# Refractory Fever In The Down Syndrome Child Due To Lag Of Temperature Regulatory Center

H Saba, Y Elshimali

**Citation**

H Saba, Y Elshimali. *Refractory Fever In The Down Syndrome Child Due To Lag Of Temperature Regulatory Center*. The Internet Journal of Pediatrics and Neonatology. 2008 Volume 9 Number 2.

**Abstract**

This is a case report of an unexplained fever in a child with Down Syndrome (DS) who went through a complete fever work up and no cause for the fever was found. The fever persisted and was refractory to all antipyretics; no antibiotics were used in the management of this case. The fever was responding only to ambient temperature accommodations, e.g., cooling the patient's environment and placing the child in bath-tub.
This is the first case report that approaches the management of refractory, constant and unexplained fever in Down Syndrome patients.

## INTRODUCTION

When unexplained fever persists, it is referred to as a fever of unknown origin (FUO). This condition is defined by the presence of a fever greater than 38.3°C (101 °F) “off and on” for more than three weeks (one week in infants). The specific cause for the fever is not identified ([2]).

This is a 12 year follow up on a case of refractory fever in a Down Syndrome child who responded perfectly to ambient modification of environmental temperature.

Unexplained fever in Down Syndrome babies has been reported in the literature ([1]) and it is considered to be a very frustrating clinical issue for pediatricians as well as the child's family.

It is very important to keep in mind that no fever of pathologic origin (infection, cancer, chronic disease, or drug fever) will disappear by just controlling environmental air without using an antipyretic, an antibiotic or any other kind of medicines. In case such as this we have to consider the disturbance of the patient's central regulation of body temperature.

## PATIENT PRESENTATION

This is a Down Syndrome patient who was born in May, 1996. At age of one month, a fever of 38.4 C was observed without any evidence of clinical illness. A thorough physical examination indicated a typical DS baby with most of the morphologic clinical features of the syndrome being present.

Laboratory tests were performed and showed that the Complete blood count (CBC) with Differential, C reactive protein (CRP), urinalysis and specific gravity were all within normal limits. Erythrocyte sedimentation rate (ESR) was not elevated. Urine Culture showed no growth after 72 hours and blood Culture showed no growth after 7 days (aerobic and anaerobic). All components of Blood Film were normal with no premature elements. The Electrolytes were: Na 138, K 4.1, Cl 100, Ca 9, and bicarbonate 22. Glucose level: 95 mg/dl. Widal test and Write Test, ALT and AST were all in the normal range.

Cerebrospinal fluid (CSF) Exam & culture were negative; and meningitis was ruled out. Chest X Ray films were unremarkable.

The baby's fever started in the beginning of summer and rose gradually in correlation to the weather getting hotter (more than 30 C indoor room temperature during the months of June, July and August).

The baby's temperature increased to reach 39 C and then to 39.5 C, and finally to 40 C in the hottest weather (32 – 33 C indoor room temperature). The lab work noted above was repeated and additional tests were done. The Peripheral Blood Smear showed no blasts and no left shift. Uric Acid was normal. IgG & IgM for CMV were negative.

TSH, T4, FT3 were within normal limits. Specific gravity of the urine ranged between 1.005–1.030 according to hydration status.

The fever was persistent and refractory to antipyretics like acetaminophen and Ibuprofen; it appeared to respond only to ambient temperature accommodation. The temperature declined to 37 C and remained in this area as long as the ambient temperature conditioning was controlled. However, the fever could recur within one hour after returning to the hot atmosphere.

The baby appeared content when his temperature was normal (37 C) but used to groan continually when he had a high temperature.

This condition persisted during August and September but declined with the drop of atmospheric temperature in October and the following months.

During autumn, winter, and spring his temperature remained within the normal limits. However, the fever recurred again during the summer of 1997 but with lower grades (not exceeding 39 C) and responded to air conditioning.

During the summer of 1998, it recurred again with lower grades (38 C) and eventually it went back to normal and stayed normal then after.

The boy is now 12 years old, doing fine, getting fevers during common illnesses, but prefers cold climates year round.

