, conflicting youth objectives, physical and moral confrontations, etc...

In the present hectic social context, where personal safety and social peace are the frontline issues, child maltreatment issues are

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unequally evaluated among different social and religious groups. In fact, the above factors are increasing child exposure to violence, and we'll continue to hear about children from different communities and diverse settings who suffer from maltreatment, abuse, and neglect of all sorts, without getting the appropriate comprehensive attention.

So what can we do? In such contexts

Pediatricians are assumed to pave the way by taking head roles in terms of diagnostic skills and referral of maltreated children, as well as providing caregivers and children with the appropriate preventive measures and assuming their expected role in true child advocacy. Realizing their importance in implementing CRC requirements in Lebanon, *the Lebanese Higher Council for Childhood* chose pediatricians, because of their familiarity with the state of children, among its group of diverse and competent professionals, with a sincere commitment to the provisions outlined in the CRC. The group was established in 2007, and was referred to as LIBAN-CAN¹. A code of conduct is currently required for those working with LIBAN-CAN specifically. Its mission aims indeed at the prevention of maltreatment as well as the identification and management of abused and neglected children. In Lebanon, the task force for accomplishing this mission is a multidisciplinary team formed of law enforcement personnel, child welfare and mental health specialists in addition to research resources and health professionals. Since its establishment in 2004, LIBAN-CAN has put its resources available for other professionals working with children such as pediatricians, and seeks for more information about diagnosis, referral and advocacy issues related to CAN and VAC.

BUILDING THE INFORMATION AND THE KNOWLEDGE BASE

Children subjected to CAN are frequently encountered in clinical and non-clinical setups; they may require urgent medical attention. However, CAN is neither a mandatory reportable nor a regularly disclosed entity, with few exceptions among medical professionals. For these reasons, the study of the prevalence and incidence of CAN and VAC is not easy to perform in Lebanon.

In 2005-2006, www.ChildOfLebanon.org studied the validity of two sets of questionnaires put by www.ispcan.org and www.arabipcan.org addressed to youth and to families respectively; the purpose of the field test was also to unveil the incidence of CAN in the setups of schools, institutions, and community within the perspective of the UNSV study. The questionnaires prove to be valid, useful, transmissible and interactive tools to study the extent of CAN in our setup.

Another study "desk review of institutions and research centers working with injured children and CAN issues", was performed from 2005-2006 in St Joseph university; allowed to gather a set of information concerning institutions qualitative and quantitative profiles, and induced a comparative study of the Lebanese laws relevant with child protection issues. This study is available at USJ university center for family and community health www.cusfc@usj.edu.lb

As it appears, there is a growing and concerted initiative in Lebanon for the recognition and control of CAN. However, the relevant lack of reporting algorithm calls for an independent, competent and participatory structure to analyze relevant maltreated child related information; such a data base would allow stakeholders, in collaboration with professionals in child related sectors, child and youth associations and dedicated NGO's, to build child protection initiatives and programs based on accurate information.

This vision of health inclusive Child Observatory, is an ongoing process growing through a participatory social network and an evaluative intersectoral team, all being keen to develop within the CRC framework, with culturally sensitive local tools. Pediatricians have a major role in such a structure, in terms of information, expertise and professional attitudes.

CONCLUSION

There are many issues in confronting violence against children in Lebanon. The whole strategy is the responsibility of the society as a whole, with special emphasis on the roles, potentials and duties of pediatricians.

LIBAN-CAN is an emerging national association that aims at the implementation of the above goals, where professionals - medical and others - as well as scientific resources are the pillars of its steering committee. Youth participation is also recognized in LIBAN-CAN through presence of youth representatives. We believe that front liners, both professionals and youth, can contribute to the development of better national understanding of the universal child rights concept. They can also play an important role in the development of an optimal, focused, socially adapted and socially accepted actions.


Finally, we would like to invite the different medical teaching institutions in Lebanon, to include a mandatory health oriented curricula on CAN and VAN in their medical and nursing education curricula. This process is also ongoing in Arab countries, as one of the major tools in medical information and child protection.

IMPLICATIONS AND FUTURE PERSPECTIVES

Lebanon and other countries in the MENA region are still challenged to plan systems, to set priorities and to provide frameworks for political and social debate on CAN and VAC, with the participation of children and youth. In this perspective, the following goals are foreseen:

¹ Lebanese Intersectoral Board of Associations Network for the prevention of Child Abuse and Neglect.
(The Higher Council of Childhood in Lebanon).

1. Meet with children in different regions of Lebanon, to exchange their output about the UNSV results and recommendations.
2. Agree on definitions of VAC and CAN.
3. Use the child questionnaires developed by ISPCAN and supported by UNICEF to unveil CAV & VAN.
4. Reach a common understanding about the ways to combat violence.
5. Enhance the already existing national and local movements towards child protection, by advocacy and awareness raising.
6. Stimulate and enforce legislative revision of laws to comply with the provision of the CRC.
7. Increase professional knowledge about the UNSV and CAN, through the development of relevant curricula.
8. Develop a Child protection act and a child budget.
9. Set a “Child Helpline” for referrals, as well as social and mental support.
10. Create a Child Defender institution, to offer quick responses to urgent child rights needs and reduce inequalities among vulnerable children.
11. Install a Child Observatory, in order to build the knowledge about child rights related issues.

These priorities are the pivots of knowledge base and information on one side, training, and rehabilitation on the other; the prevention and control of VAC and CAN requires accurate education about global child rights and local childhood issues. In this arena, pediatricians are – and should remain - the best and most efficient child defenders. Of course, this process needs social stability, common vision, and synchronized interaction between formal and informal sector, as well as standardized professional intervention and child participation. Of the above, the most challenging element is the last but not the least. 

Your Contribution Will Make The Difference

Dear colleagues;

Welcome to the second issue of LPS newsletter - *Pediatrica Online*. The LPS cabinet during its regular meetings agreed to have *Pediatrica Online* issued periodically and our ambition is to have it issued on quatrains basis. Our limiting factor is the limited number of possible original contributions from Lebanese Pediatricians and our limited knowledge of the medical topics that are of interest to vast majority of you particularly those working in remote areas.

Fortunate enough, that was not the case when I started my search for articles of the present issue, which are examples of the high professional spirits among our colleagues in medical universities and are live examples of the good support which we can get in our community had we asked for it. The published articles address the objectives of child advocacy as in Drs G. Hage & B. Gerbaka editorial, the quality of care improvement, the article of *Febrile Seizures* by Dr M. Mikati, and of new therapeutic modalities that have changed serious disease prognosis, the article of *Goodpasture disease: Case report* by Dr Ch. Mourani, a third article which I published is related to a frequently encountered behavioral question in our practice which is *Temper Tantrums*. In addition, this issue contains in the medical alerts selections, six summary articles that alert us to frequently encountered issues and controversies including: Long term prognosis of treated cancer cases, Treatment failures in Kawasaki disease, Fluoride and Iron intake, Viral infections and febrile seizures, and Predictors of bacterial meningitis.

One last word about the LPS website, I want to thank all of you who visited the website since its establishment. I also realize the difficulties that some of you have faced in entering their identification data, which is in part due to the slow system and in another part due to some structural problems. Recently and thanks to a grant from Sanofi-pasteur Pharmaceutical Company and Nestle nutrition, we are working with a specialized Website company to update our website system and make it user friendly. A process that I hope will not take more than one month. In the mean time we will keep utilizing the current system trying to make the best use of its potentials. Here, I really appreciate to have your comments on the current system, any suggested modifications or new items and please let me know as soon as possible.

“A gap between Lebanese Pediatric Society and its members” has always been a major complaint between pediatricians. Today, is your time to cover that gap by making the best use of your website and internet communication, and to start motivating your society by becoming more active in conveying your needs and informing us about your activities. Have you done something interesting in your practice? Have you read a good book about pediatrics or child health issues? Have you discovered new resources or tools that help you as a pediatrician? Are you working on an interesting project? Please let us know, contact us at lps@lpswebsite.org, and let us put our hands together to bring the required change to our society toward a real child care and advocacy.

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Proceedings of October National Pediatric Congress

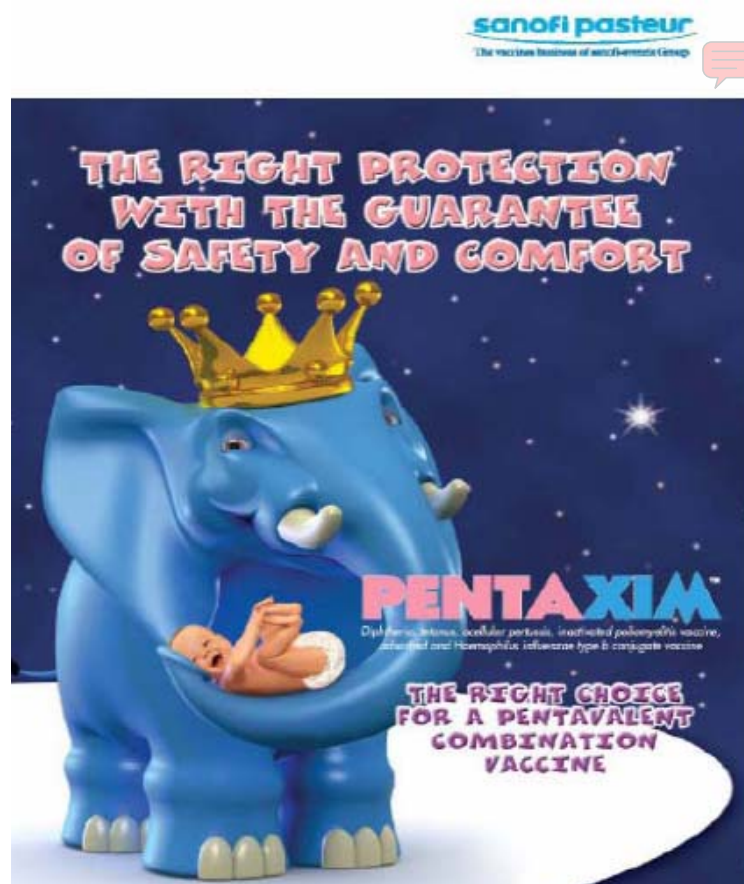
Dear Colleagues;

In spite of the current frustrating events in our country, it gives me great pleasure to inform you that LPS cabinet in its May 2007 meeting has put plans to arrange for its 6th International Pediatric Congress in November 29 through December 1, 2007. The cabinet assigned the process of Congress Organization to the Club sections of the society, with which I am working since to arrange for a special program tailored to our needs.

So far the Clubs of Neurology, Hem-Oncology, Gastroenterology, Neonatology, Pulmonology, and Community Pediatrics have agreed to participate in that congress. The above clubs started already their preliminary meetings and they are working relentlessly to fulfill the endeavor of our society in promoting Continued Medical Education among its members through an attractive program.

Each Club will present 1 or 2 sessions, 2 hours duration each. Each session consists of 6 scientific presentations, 15 minutes each. The final topics have not been finalized yet in all sections. Our priority is for presentations that deal with new updates related to the fields of the different participating clubs. The Congress will also contain workshops and presentations by invited foreign speakers.

Finally, I would appreciate your contribution in the success of that event by giving your ideas, suggestions and/or presentations. Hopefully the turmoil of violence will end soon, we will keep you updated about any developments related to the Congress through our website and e-mail, should you have any questions or any suggestions please feel free to contact me at alifawaz@cyberia.net.lb or lps@lpswebsite.org.



FEBRILE SEIZURES

MOHAMAD A/G MIKATI MD*, MOHAMAD H. ITANI MD, AMAL C. RAHI MPH.

Febrile seizures is a benign childhood condition that is sometimes frightening to the parents, and is associated with significant care giver anxiety, and concerns about future epilepsy in affected children. In this review article, Dr Mikati et al, provide a practical approach to management of febrile seizures, through an up-to-date review of the medical literature about the definition of febrile seizures, its genetic background, its recurrence risks, risk of subsequent epilepsy and the different therapeutic modalities with their side effects. After reading this article you should be able to identify simple and complex febrile seizures, assess the risk of recurrence, the risk of further epilepsy, and to develop a therapeutic strategy for the management of febrile seizure.

DEFINITION

Febrile seizures; are seizures that occur between the age of 6 months and five years with a temperature of 38°C or higher and are not the result of central nervous system infection or any metabolic imbalance. The disorder has been reported in infants as early as 3 months of age and as late as 7 years. The child may look strange for a few moments, then stiffen, twitch and roll his eyes. He or she will be unresponsive for a short time, breathing will be disturbed, and skin may appear a little darker (bluish) than usual. The seizures usually last less than one minute but can last for up to 15 minutes. After the seizure, the child quickly returns to normal. They are either simple (referred to as typical) or complex (atypical):

- A simple febrile seizure is a primary generalized usually tonic-clonic attack associated with fever, lasting for a maximum of 15 minutes, not recurring within a 24-hour period.
- A Complex febrile seizures, on the other hand, are either more prolonged (more than 15 minutes), focal, or recur within 24 hours during the same febrile illness.

Important information to parents about Febrile Seizures

- Febrile seizures occur in 2-5% all children between the ages of 6 months and 5 years.
- Seizures are sometimes frightening, but they are usually harmless.
- Febrile seizures usually happen during the first few hours of a febrile illness.
- The seizures usually last less than 1-2 minutes but can last for up to 15 minutes or more. The child should be brought to medical attention to prevent the seizures from lasting longer than 15-30 minutes; as such seizures may be associated with brain injury.
- After the seizure, the child usually quickly returns to normal.
- Febrile seizures do not necessarily lead to later development of epilepsy.

EPIDEMIOLOGY

2-5 % of neurologically healthy infants and children experience at least one, usually simple, febrile seizure. Recurrence risk after a first simple febrile seizure is 30% on the average. However this figure may vary according to several "risk" factors (table1). It increases to 50% in infants less than one year of age and to another 50% after two or more febrile seizure episodes. In 1985 Knudsen reported six 'additive' predictive factors for recurrence: complex nature of the febrile seizure, age less than 14 months, family history of febrile seizures, family history of epilepsy, attendance at day care, and developmental delay. The risk of recurrence for an individual child ranged from 12% if none of these factors were present to 100% if all were present. Other risk factors include short duration of illness before the seizure, low body temperature at the time of seizure, and age at first seizure less than 18 months.³²

Those findings were further documented in the study of Bessiso et al¹² that found male sex and complex seizure as important recurrence risk factors. EI-Radhi²³ found that children whose body temperature was below 39°C at the onset of the seizure, were 2.5 times more likely to have multiple convulsions within the same illness and more likely to experience recurrent febrile convulsions in subsequent

Table 1. Risk Factors for Recurrent Febrile seizures.

1. Age at 1st seizure < 18 months.^{9,32,42}
2. Short duration of fever before seizures.⁹
3. Complex nature of febrile seizures.^{32,12}
4. Positive family history of febrile seizure^{9,32}
5. Positive family history of epilepsy.^{32,49}
6. Low body temperature at time of 1st seizure.^{9,23}
7. Low serum sodium level.²⁹
8. Male sex.¹²
9. Attendance at day car center.³²

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illnesses than those with a temperature above 39°C. Hugen and colleagues²⁸ found a linear association between serum sodium levels and recurrent febrile convulsions - the lower the level, the higher the risk.

Table 2. Relative Risk For Recurrence of Febrile Seizures^{8,9,31}

No. of Risk Factors (Table 1)	Relative Risk
No Risk Factors	12%
One Risk Factor	25-36%
Two Risk Factors	50-59%
Three or More Risk Factors	73-100%
Average Risk	30%

The Risk of Brain Damage

A number of hospital based studies have reported deficits in speech, drawing, arithmetic, attention and intelligence in patients with febrile seizures. However those series are considered biased, due to referral patterns,²² and were not confirmed by other controlled and population based studies. There are no long-term adverse effects of having one or more simple febrile seizures. Specifically recurrent simple febrile seizures do not damage the brain.^{17,18,22,34,61} However prolonged febrile seizures and febrile status are thought to result in increased risk for cerebral injury and later epilepsy and thus should be prevented.⁷

The Risk of Developing Epilepsy

2-7 % of children who experience febrile convulsions proceed to develop non febrile seizure disorders and epilepsy later in life. In contrast 15% of children with epilepsy have had febrile seizures.^{14,30} This implies that most patients who develop epilepsy in later life do not necessarily have febrile seizures in childhood.

There are several predictors of epilepsy after febrile seizures (table 2). Complex febrile seizures, neurodevelopmental abnormalities, a family history of epilepsy, recurrent febrile seizures and a brief duration of fever before the initial febrile seizure were all associated with an increased risk of epilepsy in the study⁹. However, in other studies multiple recurrences did not predict subsequent epilepsy.^{12,13} Verity and Golding in 1991 demonstrated that a higher risk for later epilepsy occurs in patients with complex febrile seizures (6%) particularly focal febrile seizures (29%) as compared to simple febrile seizures (1 %).⁶¹

Prolonged febrile seizures may precede intractable complex partial seizures.¹⁴ Choueiri et al (2001) showed that 36% of patients with temporal lobe epilepsy had prior febrile seizures and that only 6% of patients with primary generalized epilepsy had such a history. The above-mentioned increased risk for later epilepsy after febrile seizures is thought to be predominantly due to genetic predisposition and probably only to a lower extent due to structural damage to the nervous system caused by recurrent febrile seizures. However, this issue is not yet fully resolved.¹⁹

Table 3. Predictors of Epilepsy

1. Complex Febrile seizures. ^{10,42,61}
2. Neurodevelopmental abnormalities. ⁴²
3. Family history of epilepsy. ^{10,42}
4. Recurrent febrile seizures. ¹⁰
5. Short duration of fever before febrile seizure. ¹¹

No. of Risk Factors (Table 3)	Relative Risk of Epilepsy ^{10,42,61}	Risk of Later Cognitive Impairment ^{17,18,61}
No Risk Factors	1%	Similar to general population irrespective of risk factors *
Four or more Febrile Seizures	4.2%	
Complex Febrile Seizure (Any type)	6%	
Complex Febrile Seizure (Focal type)	29%	
Fever < 1 hour before Febrile Seizure	10.7%	
Family History of epilepsy	17.7%	
Neurodevelopmental abnormality	33%	
Average Risk	2-7%	

* Risk factors include: Age of onset (<1year or > 1 year), Presence or absence of complex febrile seizures, Recurrence rate of febrile

convulsions (0,>1,<3,>4), Presence or absence of subsequent unprovoked seizures, Prior use of antiepileptic drugs, Duration of the seizure free period and Presence of any deficits in febrile convulsion patients.

GENETIC FACTORS

Positive family history of febrile and afebrile seizures has been documented in several studies.^{19,31,40,41,47,59,62} Segregation analysis on nuclear families found that nearly dominant seizure susceptibility was found in families of probands with multiple febrile convulsions while families of probands with single febrile convulsions followed the polygenic model of inheritance.⁴⁹ In a study in India by Wadhwa et al out of 144 cases of febrile seizures (95 simple and 49 complex), 20% had familial prevalence of febrile seizures (same percentage in both groups). On the other hand 13.9% had family history of afebrile seizures (13.2% in the simple and 40.8% in the complex group).⁶² Choueiri et al (2001) showed that patients with febrile seizures were more likely to have a family history of febrile seizures (20%) than patients with epilepsy.¹⁹ Similarly, it has been documented that the familial type of febrile seizures is not necessarily associated with the initial febrile seizure being complex in nature.⁵⁹

It has been recognized that there is a significant genetic component for susceptibility to this type of seizure. Six susceptibility febrile seizures loci have been identified on chromosomes 8q13-q21 (FEB1), 19p (FEB2), 2q23-q24 (FEB3), 5q14-q15 (FEB4), 6q22-q24 (FEB5), and 18p11 (FEB6). Furthermore, mutations in the voltage-gated sodium channel alpha-1, alpha-2 and beta-1 subunit genes (SCN1A, SCN2A and SCN1B) and the GABA(A) receptor gamma-2 subunit gene (GABRG2) have been identified in families with a clinical subset of seizures termed “generalized epilepsy with febrile seizure plus syndrome” (GEFS+).^{41,51,63} The syndrome has its onset in early childhood and remits in mid childhood. It is characterized by multiple febrile seizures and several types of afebrile generalized seizures including generalized tonic clonic, absence, myoclonic or atonic and myoclonic astatic seizures with variable degree of severity. 3 types of GEFS+ have been described linked to 3 different genes.^{51,55} (GEFS +1, SCN1A) 2q23-q31 β subunit of the voltage-gated sodium channel,⁶¹ (GEFS +2, SCN1B) 19q13, α subunit of the voltage-gated sodium channel,²⁴ and (GEFS +3, GABA receptor γ 2) 5q31, GABA(A) receptor gamma-2 subunit gene.^{6,41}

WORK-UP OF THE CHILD WITH FEBRILE SEIZURES

Good history & neurological examination are the corner stones in the evaluation of a child with febrile convulsions (refer to Figure 1 at the conclusion of the article).

o **Lumbar Puncture**

Seizures are the major sign in 13-16% of children presenting with meningitis. 30-35% of children less than 18 months of age have negative meningeal signs. According to the American Academy of Pediatrics practice parameter, LP is strongly recommended in infants less than one year of age after their first febrile seizures since clinical signs of meningitis can be minimal to absent in that population. In children between 12-18 months of age after their first febrile seizure LP should be considered because signs and symptoms in this age group may be subtle. In older children LP should be considered in case of positive neck stiffness, Kernig’s or Brudzinski’s meningeal signs, or when the clinical condition of the child is suspicious of meningitis. If the child has already on antibiotics when febrile seizures occur, the clinician should be aware that treatment with antibiotic may mask the signs and symptoms of meningitis and LP in that case should be strongly considered. Moreover the presence of an identified source of fever like otitis media does not eliminate meningitis. A child between 12 and 18 months should also be considered for lumbar puncture since they usually have slight symptoms of meningitis clinically.^{28,46} Table 5 summarizes indication of LP in a child with first febrile seizure.