## DISCUSSION

First of all, obtaining a good clinical history is very important in febrile babies with Down Syndrome. In addition to the common causes of fever (infection, cancer, chronic diseases, dehydration, etc.), it is important to keep in mind that the fever might be a reaction to antibiotics (drug fever); the discontinuation the antibiotics might resolve the case ($_3$). However, no antibiotics or any other drugs were given to this patient (except for acetaminophen or Ibuprofen occasionally with no response) and the prospect of fever was ruled out. Fever due to dehydration from hot weather or decreased fluids was ruled out due to giving enough oral fluids (water and milk). Plasma electrolytes (Na, K) plus specific gravity of the urine were normal on repetitive titrations, and no dehydration was noticed, so Nephrogenic Diabetes Insipidus could be ruled out. No masses or lymphadenopathy were identified and since the peripheral smear was normal, the lymphoma, leukemia and other malignancies were ruled out; there was no need for bone marrow biopsy.

On the physical exam, along with thorough observation of sweating and other autonomic functions, congenital malformations (like Riley Day syndrome, and ectodermal dysplasia) were excluded.

Due to the risk of developing hypothyroidism in DS children, titration of TSH Yearly was done. It stayed normal until age 7 when it started to rise (more than 100 units \ l) suggesting secondary hypothyroidism, which is expected in DS children. The child was put on Eltroxine, established control, and eventually the hyperthyroidism was ruled out.

It should be noted that a hypothalamic abnormality could not be ruled out because MRI scanning was not available that time (1996). It could be a possible cause for lack of body temperature regulation and it is recommended to do MRI as scanning test in the future. However, if this abnormality existed, it would have had a temporary effect and be resolved in time.

Fevers do not typically decline after one hour of air conditioning, repeatedly. A fever due to weather condition could be the diagnosis of exclusion in countries that have appropriate and widely distributed cooling facilities. But in poor countries, especially these in Africa, Asia and Middle East; it is vitally important to consider this cause of refractory fever in Down Syndrome babies and to observe the child fever under different room temperatures. By following this step, the time, the cost and the effort will result in enhanced treatment.

In this case, conditioning ambient atmosphere (24 – 25 C in room temperature) was very effective in decreasing and maintaining the baby's temperature around 37 C. After age of 3 years, a stable condition was achieved and the child became able to regulate body temperature even in hot weather like other children. He became afebrile and stayed so through this long follow up (12 years).

Taking into consideration that Down Syndrome is the most common chromosomal disease in any society and that the published data about refractory fever in Down's is rarely reported, this will be the first case about the management of unknown fever in a Down Syndrome baby. As noted above, this is most likely due to delay in maturation of the regulatory center of temperature in the hypothalamus which results in lack of accommodation and adaptation to hot temperature.

No reports or reference about autonomic regulation disturbances in children with Trisomy 21 have yet been reported.

In conclusion, the best description for this condition would be to call it seasonal fever or hot weather fever which can be distinguished from any other kind of fever which doesn't respond to atmosphere accommodation or respond to antipyretics, regardless of the season.

This identified pattern was noticed in three more babies with Down Syndrome with reported fevers of (38.5- 41) C with no evidence of clinical illness. Interestingly, these cases were handled similarly to the above reported case. All responded to ambient temperature accommodation like being placed in the bath-tub and controlling air temperature. No antibiotics were used in any of these cases with the outcome being very satisfactory. Follow up for 6 years on one of these cases showed a favorable outcome.

At this point, we are not aware of the incident of “seasonal” fever in other syndromes than Down's. Further observation and clinical follow up to unknown fever in other chromosomal, genetic or metabolic diseases will add more value to the understanding of fever that responds only to external modification of environmental temperature.

## CORRESPONDENCE TO

Hazar I. Saba, MD.
Department of Pediatrics
Al-Basel Hospital, Tartus, Syria.
Email: hazarsaba@gmail.com
Phone: 00963 - 944 - 648958

### References

1. Leal Hernández M, Abellán Alemán J, Martínez Crespo J, Vicente Martínez R.
Unexplained fever in patient with Down's syndr: Aten Primaria. 2001 Jun 30;28(2):141-3.
2. MedicineNet.com, http://www.medicinenet.com/script/main/art.asp?articlekey=53595.
3. Nakajima W, Ishida A, Takahashi M, Sato Y, Ito T, Takada G.
Aseptic meningitis associated with cephalosporins in an infant with trisomy 21.
J Child Neurol. 2007 Jun;22(6):780-2.

## Author Information

**Hazar I. Saba, MD**
Staff Pediatrician, Department of Pediatrics, Children Hospital, Damascus University and Al-Basel Hospital

**Yahya I. Elshimali, MD**
Assistant professor of Pathology, University of California & Charles Drew University For Sciences And Medicine