Table 5. Practice Parameters of performing lumbar puncture in a child with febrile seizures⁴⁶

1. Suspicious findings on physical exam particularly positive meningeal signs.
2. Complex febrile seizures.
3. Physician visit within 48 hours before the seizures i.e. seizures occurring after 48 hours of a febrile illness.
4. Seizures on arrival to emergency department.
5. Prolonged postictal state as children with simple febrile seizures usually recover quickly.
6. Initial seizure after 3 years of age.
7. Children younger than 18 months of age who show no signs or symptoms of meningitis.
8. Children evaluated by less experienced clinicians.
9. Children who can not be available for follow-up.
10. Increase risk of missing the proper diagnosis of meningitis occur e.g. antibiotic therapy prior to the onset of febrile seizures.

N.B.: A recognized source of infection e.g. Otitis media does not exclude the diagnosis of meningitis.

o **EEG**

If the child is presenting with his first simple febrile seizure, and is otherwise neurologically healthy, an EEG should not

normally be performed as part of his evaluation (Provisional Committee on Quality Improvement 1996).⁴⁶ However the performance of an EEG would not predict the future recurrence of febrile seizures or epilepsy even if the result is abnormal.^{2,21} If an EEG is done, it should be performed for at least half an hour in wakefulness and in sleep according to international guidelines in order to avoid misinterpretations and erroneous conclusions. EEGs performed within two weeks of a febrile seizure often have non-specific usually posterior slowing. Thus, in many cases the EEG is delayed till after two weeks have passed or if done during that period it often needs to be repeated. Because of all the above reasons, performance of an EEG should be highly restricted to only special cases in which epilepsy is highly suspected. (Table 4).

Facts about EEG in simple febrile seizures

- EEG does not predict future epilepsy.
- If done, it often should be performed properly and at least two weeks after the simple febrile seizures.
- EEG should be restricted to those cases highly suspicious of epilepsy.

○ **Blood studies**

Blood studies including serum electrolytes, calcium, phosphorus, magnesium, and CBC are not routinely recommended in the workup of a child with a first simple febrile seizure. Blood glucose should be determined only in case the child had a prolonged obtundation post ictally. Serum electrolyte values may be abnormal in children after a febrile seizure, but this should be manifested by physical examination and history taking.⁴⁶

○ **Neuroimaging**

According to The American Academy of Pediatrics practice parameter⁴⁶ a CT scan or magnetic resonance imaging is not recommended in evaluating the child after a first simple febrile seizure. Adamsbaum et al (2004) reviewed neuroimaging studies requested for children attending emergency room department in France. They concluded that no imaging studies are indicated in case of typical febrile seizures, i.e. generalized, brief and occurring between 1 and 5 years of age. No abnormalities were detected by neuroimaging procedures even though most of their cases had severe or focal febrile seizures.¹ We believe that more data are needed in this area. We recommend that workup of children with complex febrile seizures needs to be individualized. This often includes EEG and neuroimaging particularly if the child has an abnormal neurological exam.

TREATMENT

If a child develops a febrile seizure, parents should act immediately by providing First Aid measures (Table 6) to prevent brain injury resulting from upper airway obstruction. In general antiepileptic therapy, continuous or intermittent, is not recommended for children with one or more simple febrile seizures. Parents should be counseled about the relative risks of recurrence of febrile seizures and recurrence of epilepsy (Tables 2 & 4), educated on how to handle a seizure and should be given emotional support. If the seizure lasts for more than few minutes then acute treatment with intravenous or rectal diazepam may be needed. Intravenous phenobarbital, phenytoin, or valproate may be needed in the case of febrile status epilepticus. If the parents are very anxious concerning their child's seizures, intermittent oral diazepam can be given during febrile illness to help prevent, In addition antipyretics may comfort the child.⁸

Antiepileptic therapy may be considered for children with complex febrile seizures. Nevertheless currently available data indicates that the possibility of future epilepsy does not change with or without therapy.

A. Intermittent therapy during fever

1. Antipyretics:

Though it is sometimes hoped that antipyretics would consequently reduce; febrile seizure episodes. However, review of the literature reveals that this is almost definitely not the case. Schnaiderman et al (1993), studied the effect of acetaminophen prophylaxis (10 mg/kg every 4 hours) or sporadic doses (given only when the body temperature was 38°C or above) during a febrile illness. Four children in each group had a second febrile seizure within 24 hours. It was concluded that neither regimen reduced the number of fever episodes, the duration of fever, or the recurrence of febrile seizures.⁵² Camfield et al (1980) studied 79 children with a first simple febrile seizure and who had normal psychomotor development. Extensive instructions on antipyretic use were provided to the

Table 6. First Aid Measures

- Place your child on the floor or bed away from any hard or sharp objects.
- Turn his or her head to the side so that any saliva or vomit can drain from the mouth.
- Do not put anything into his or her mouth; your child will not swallow his or her tongue.
- Call your pediatrician.
- Take your child to Emergency Room if seizures persist more than 5-10 minutes.

parents and acetaminophen was to be given during a febrile illness as 15 mg/kg every 4 hours with either daily phenobarbital or placebo (5 mg/kg/day). There was a significant difference in the incidence of recurrence of febrile seizures between the acetaminophen and phenobarbital group (5%), and the acetaminophen and placebo group (25%). This implied that a single dose of Phenobarbital is more effective than antipyretic therapy in preventing febrile seizure recurrence.¹⁶ In addition, the high recurrence rate in the placebo group suggests that antipyretics did not have an effect on the rate of recurrence.¹³ In the randomized, double-blind, placebo-controlled study by van Stuijvenberg et al, 230 children 1-4 years of age, who had at least one risk factor for febrile seizure recurrence were randomly assigned to ibuprofen syrup 20 mg/ml, 5mg/kg/dose or placebo to be administered every 6 hours during fever 38.5°C or higher until the child was afebrile for 24 hours. After a follow up time of about one year, 67 of the children had a first febrile seizure recurrence (31 in the ibuprofen and 36 in the placebo group). In all fever episodes, ibuprofen was found to significantly reduce the body temperature as compared to placebo. However, in episodes with febrile seizure recurrence, a similar increase in temperature was found in both groups. The results suggested that intermittent antipyretic treatment during fever did not prevent febrile seizure recurrences in children at risk.⁶⁰ The study by Van Esch et al (1995); compared acetaminophen 10mg/kg with ibuprofen 5mg/kg as antipyretic agents in 70 randomized children with febrile seizures. Both ibuprofen and acetaminophen were shown to be effective antipyretic agents in these children. Ibuprofen was significantly more effective in reducing body temperature (more rapidly and to a greater degree), but no significant differences were found with respect to seizure recurrence (two had recurrence after ibuprofen vs. three after acetaminophen).⁵⁸ One explanation of the ineffectiveness of antipyretics in reducing febrile seizure recurrence might be that in some children seizures occur at a somewhat lower temperature and the antipyretic does not lower the temperature completely to normal.⁴³ In addition febrile seizures often occur as the temperature is rising before antipyretics have had the chance to exert their effects.

2. Oral diazepam and other benzodiazepines:

In the study by Autret et al (1990) oral diazepam (0.5mg/kg and then 0.2mg/kg every 12 hours during a febrile illness) was found to be ineffective in reducing febrile seizure recurrence (occurred in 16% of children) compared to placebo (19.5%). This was thought to be due to poor compliance by the parents.⁴ Uhari et al (1995) randomized 180 children into, diazepam and acetaminophen, diazepam and placebo, paracetamol and placebo, or two kinds of placebo. Either diazepam or placebo was given as an initial rectal dose of 2.5mg for children weighing less than 7 kg, 5 mg for children weighing 7-15 kg. and 10 mg for those weighing more than 15 kg, followed after 6 hours by oral doses of 0.2 mg/kg tid for the first two days of a febrile illness (when body temperature is >38.5°C). Acetaminophen was given at a dose of 10 mg/kg four times per day. The four groups were followed for two years and compliance was excellent. In this study, the relatively low doses of acetaminophen and of diazepam that the authors used were ineffective for febrile seizure prevention.⁵⁷ On the other hand, Rosman et al (1993) found that intermittent oral diazepam treatment using the dose of 0.33mg/kg every 8 hours during fever was effective as compared to placebo against febrile seizure recurrence in 406 randomized children with at least one prior febrile seizure. Results of the 1.9-year follow up were that oral diazepam reduced the risk of recurrent febrile seizures by 44% per person-year. Difference in time to first recurrent febrile seizure was only significant after adjustment for covariates⁵⁰ Intermittent oral nitrazepam, clobazam, and clonazepam (0.1/kg/day) have also been shown to be effective in reducing the risk of recurrence of febrile seizures.⁶⁵

3. Rectal diazepam:

Intravenous lorazepam remains the preferred medicine and the preferred route for the initial treatment of generalized convulsions. However, other medications and other routes need to be considered. Rectal diazepam is usually used to stop ongoing seizures in hospital or by parents at home. Echenne et al (1983) used rectal diazepam by parents at home to stop simple febrile. The results (21 families with an average follow-up of 2 years) were compared with those in two groups of controls. The efficacy and innocuousness of prophylactic treatment were remarkable. If used at home by parents, the latter should be carefully instructed about the specific dose to be administered to the child.²⁵ It has also been used as a prophylaxis to reduce recurrence at the time of febrile illness. In the study by Knudsen and Vestermark (1978), children were randomized to either rectal liquid diazepam (0.5mg/kg every 12 hours) during illness or daily phenobarbitone. Both treatments were equally effective - or ineffective because there was no placebo - and adverse effects were minimal.³³ In the study by Lee et al (1986), intermittent diazepam prophylaxis 0.5 mg/kg administered as a rectal suppository every 8 hours for up to 48 hours when the temperature exceeded 38.5°C was found to be as effective as continuous oral sodium valproate. Again in this study also there was no placebo group.³⁶

4. Other routes for benzodiazepines administration:

Intramuscular absorption of benzodiazepines is erratic. McIntyre compared the efficacy of rectal diazepam versus buccal medazolam for treatment of acute tonic-clonic seizures. Both drugs were found to produce equivalent therapeutic effects in controlling the seizures within 10 minutes. Other routes of midazolam administration include intranasal, sublingual or rectal. Upper respiratory infection, prominent secretions, or vigorous head movement can prohibit intranasal use. Sublingual application of the drug is impractical with tonic seizures. Rectal access requires the removal of clothing (especially difficult in tonic seizures and for those with underlying motor impairment). Although buccal mucosa can be blocked by copious saliva, it has clear advantages over other ports of entry.^{38, 54}

B. Long-term Anti-Epileptic Drug (AED) therapy

1. Phenobarbital:

In a recent meta-analysis of 47 trials on AEDs and seizure prevention phenobarbital was specifically found to be effective for prevention of recurrences of febrile seizures with a relative risk of 0.51 (95% CI 0.31-0.82).⁵⁶ In the placebo-controlled trial of Camfield et al (1980) in children with a first simple febrile seizure daily dose 4-5 mg/kg of phenobarbital was found to be effective in preventing recurrence (5% vs. 25% in the placebo group).¹⁶ Another randomized study on 355 children with simple febrile seizure found that recurrence rate in intermittent phenobarbital therapy did not differ with the placebo while continuous treatment with phenobarbital was significantly better than placebo (6% vs 30%).⁶⁶ In the study by Farwell et al (1990) in children with complex febrile seizures, where non-compliance was a problem, phenobarbital did not appear to have an advantage over placebo in reducing recurrence rate of seizures. After 2 years, 46% of the phenobarbital group had recurrence as compared to 38% in the placebo group.²⁶ In conclusion most trials of phenobarbital have shown benefit of this drug in preventing recurrence or in reducing the number of febrile seizures on condition it be given on a daily basis, with compliance monitored and therapeutic blood levels maintained.⁸ Bacon et al (1981) compared phenobarbital, phenytoin, and placebo in children who had their first seizure before two years of age. Assessment was done after one year of treatment. Phenobarbital significantly reduced febrile seizure recurrence only in children who were less than 14 months of age at the time of their first febrile seizure but not among older children while phenytoin did not differ from placebo. Their conclusion was that continuous prophylaxis against febrile seizures should be considered for each case alone. However, phenobarbitone is advisable as prophylaxis for children who had their first seizure before 14 months of age.⁵

2. Carbamazepine

Comparing children treated with phenobarbital and those treated with carbamazepine, the study by Anthony and Hawke (1983) showed that 47% of the carbamazepine group had recurrence vs. 10% of the phenobarbital group.³ Another study showed that 13 of 16 children, who have failed phenobarbital, had recurrent febrile seizures after 18 months of treatment with carbamazepine.¹⁵

3. Valproic acid

In the study by Lee and Melchior (1981), phenobarbital did not show better outcome of seizure recurrence as compared to no treatment, while valproic acid was significantly better than both, in preventing recurrences.³⁵ Herranz et al (1984) found that phenobarbital 4.8mg/kg/d was effective in 80% of the patients and valproate 35.2 mg/kg/d was effective in 91.7% of the patients. Side effects after valproic acid were observed in 45% of patients, were significantly lower than those observed after phenobarbital (76.7%).²⁷ Several other studies have found valproic acid to be as effective as phenobarbital and significantly better than placebo.^{37,45,65} The study by Mamelle et al 1984 showed that children treated with either phenobarbital or valproate had significantly better seizure outcome than the placebo group.³⁷ The study by Minagawa and Miura (1981) found that a regimen of 20-25 mg/kg/d bid of valproic acid was less effective than a regimen of 30mg/kg/d bid and also less effective than phenobarbital and primidone treatments.³⁹ In a pooled analysis of trial results in Britain in 1988 for febrile seizures treatment neither phenobarbital nor valproic acid were found to be effective.⁴⁵ However, in a more recent meta-analysis (1997) of randomized, placebo-controlled, published trials on prophylaxis for febrile seizures found that children receiving either phenobarbital or valproic acid had significantly lower risks of recurrence than placebo, while intermittent diazepam did not show significant advantage over placebo.⁴⁸

2. Adverse effects of AED therapy

Cognitive and behavioral side effects are mostly encountered during phenobarbital treatment. Available data suggest that 20% to 40% develop behavioral adverse effects (hyperactivity, irritability, sleep disorders) and a smaller proportion suffer from idiosyncratic reactions.⁸ Wolf et al (1981) compared phenobarbital treated children with children receiving no therapy on psychometric tests (Wechsler Preschool and Primary Scale of Intelligence WPPSI, the Matching Familiar Figures Test, and the Children's Embedded Figures Test). No significant differences were found on any scale at the initial evaluation or at the 3-month follow-up.⁶⁷ Farwell et al (1990) documented a decline in intellectual ability of children receiving phenobarbital. They noted an average of 7.03 IQ points lower in children receiving phenobarbital as compared to the placebo group after 2 years of treatment. Six months after stopping the medication the IQ was still 5.2 points lower in the phenobarbital-assigned group.²⁶ A continuation of the above study found that 3-5 years later, the difference in IQ was not significant. However, the phenobarbital group scored significantly lower on the reading achievement standard score of the Wide Range Achievement Test.⁵³ Hirtz et al (1993). studied the effect of phenobarbital on total sleep time and night awakenings and found that only a subset of predisposed children had significant increases in night awakenings due to phenobarbital as compared to placebo²⁸. In the study by Knudsen and Vestermarck (1978) side effects including irritability, hyperkinesias and listlessness were documented in 45% of the patients.³³ Herranz et al (1984) observed side effects in 76.7% of the phenobarbital treated patients (13.3% required drug discontinuation) and 45% of the valproate patients (14.3% required drug discontinuation).²⁷ Hyperactivity and sleep disturbances lead to discontinuation of phenobarbital in 21% of the patients in the study by Lee and Melchior (1981).³⁵ The study by Domizio et al (1993) compared children in the phenobarbital treated group with those treated with other AEDs with respect to side effects. In the phenobarbital group 76% had behavioral disturbances (most commonly

hyperactivity) as compared to 31 % in the other group.²⁰ According to the AAP practice parameter reduced performance while on therapy with phenobarbital has been documented.⁴⁶

The use of Valproic acid in the treatment of febrile seizures has been discouraged because of fears of life threatening liver toxicity in infants and children. It is specifically not recommended for routine use in children less than 3 years of age.⁸ Thrombocytopenia, pancreatitis, and weight disturbances are other adverse effects encountered with valproic acid treatment. In the treatment of febrile seizures, valproic acid has been shown to cause vomiting and altered appetite as well as increased activity.^{8,35}

In the study by Uhari et al (1995) 39% of the children on intermittent oral diazepam (0.3 mg/kg) had moderately severe side effects of somnolence and ataxia.⁵⁷ Rosman et al (1993) documented that 25-30% of the children on intermittent oral diazepam developed ataxia, lethargy, and irritability, and 5% had speech abnormalities, sleep disorders, and altered activity.⁵⁰ Furthermore, diazepam given at the time of febrile illness might mask an underlying infection by causing lethargy, which is usually attributed to the drug.⁸

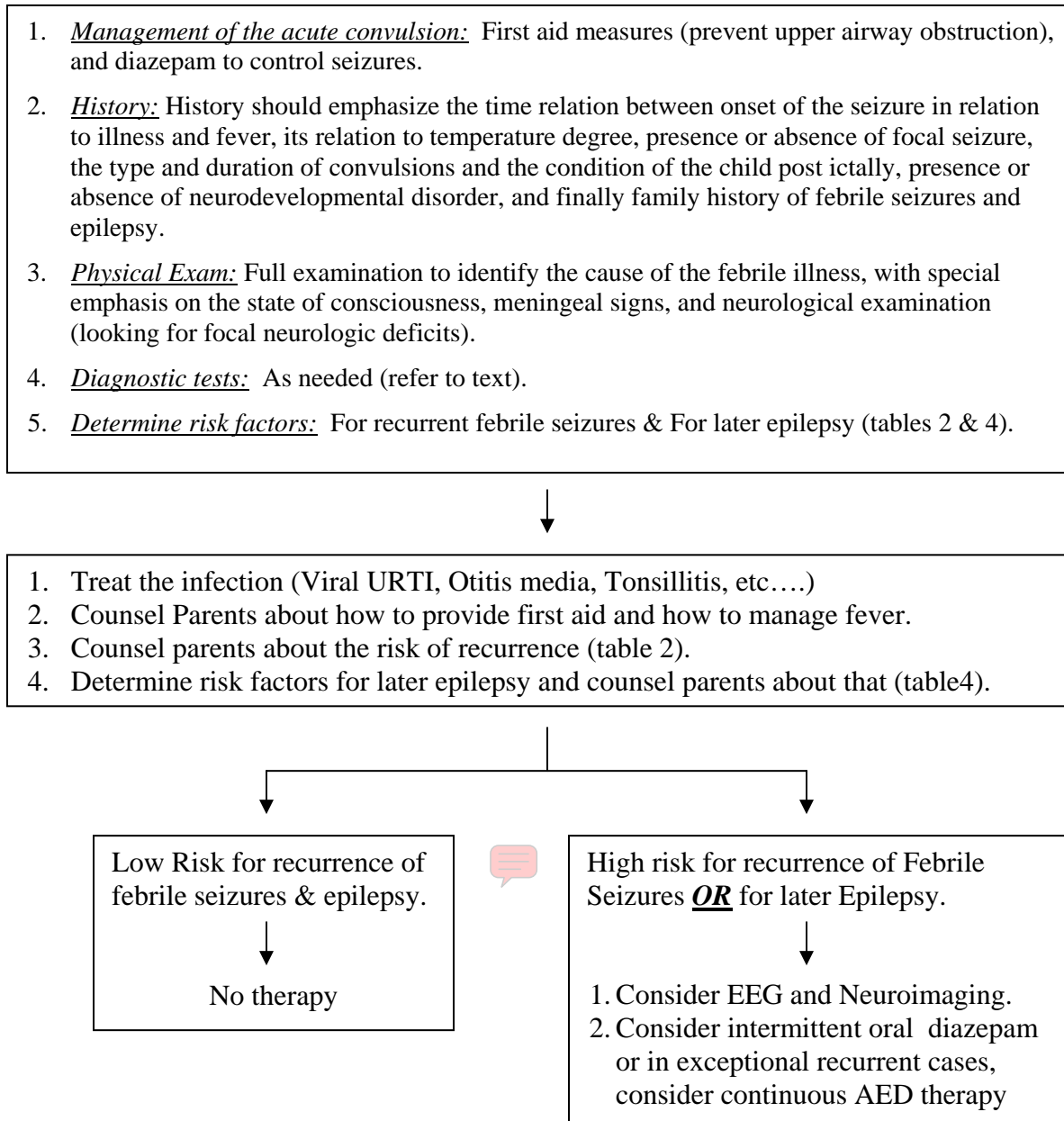
CONCLUSION

Febrile is a benign childhood disorder affecting 2-5% of children between 3 months to 5 years of age. They are either simple or complex. Their average relative risk of recurrence is about 30%. The risk of recurrence may increase or decrease in each individual child depending on prevalence and number of certain risk factors (Table1). The risk of developing epilepsy after febrile seizure is on the average 6%, but varies depending on the presence and number of risk factors in any given child (Table3).

The immediate treatment of febrile convulsion is summarized in [Figure 1](#) (next page). It includes first aid measures, with administration of IV or rectal diazepam. Febrile status epilepticus requires the use of additional medications such as IV Phenobarbital or long term AED therapy is not indicated in simple febrile seizures. In individual cases, intermittent diazepam treatment may be given during the febrile illness in children with high parental anxiety or in those cases with multiple risk factors for recurrent febrile seizures. The use of continuous Phenobarbital or valproic acid prophylaxis is limited to patients with complex febrile seizures or to those cases with multiple risk factors for development of future epilepsy.



Figure1. Febrile Seizures Management Algorithm (Mikati et al 2007).



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FAVOURABLE OUTCOME OF ADVANCED RENAL FAILURE IN AN ADOLESCENT WITH GOODPASTURE DISEASE: CASE REPORT

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Abstract

Goodpasture disease is the clinical entity of acute glomerulonephritis and pulmonary alveolar hemorrhage associated with antiglomerular basement membrane antibodies and with severe renal prognosis. This disease has rarely been reported in childhood and its treatment is controversial when advanced renal failure is initially diagnosed. This is a case of a 16 y.o. patient who was referred to us with a rapidly progressive advanced renal failure and a mild pulmonary hemorrhage. In spite of an initial serum creatinin level of more than 8 mg/dl, he was treated with corticosteroids, cyclophosphamide and plasma exchange and had a very good outcome.

GS = Goodpasture Syndrome; GBM = Glomerular basement membrane; WBC = White blood cells; BUN = Blood urea nitrogen; SGOT = Serum glutamic-oxaloacetic transaminase; SGPT = Serum glutamic-oxaloacetic transaminase; γ GT = Gamma glutamic transaminase; AgHbs = Hepatitis B surface antigen; HCV = Hepatitis B virus; CMV = Cytomegalovirus; EBV = Epstein-Barr virus; HIV = Human immunodeficiency virus; c-ANCA = Cytoplasm antineutrophil cytoplasmic antibodies; p-ANCA = Perinuclear antineutrophil cytoplasmic antibodies; C3 & C4 complements 3 & 4; IgG and IgA = Immunoglobulin G & A; ANA = Anti nuclear antibodies; anti-DNA = Anti deoxy-ribonuclear antibodies; ASO = Antistreptolysin A; RA = Rheumatoid arthritis factor; CT = Computerized tomography; ESRD = End stage renal disease; NC1 epitope = Non collagenous 1 epitope.

Introduction

Goodpasture syndrome (GS) is the clinical entity of acute glomerulonephritis and pulmonary alveolar hemorrhage that was first described by Ernest Goodpasture in 1919.

Goodpasture disease is the pulmonary renal syndrome specifically associated with antiglomerular basement membrane (GBM) antibodies. These anti-GBM antibodies produce a characteristic linear deposition along the GBM, which is one manner in which GS is differentiated from Wegener granulomatosis.^{1,2}

Fewer than 20 cases of immunologically confirmed cases of anti-GBM renal disease have been reported in children at all ages with a medium age of 16 and with no predilection in either sex.¹ But, in spite of the rarely described cases, this disease should be looked for in childhood when facing a pulmonary-renal syndrome.⁵

To avoid confusion between GS and Goodpasture disease, the term anti-GBM disease is used and because of the limited experience with the disease in children, much of the information presented in this article is derived from the literature about adults.

Rapid diagnosis of anti-GBM disease is mandatory using both the dosage of anti-GBM antibodies and renal biopsy. Treatment should be specific and rapid and consists in removing the pathogenic antibody with plasma exchange and

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preventing new antibody production with immunosuppression (corticosteroids / cyclophosphamide).^{1,2,4,7,8}

In this article, we report the case of an adolescent who presented with mild respiratory symptoms (hemoptysis and cough) but rapidly progressive advanced renal failure and who had an excellent response to immunosuppression and plasma exchange despite an initial creatinine of nearly 9mg/dl.

Case report

A 16-year-old patient was transferred to our university hospital for abdominal pain, cough, hemoptysis, fever, rapidly progressive renal failure and general weakness for three weeks. Initially, he had been treated with amoxicillin and clavulanic acid at home without improvement. He had no renal or pulmonary history, or any other medical problem. On day 11, he was admitted to a hospital where the initial laboratory findings showed:

WBC 16200/ μ l, hemoglobin 10.5 g/dl, hematocrit 31% and platelet count 330000/ μ l on complete blood counts, creatinine 2.1 mg/dl, albumin 4g/dl. Urinalysis showed: protein (1+), RBC >100/HPF and WBC 6-8/HPF. A urine culture and 3 blood cultures showed no growth. 24 hour urine collection revealed Proteinuria of 3.3g/24h and creatinine clearance 45 ml/min/1.73m². His BUN, electrolytes, calcium, phosphorus, magnesium, SGOT, SGPT, alkaline phosphatase, and LDH were normal. Chest X-ray, abdominal CT scan, abdominal ultrasound and esophago-gastro-duodenoscopy were normal.

Viral and immunological studies revealed: Negative AgHbs, anti-HCV, CMV, EBV, HIV1 and 2, and toxoplasmosis serologies. Positive ANA (1/100) but negative anti-DNA antibodies. Negative ASO, RA test, Coomb's (direct and indirect), Widal, Wright, Weil-Felix, cANCA and pANCA. Normal C3, C4 and IgA levels.

On the second hospital day the patient's renal function deteriorated with serum creatinine of 4.62 mg/dl, creatinine clearance was 18 ml/min/1.73m² and his proteinuria was 2.7 g/24h. He was receiving amoxicillin-clavulanic acid then ceftriaxone IV.

On day 18, because of the continuous rapid deterioration of his renal function, the patient was started on pulse methylprednisolone (500 mg the first 2 days then 750 mg for 1 day) along with cyclophosphamide 2 mg/kg/d.

On day 19, a percutaneous renal biopsy revealed only hypertrophic glomeruli with circumferential fibro-cellular crescents that compressed the glomerular tufts which were congestive and contained polymorphic leukocytes and a fibrinogen exudate. The basal membrane was thick and linear IgG and C3 deposition along the GBM was seen with immunofluorescence testing. His serum anti-GBM antibodies were positive (titers 2.4). During corticosteroid therapy, the patient didn't present any hemoptysis or epistaxis but had persisting fever with a progression of his renal failure.

On day 21, his renal function deteriorated further with a creatinine clearance of 4 ml/min.

Blood work-up showed: hemoglobin 9.4g/dl, hematocrit 27.4%, White blood cells 16700/ μ l, platelets 365000/ μ l, BUN 39.7mg/dl, creatinine 8.86 mg/dl, albumin 30 g/l, proteins 75 g/l, total cholesterol 3.64 mmol/l, triglyceride 2.6 mmol/l. Electrolytes, calcium, phosphorus, magnesium, glucose, SGPT, SGOT, γ GT, and bilirubin were normal. Since plasmapheresis was indicated but was not available in this primary hospital, the patient was then transferred to our hospital.

On admission, his blood pressure was 120/70, pulse rate 75/min and body temperature 36.5°C.

His physical exam was normal, particularly heart sounds were normal and lung fields were free of crackles bilaterally. He had no peripheral edema and his peripheral pulses were present and symmetrical. Anti-GBM antibodies were positive (1.1).

Pulse methylprednisolone was increased to 1g/d, the rest of the treatment was maintained and a series of 15 plasmapheresis sessions were performed on every other day basis with both plasma and albumin. On the second day the methylprednisolone was decreased to 250 mg/day, to 70 mg/day on the third day, and then it was discontinued and patient was put on oral Prednisone 1 mg/kg/day. The patient had a very good evolution: remained normotensive, had no respiratory symptoms, oliguria, peripheral edema or fever. He was transfused 3 times but no dialysis was performed. Finally the patient was discharged on cyclophosphamide 2 mg/kg/d and Prednisone 1 mg/kg/d, 4 weeks after admission. On discharge, his blood work-up showed: hemoglobin 10.3 g/dl, hematocrit 30.5%, WBC 15700/ μ l, platelets 199000/ μ l, BUN 1.3g/l. his serum creatinine had dramatically decreased to the level of 2.21 mg/dl. His anti-GBM antibodies were still positive but had decreased to the level of 0.4. His proteinuria was 1 g/l, and creatinine clearance had increased to 46 ml/min.

Discussion

Patients with anti-GBM disease may present with a spectrum of conditions ranging from pulmonary hemorrhage with minimal or no renal involvement to full-blown renal failure with limited or no pulmonary involvement. Our patient is a 16 year-old young man who presented to our university hospital with nearly all the features of anti-GBM disease:

1. Clinical features:

- Systemic illness: fever, malaise, headache, anorexia, nausea, and fatigue.
- Renal involvement: hematuria (but without oliguria or edema).
- Pulmonary involvement: cough, and hemoptysis

2. Biologic and serologic features:

- Anemia out of proportion to hemoptysis or renal failure (a hemoglobin level less than 12 mg/dl is observed in 90-100% of adults).
- Leukocytosis (about 40-50% of adults have a white blood cell (WBC) count of greater than 10,000/mm³. A leftward shift is common).
- Azotemia (occurs in 55-71% of adults with anti-GBM disease).
- Hematuria.
- Proteinuria (occurs in 76-100% of adults. Nephrotic syndrome is unusual).
- Erythrocyte sedimentation rate only mildly elevated (unlike in patients with vasculitis).
- Positive anti-GBM antibodies (elevated in more than 90%).
- Negative anti-DNA antibodies (but positive ANA antibodies).
- Normal ASO titers and complement studies.
- Negative ANCA titers (elevated in more than 10-40%; which eliminates the possibility of an association with a pauci-immune ANCA-associated rapidly progressive glomerulonephritis -like the Wegener granulomatosis- and is a negative prognostic factor).

3. Histologic features:

Linear IgG deposition along the glomerular capillary walls on the immunofluorescence portion of the renal biopsy is highly suggestive of the disease, especially in the setting of crescentic glomerulonephritis and linear C3 along the GBM is present in two thirds of biopsy samples.

Anti-GBM disease is a dangerous disease that can be life-threatening. Fulminant pulmonary hemorrhage, when present, can lead to respiratory failure, and is the main cause of death early in the course of the disease. The renal prognosis is poor; renal failure usually requires dialysis, and patients requiring dialysis at presentation usually go on to develop ESRD (fifty percent of patients require maintenance dialysis within 6 months of disease onset).^{1,2,6,13} According to the current literature about adults, the incidence of ESRD in anti-GBM disease is 25-69%. More recent reports indicate a better outcome with the aggressive use of plasma exchange. In the few pediatric cases of anti-GBM disease reported, approximately 90% of the children developed ESRD, and 3 died.¹

When facing a rapid increase of serum creatinine in the presence of an acute glomerulonephritis and a clinical history of hemoptysis, anemia or acute sinusitis, immunologic studies should be done. In case of normal complement level and positive anti-GBM antibodies, Goodpasture disease should be highly suspected and the patient should be urgently referred to a nephrology center, where a renal biopsy should be performed and starting pulse solumedrol with cyclophosphamide and then plasma exchange.^{1,2}

Table 1. Poor Prognostic Factors in Goodpasture Disease.

- Large crescents in more than 80% of the glomeruli (especially if fibrocellular or acellular)
- Initial serum creatinine level of more than 500 $\mu\text{mol/L}$ or GFR of less than 5 ml/min/1.73m² on presentation.
- Oliguria.
- Presence of anti-GBM antibody.
- Negative ANCA antibodies (10-40% of Anti-GBM antibody disease have positive ANCA findings and are considered to have a better prognosis because of their good response to immunosuppressive treatment).

Our patient had 4 out of 5 poor prognostic factors associated with Goodpasture disease (Table 1) (large crescents in more than 80% of the glomeruli, initial GFR of 4 ml/min, anti-GBM antibodies, and negative ANCA antibodies).

Before the advent of plasmapheresis, renal survival after plasmapheresis (with no need for dialysis or transplantation) was less than 25% in adults. Currently, intensive plasmapheresis, as in our patient, has been advocated as the treatment of choice in Goodpasture disease as it removes the circulating anti-GBM antibodies and other mediators of inflammation and it.

The combination of plasmapheresis with immunosuppression has been shown to be effective in the treatment of pulmonary hemorrhage and significantly improves renal function. Therapy usually consists of 14 plasma exchanges sessions during 2-3 weeks with concomitant administration of cyclophosphamide and steroids to prevent rebound antibody formation.^{1,2,4,7,8} Early diagnosis and treatment allow a better outcome.^{4,8,9,12}

Patients with advanced disease (serum creatinine level of >6-7 mg/dl and crescents in >75% of glomeruli) are thought unlikely to improve with any therapy and are spared the significant risks of aggressive treatment.^{1,2,8,13} Supportive care and, eventually, renal transplantation are recommended.^{1,2} But we believe as some other authors suggest that patients with the Goodpasture syndrome and severe renal failure should be considered for urgent immunosuppression therapy, including plasma exchange, to maximize the chance of renal recovery. Patients needing immediate dialysis are less likely to recover.^{1,2}

In our case and in spite of all the negative prognostic factors, the initial creatinine level above 8 mg/dl and the presence of crescents in 100% of the glomeruli, plasma exchange had a significant effect on the renal function when added to pulse methylprednisolone and cyclophosphamide and the patient was discharged from the hospital with a creatinine level of 2.21mg/dl, a creatinine clearance of 46ml/min, and did not require dialysis during his hospitalization.

Only the anti-GBM antibodies directed against the N-terminus of the NC1 epitope are the only antibodies correlated with the clinical prognosis of the disease and could be used both to diagnose and follow the progression of the disease but they were not available in our hospital so we only relied on the serum creatinine and electrolytes, and on the creatinine clearance to follow the progression of our patient's disease.

Conclusion

Pediatric form of Goodpasture disease is a rare entity with a life-threatening course sometimes and with a very poor renal prognosis especially with advanced renal failure on presentation. Diagnosis should be suspected when facing a rapidly progressive glomerulonephritis with a history of hemoptysis or cough and with positive anti-GBM antibodies. Treatment should be rapidly installed combining corticosteroids, cyclophosphamide and plasmapheresis. We recommend this treatment even with extremely high serum creatinine level on presentation.

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TEMPER TANTRUMS

MOHAMAD H. ITANI*

Tantrums are normal part of young children growing up process. When children feel frustrated, angry, or disappointed, they often express their emotions by crying, screaming, or stomping up and down. Parents often feel angry, helpless, or embarrassed from their child uncontrolled and “strong emotions”, that are hard for their young child to hold inside.

From the developmental point of view, temper tantrums teaches the child to master self-control of his feelings in response to the surrounding environmental reaction/s. Almost all children practice variable degrees of tantrums between the age of 1 and 3. "The terrible two's" is an English term used to describe that 2 years period sufferings, and the good news is that by age 4, temper tantrums usually stop.

ETIOLOGY

Toddlers are busy learning many things about their surrounding environment. They are eager to become independent and to have control on their environment (or at least to have control on their belongings). For that reason they always want to make their own choices but rarely succeed in that. On the other hand, they have limited ability to cope with, the resulting, frustrations and discover by instinct that crying and screaming that used to fulfill their basic needs of hunger, fear and love is a good strategy to follow in response to their daily frustrations. Controlling temper may be one of the most difficult lessons for the parents to learn, and for the pediatrician to teach.

PRECIPITATING FACTORS

The followings are some of the reasons that may precipitate temper tantrums particularly in toddlers:

- Limited language development that prevents parents from understanding what their child is saying.
- Limited language development in toddlers prevents them from using proper words to describe their feelings and needs of hunger, sleep, and stress. After 3 years of age, most children can express such feelings, so temper tantrums taper off. Children who are not able to express their feelings very well with words are more likely to continue to have tantrums.
- Limited cognitive development in toddlers prevent them from full understanding of what parents are saying or asking, and may get easily confused.
- Their limited cognitive development also prevents them from solving their problems on their own and get discouraged easily.
- Illnesses are common in toddlers, which make their temper fussy during illness and their tantrums easily provoked.
- Toddlers have profound attachments to objects as well as to care givers. Tantrums may be provoked as a reaction to stress to separation from mother, toy or changes at home.
- Toddlers are self centered and may get jealous easily of a friend or sibling. Children often want what other children

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have and even the attention others may receive, therefore parents should not try to tease their children by playing and loving other kids in their presence.

- Toddlers get frustrated easily if challenged with activities that are beyond their psychomotor developmental milestones i.e. do not force the child to walk, run or draw if he/she is not yet able to walk or run, climb down stairs or drawing things.

PREVENTION OF TANTRUMS

It is important to tell the parents that they will not be able to prevent all tantrums; however they can do much to decrease their severity and duration.

With close observation parents can tell the onset of temper tantrums: First; child seems moody, cranky, or difficult to manage, then he/she starts to whine and whimper and at finally he/she starts to cry, scream, stomp up and down, kick, fall to the ground, or hold his breath and looks as if nothing will make him/her happy. Other times, a tantrum may come on suddenly for no obvious reason.

Tantrums usually occur only in front of parents. This is one way in which the child tests family rules and limits. Many children will not act out their feelings around others and are more cautious with strangers. Children feel safer showing their feelings to the people they trust. The following suggestions may help parents in reducing frequency and severity of their child tantrums:

- **Do not tease or challenge your child** if he looks moody or fussy.
- **Encourage your child to use words to tell about his/her feelings.** On your behalf, try to understand how your child is feeling and suggest simple words that he/she can use to describe that feeling in future e.g. consistently tell the child when he has tantrum "you're acting *mad*".
- Set reasonable family limits and don't expect your child to be perfect. Always, **try to give simple reasons for the rules you set,** and don't frequently change those rules.
- Think carefully about the rules you set and don't set too many rules. **Discuss your rules with those who take care of your child** which rules are really needed and be firm about them.
- **Respond the same way every time your child breaks the rule.**
- Keep daily routine in the child life as much as possible, so your child knows what to expect.
- **Avoid situations that will frustrate the child,** such as playing with children or toys that are too advanced for his age and abilities.
- Avoid long outings or visits where your child has to sit still or can not play for long periods of time.
- If you have to make a trip, **take your child favorite book or toy to entertain your child on the way.**
- Prepare healthy snacks to give for your child when going long trips, hunger may precipitate tantrums easily.
- Make sure your child is well rested, especially before busy day or stressful activity.
- Direct your child to **avoid activities that are likely to lead to tantrum,** and suggest different activities.
- If possible, **change location, act silly, playful, or make a joke such acts can help to ease a tense situation.** Sometimes, something as simple as changing locations, changing the room, can prevent a tantrum e.g. if you are indoors, try taking your child outside to distract his attention.
- Many times, you will have to tell your child "No" to protect him/her from harm or injury e.g. the kitchen and bathroom can be hazardous places for your child. Preventing the child from playing in restricted areas is a common cause of tantrum. We advice to have your **home designed as "Childproof"** and to make dangerous areas or objects off his/her reach.
- You may feel guilty by continuously saying "No" to your child. Do not feel so, be consistent in your approach and try not to send mixed signals. When parents do not clearly enforce certain rules it becomes harder for the child to understand which rules are firm and which are not.
- **Be choosy about saying "No".** When you say no to every demand or request your child makes, you frustrates the child further.
- **Keep an eye on your child at all times, particularly after telling him/her "No".** Never leave your child alone in a situation that could be hazardous. Take away dangerous objects from your child immediately and **replace** them with something safe. It is up to you to keep your child safe and teach
- **Listen carefully to the child requests.** When a request is not too unreasonable or inconvenient, consider saying "Yes". When your child's safety is involved, do not change your decision because of your fear from his/her tantrum.

- **Let the child choose whenever possible** e.g. if your child resists a bath, make it clear that he will be taking a bath, but offer him an second simple complementary offer for which he can make his own decision e.g. Instead of saying, "Do you want to take a bath?" Try saying, "It's time for your bath. Would you like to walk to the bathroom or you prefer to have me carry you?"
- **Make sure to have fun with your child during the day.**
- **Set a good example for your child.** Avoid arguing or yelling in front of your child.
- Try to show your child how to protect him/herself from getting hurt. **Be consistent and clear about safety.**

DO NOT OFFER REWARDS

- Do not reward your child for stopping a tantrum. Rewards may teach the child that temper tantrums will help him/her to get things his/her way.
- When temper tantrums do not accomplish any thing for the child, they are unlikely to continue.

WHAT TO DO WHEN TANTRUMS OCCUR

Whenever a child develops temper tantrum, advice parents to follow the following suggestions:

1. Distract the child by calling his attention to something else, such as a new activity, book, or toy. Sometimes just touching or gently restrain or holding the child and stroking on his back will calm him/her. You may need to. Interrupt his/her behavior with a light comment like, "Did you see what the kitty is doing?" or "I think I heard the doorbell". Humor or something as simple as a funny face can also help.
2. Try to remain calm. If you shout or become angry, it is likely to make things worse. Remember, the more attention you give this behavior, the more likely it is to happen again.
3. Minor displays of anger such as crying, screaming, or kicking can usually be ignored. Stand nearby or hold your child without talking to him until he calms down. This shows your support to the child without reinforcing his behavior. If you cannot stay calm, leave the room.
4. Some temper tantrums cannot be ignored. The following behaviors should not be ignored and are *not* acceptable:
 - Hitting or kicking parents or others
 - Throwing things in a dangerous way
 - Prolonged screaming or yelling
5. Use a cooling-off period or a "time-out" to remove your child from the source of his anger. Take your child away from the situation and hold him or give him some time alone to calm down and regain control. For children old enough to understand, a good rule of thumb for a time-out is 1 minute of time for every year of your child's age. (For example, a 4 year old would get a 4-minute time-out.) but even 15 seconds will work. If you cannot stay calm, leave the room. Wait a minute or two, or until his crying stops, before returning. Then help him get interested in something else. If your child is old enough, talk about what happened and discuss other ways to deal with such episodes next time.
6. You should never punish your child for temper tantrums, for the fear of keeping his anger or frustration inside, which can be unhealthy. Your response to tantrums should be calm and understanding. As your child grows, he will learn to deal with his strong emotions. Remember, it is normal for children to test their parents' rules and limits every now and then.
7. For more information, check the American Academy of Pediatrics website www.aap.org parents corner.

WHEN TEMPER TANTRUMS ARE SERIOUS?

The child behavior between tantrums should be normal and healthy. Temper tantrums should decrease in frequency by the middle of the fourth year of life, after that age children usually outgrow these outbursts. However some children may take their time to learn how to control their temper and they do so at their own pace. However temper tantrums may be an early sign of emotional disturbances or a sign of associated cardiac or neurological disorder particularly if associated with fainting episodes (Table 1).

Table 1. Red Herrings in Temper Tantrums

- Severe or frequent episodes of anger may be early signs of emotional problems.
- Outbursts associated with self harm or injury.
- Outbursts associated with others harm or injury.
- Outbursts associated with breath holding and fainting episodes.
- Worsening of anger outbursts after the age of 4 years.

PEDIATRICIAN ROLE

Pediatricians should reassure parents about the benign nature of temper tantrums in toddlers and that tantrums are a way for the child to let off steam when he/she is upset.

The pediatrician should encourage parents to anticipate the tantrum episodes by identifying the precipitating event i.e. by keeping a record of the reason behind each tantrum episode, its duration, their response to that episode and its outcome and discuss those records during regular well child care visits.

The pediatrician should make sure that there are no serious physical or psychological problems causing the tantrums.

The pediatrician should give advice to help the parents on how to deal with their child anger outbursts. A good reference site for that is at www.lpswebsite.org at parent's corner where they may find instructions about temper tantrum management in *Arabic*, by pressing corresponding icon.

CONCLUSION

Tantrums are not easy to deal with, and they can be a little scary for the parents and the child. Using a loving and understanding approach will help the children and their parents through this critical period of development.

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THE ALERT: CURING CANCER IS NOT ENOUGH

THE ARTICLE: Chronic health conditions in adult survivors of childhood cancer. Oeffinger KC, Mertens AC, Sklar CA, et al.

THE SOURCE: N Engl J Med. 2006;355:1572-1582.

Due to continued success in the treatment of childhood cancer, approximately 80% of children diagnosed with cancer today will become long-term survivors.) This is a major medical achievement given the fact that prior to 1970 most childhood cancer was uniformly fatal. However, late effects from chemotherapy and radiation, especially cardiac dysfunction and secondary malignancies, have long been recognized as potential problems. Several excellent studies examining late mortality in childhood cancer survivors have been published; however, studies analyzing the long-term morbidity of childhood cancer survivors are lacking.

The Childhood Cancer Survivor Study is a large retrospective cohort study that follows patients diagnosed with childhood cancer between 1970 and 1986 and compares outcomes to those in a control cohort of siblings. Utilizing this cohort of 10,397 survivors and 3,034 siblings from 26 centers in North America, the authors report the frequency and relative risks of developing chronic health conditions following treatment for childhood cancer. Survivors and siblings had mean ages of 26.6 (range, 10.8 to 48.0) and 29.2 (range, 18.0-56.0) years, respectively. Among survivors, the cumulative incidence of a chronic health condition was 73.4% at 30 years after the cancer diagnosis. The cumulative incidence of a severe or life-threatening chronic health condition or death at 30 years after cancer diagnosis was 42.4%.

The adjusted relative risk for a chronic condition in a survivor as compared to a sibling was 3.3 (95% CI, 3.0-3.5) and for a severe or life-threatening condition it was 8.2 (95% CI, 6.9-9.7). The relative risks were greatest for cardiovascular disease, second malignancy, renal dysfunction, musculoskeletal problems, and endocrinopathies. Moreover, the incidence of these chronic conditions increased over time and did not appear to plateau. Patients with diagnoses of bone tumors, CNS tumors, or Hodgkin's disease had the highest relative risk for developing a chronic condition.

The authors conclude that survivors of childhood cancer have a high risk of developing chronic health conditions like cardiovascular disease, second malignancy, renal dysfunction, musculoskeletal problems, and endocrinopathies and therefore, require close monitoring as part of their routine health supervision.

THE ALERT: PREDICTING TREATMENT FAILURES IN KAWASAKI DISEASE.

THE ARTICLE: Prediction of intravenous immunoglobulin unresponsiveness in patients with Kawasaki disease. Kobayashi T, Inoue Y, Takeuchi K, et al.

THE SOURCE: Circulation. 2006;113:2606-2612.

Kawasaki Disease (KD) is one of the most common pediatric systemic vasculitides and is the leading cause of acquired heart disease during childhood in the US.

Most children will recover, but 15-25% will develop coronary artery abnormalities (CAA) if untreated, which places them at risk for myocardial infarction, sudden death, or ischemic heart disease. Treatment with intravenous immunoglobulin (IVIG) and aspirin greatly reduces the frequency of CAA (<5%) and usually causes a rapid defervescence and reduction of other signs of inflammation. However, 10-20% of treated KD patients will continue to have fever and other symptoms of KD. These IVIG non-responders have an increased risk for developing CAA (15% vs 0.2% of IVIG responders in this study; 12.2% vs 1.4% in another study). The authors from Gunma University and Takasaki University, Japan, carried out a retrospective analysis of 750 cases of KD patients treated from September 2000 to January 2006 at 13 medical institutions in 2 prefectures in Japan. The purpose of the analysis was to develop a model for predicting IVIG unresponsiveness.

Data on the study patients were divided into 2 datasets: the earlier (development) dataset (9/00-8/04, 546 patients) was used to develop a predictive model, while the later dataset (9/04-1/06, 204 patients) served as the validation dataset. Patients were excluded if they had evidence for another disease besides KD (such as a viral or bacterial infection), had atypical KD (did not have fever associated with at least 4 of the following symptoms: bilateral conjunctival injection, changes in the lips or oral cavity, cervical lymphadenopathy, polymorphous exanthem, or changes in the extremities), had CAA prior to MG treatment, or did not receive the full 2g/kg treatment of IVIG.

All patients were treated with Ig/kg/d of IVIG x 2 days along with aspirin (30mg/kg) and dipyridamole (2mg/kg x 2 days) to prevent blood clots. The aspirin dose was reduced to 5mg/kg per day after C-reactive protein normalized. IVIG non-response was defined as persistent fever that lasted more than 24 hours or recrudescence fever associated with KD symptoms after an afebrile period following IVIG treatment. No significant differences were found between the 2 datasets in terms of patient age (mean age 29.1 vs 28.4 months), sex (male sex 58% vs 50%), days of illness at initial treatment (mean 4.9 days vs 4.8 days), frequency of IVIG non-response (21 % in both), or frequency of CAA (8% vs 5%).

In univariate analysis, 10 laboratory variables were found to be significant predictors of IVIG non-responsiveness: the percentage of white blood cell representing neutrophils (% neutrophils), platelet count, total bilirubin, AST, ALT, sodium concentration, chloride concentration, total protein, albumin, and CRP. Stepwise forward logistic regression analysis was carried out on these 10 variables and the demographic variables of male gender, age in months, and days of illness at initial treatment. Sodium, % neutrophils, days of illness at initial treatment, AST, age, platelet count, and CRP were found to be independent predictors of IVIG non-responsiveness and were used to develop a risk scoring model. Both datasets were used to develop this simple scoring:

Sodium \leq 133 mmol/l	2 Points
Days of illness at initial treatment \leq 4	2 Points
AST \geq 100 IU/l	2 Points
% neutrophils \geq 80%	2 Points
CRP \geq 10mg/dl	1 Points
Age \leq 12 months	1 Points
Platelet count \leq 30 x 10 ⁴ mm ³	1 Points

The median score was 3, range 0 to 10. Low risk was defined as a score from 0 to 3, and included 56% of the patients; high risk was defined as \geq 4, and included 44% of the patients. Sensitivity and specificity were 86% and 68% with this scoring model. IVIG non-responsiveness was 5% in the low-risk group and 43% in the high-risk group; occurrence of CAA was 1 % in the low-risk group, 16% in the high - risk group. Risk factors had an additive effect i.e. patients with very high scores, \geq 7, had a 75% IVIG non-response rate and 36% CAA frequency.

THE ALERT: FLOURIDE, WHEN IS IT TOO MUCH OF A GOOD THING?

THE ARTICLE: Dose-effect relationship between drinking water fluoride levels and damage to liver and kidney functions in children. Xiong XZ, Liu FL, He WH, et al.

THE SOURCE: Environmental Research. 2006.

Researchers from Tongji Medical College in the People's Republic of China (PRC) evaluated the effects of fluoride in drinking water on liver and kidney function in children. Four areas in Henan Province with different levels of fluoride in drinking water were selected: 0.76 ppm (0.61-0.87), 1.47 ppm (1.1-2.0), 2.58 ppm (2.15-2.96), and 4.51 ppm (3.1-5.69). Dental fluorosis among the children was found to be 15%, 41 %, 79%, and 94%, respectively. Two hundred and ten children (age range 10-12 years) were placed into groups matched for age, sex, and nutrient status. The control group consisted of 30 children from the 0.76 ppm fluoride area. The test groups consisted of 60 children each from the 1.47 ppm, 2.58 ppm, and 4.51 ppm areas. Serum fluoride, total protein, albumin, AST, ALT, LDH and urine fluoride, Creatinine, NAG (N-acetyl- β -glucosaminidase), and GGT (γ -glutamyl transpeptidase) were determined from each child. NAG is a specific marker of proximal convoluted tubule (PCT) function and has been studied in fluoride nephrotoxicity. GGT is found in high concentration in the liver, bile ducts, and kidney.

Fluoride levels in serum and urine increased as the levels of drinking water fluoride increased. There were no significant differences in the levels of total protein, albumin, AST, or ALT among the groups. However, serum LDH, urine NAG, and urine GGT were significantly higher among children from the area with the highest level of water fluoride compared to control children.

The authors conclude that water fluoride levels above 2.0 ppm may cause damage to liver and kidney function in children.

THE ALERT: IRON & COGNITION, PROFOUND IMPACT OF A SIMPLE THERAPY.

THE ARTICLE: Double burden of iron deficiency in infancy and low socioeconomic status. Lozoff B, Jimenez E, Smith JE.

THE SOURCE: Arch Pediatr Adolesc Med. 2006;160:1108-1113.

Iron deficiency anemia or other forms of severe iron deficiency have consistently been shown to affect cognitive function in children from all parts of the world. The effect on IQ has been estimated as a decrease of 1.7 points for each 1.0 g/dL decrease in hemoglobin. In this study, investigators from the University of Michigan ; Oakland University, Rochester, Mich; and Hospital Nacional de Niños, San Jose, Costa Rica, evaluated long-term follow-up data on 185 individuals from a middle- and lower-class urban community in Costa Rica. These study participants had been the products of full-term pregnancies, had been free of acute or chronic medical problems, and were enrolled between 12 and 23 months of age. Abnormal iron status in infancy was assessed by venous concentrations of hemoglobin (≤ 12 g/dL), transferrin saturation ($<10\%$), erythrocyte protoporphyrin (≥ 100 mcg/dL), and serum ferritin (<12 ngL mL). Chronic iron deficiency was defined as a hemoglobin concentration ≤ 10 g/dL or higher hemoglobin concentrations that did not fully correct after 3 months of treatment. Anemia resolved in all children within 3 months of treatment. At the 4 follow-up evaluations at 5, 11-14, 15-18, and 19 years, less than 5% of the subjects had evidence of iron deficiency. Trained Costa Rican psychologists blinded to the participants' hemoglobin status performed the cognitive assessments. The validated instruments included the Mental Development Index of the Bayley Scales of Infant Development, The Wechsler Preschool and Primary Scale of Intelligence, and Wechsler Intelligence Scale for Adults, and testing was done at enrollment and at each of the 4 follow-up periods. Seventy-eight percent of patients were available for evaluation at 18 or 19 years after receiving iron therapy.

The most important finding of this study was that there was no evidence of catch-up in cognitive test performance for individuals with chronic iron deficiency in infancy and that the gap in cognitive scores continued to increase for children from low socioeconomic status (SES) families. The difference in cognitive scores averaged between 8 and 9 points between children with good iron status and those with chronic deficiency. The investigators also determined that chronic iron deficiency was found in a higher proportion of males and those of low SES, as has been reported in earlier studies.

THE ALERT: VIRAL INFECTIONS IN THE ETIOLOGY OF FEBRILE SEIZURES

THE ARTICLE: Role of viral infections in the etiology of febrile seizures. Millichap JG, Millichap Jj.

THE SOURCE: *Pediatr Neurol.* 2006;35:165-172.

The role of viral infections and fever in the etiology and mechanism of febrile seizures is reviewed by researchers at Children's Memorial Hospital, Chicago, Ill; and East Carolina University Brody School of Medicine, Greenville, NC. In a previous review of studies published between 1924-1964, except for roseola infantum that was reported in 128 (4%) of 3168 patients, viral infection as a cause of febrile seizures was rarely diagnosed. However, in reports published since 1995, primary human herpesvirus (HHV)-6 was detected in 101 (24%) of 416 patients with febrile seizures <3 years of age; and of 902 children <3 years of age with primary HHV-6 infection and fever, 149 (16.5%) had a seizure. A geographic variation in incidence and lesser role for HHV-6 infection in the etiology of febrile seizures is reported in Asia compared with the US and Canada. In Asia, influenza A is the most frequent cause.²

HHV-6 infection with seizure is associated with a higher body temperature than a seizure in patients without HHV-6 infection, and the degree of fever has been invoked as the essential convulsive trigger. Other postulated factors include a specific invasive property of HHV-6 virus or reactivation of the virus to infect neural tissue (neurotropism) and/or the CNS. HHV-6 DNA was detected by polymerase chain reaction in 2 of 7 CSF samples tested in a prospective study,³ and in a total of 20 (14.5%) of 138 samples collected in 10 studies. Pleocytosis in the CSF was noted in only 2 (2.5%) of 79 patients tested. Evidence for a direct viral invasion of the CNS due to HHV-6 causing an encephalitic process associated with febrile seizures is inconclusive. By definition, the diagnosis of a febrile seizure excludes infections that cause seizures by primary involvement of the brain, but complex febrile seizures (defined as febrile seizures lasting >15 minutes, focal seizures, or the presence of repeated seizures in a 24-hour period) may have a different mechanism from the simple type, and may be difficult to differentiate from an encephalopathy.

The essential mechanism of viral infections in the etiology of febrile seizures is the degree of fever. A threshold convulsive temperature, varying with the individual, the virus, and dependent on genetic and environmental factors, is

modified by age, cerebral maturation, and metabolic changes associated with fever. References to viral neurotropism and viral reactivation as etiological factors and cytokine responses as indicators of disease severity deserve further investigation.

THE ALERT: FIVE FINDINGS HELP PREDICT LOW RISK FOR BACTERIAL MENINGITIS.

THE ARTICLE: Clinical prediction rule for identifying children with cerebrospinal fluid pleocytosis at very low risk of bacterial meningitis. Nigrovic LE, Kuppermann N, Macias CG, et al.

THE SOURCE: JAMA. 2007;297:52-60.

Investigators from the Pediatric Emergency Medicine Collaborative Research Committee of the AAP report a multi-center, retrospective study to validate the previously reported Bacterial Meningitis Score (BMS), a clinical prediction rule to identify patients at low risk of bacterial meningitis based on 5 variables: positive cerebrospinal fluid (CSF) Gram stain, CSF absolute neutrophil count (ANC) ≥ 1000 cells/ μL , CSF protein ≥ 80 mg/dL, peripheral blood ANC $\geq 10,000$ cells/ μL , and history of seizures at the time of presentation. The group consisted of investigators from 20 centers (17 free-standing pediatric centers and 3 general emergency departments). These centers evaluate over 1 million children every year. Medical records of all children between the ages of 29 days and 19 years seen at these centers between January 1, 2001 and June 30, 2004, with a diagnosis of meningitis were reviewed. Children were included in the study if they had a lumbar puncture in one of the emergency departments of the 20 centers and had either CSF pleocytosis (defined as ≥ 10 white blood cells/ μL corrected for presence of red blood cells at a ratio of 1:500 compared to the peripheral blood) or a CSF culture yielding a bacterial pathogen. Bacterial meningitis was defined as a positive CSF culture or CSF pleocytosis associated with either a positive blood or a positive latex agglutination test for a bacterial pathogen. Children were excluded if they required hospital admission for reasons other than the risk of meningitis (eg, critical condition, presence of purpura, presence of a ventricular shunt, active Lyme disease), or if they were treated with antibiotics in the 72 hours prior to lumbar puncture.

Of the 4369 patients identified with meningitis 3295 met the inclusion criteria. One hundred and twenty-one (3.7%; 95% CI, 3.1-4.4%) had bacterial meningitis and the remaining 3174 (96.3%; 95% CI, 95.5-96.9%) had aseptic meningitis. All patients with bacterial meningitis and 2518 (80%) with aseptic meningitis were admitted to the hospital. Due to missing data in 392, the BMS could only be calculated for 2903 (88%) patients. Among these patients the frequency of bacterial meningitis increased with an increasing number of BMS risk factors: the risk of meningitis was 0.1% when no risk factors were present, 3% with 1 risk factor, 27% with 2 risk factors, 70% with 3 risk factors, and 95% with ≥ 4 risk factors. All BMS risk factors were significantly associated with meningitis, with Gram stain most strongly associated. Only 2 (0.1%) of 1714 patients defined as very low risk by the BMS (no risk factors) had meningitis (negative predictive value 99.9%; 95% CI, 99.6-100%); both of these patients were 1 to 2 months of age and had E coli meningitis. Of the 1189 determined not to be very low risk, 119 (10%) had bacterial meningitis. The sensitivity of the BMS for bacterial meningitis was 98.3% (95% CI, 94.2-99.8%), the specificity 61.5% (95% CI, 59.7-63.3%), the positive likelihood ratio 2.56 (95% CI, 2.43-2.69), and the negative likelihood ratio 0.03 (95% CI, 0.01-0.11).