

Thousand Faces of Mastocytosis: Mistaken Medical Diagnoses, Patient Suffering & Gender Implications

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The goals of this paper are to help a larger circle of medical professionals by creating greater awareness of Mastocytosis. Our focus is on the complexity and seriousness of the symptoms, and medical tests which are helpful in diagnosis. We include first hand experiences from 12 Mastocytosis patients who are long-term sufferers of this elusive but cruel malady. Finally, we will make recommendations to the medical community, as well as the Mastocytosis sufferers, about how to recognize and live with this disease. It is our sincere hope that our participants' struggles and their experiences with Mastocytosis, as well as with their medical professionals, will improve the diagnostic process for Mastocytosis. It is also our sincere hope that the possible gender biases in dealing with female patients will be reduced or eradicated in the face of a plethora of Mastocytosis symptoms. It is not blame we seek, and we certainly do not wish to point fingers. Our aim is the creation of more accessible knowledge, faster diagnosis, mutual respect between patients and caregivers, and better ways of dealing with this frightening disorder.

In this paper, we are going to explore the many faces of a very rare and serious disease called Mastocytosis. Because of the lack of

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clarity in the causes, symptoms, triggers, and because of its multifaceted manifestations and progression, Mastocytosis is a disease that is exceptionally hard to diagnose. Patients who suffer from a myriad of symptoms usually go from doctor to doctor, without reaching a definitive diagnosis. According to patient revelations at Canada Mastocytosis Support², accurate diagnosis takes extraordinary vigilance on the patients' part, but even then, may take anywhere from two to 10+ years. It is possible that many patients never get an accurate diagnosis, and may live their lives wondering what ails them. The debilitating symptoms of Mastocytosis deprive patients of quality of life. Mastocytosis can ruin careers, lead to lost relationships, and often curtails the most basic life activities. Some patients even confess to having contemplated suicide as a way out of their suffering. For all these reasons, patients believe in the importance of early diagnosis. Continuation of symptoms, left untreated, will usually worsen and over time, may become disabling. Prompt diagnosis is also of importance to limit the severe reactions as the disease progresses (Metcalfe, 2008).

Mastocytosis patients who have access to good quality and universal healthcare coverage may be shuttled from physician to physician, from specialist to specialist, in their search for finding an answer. Despite comprehensive healthcare coverage, affected individuals still have to deal with the emotional drain, increasing anxiety and frustration because of their negative experiences with symptoms as well as the frequent lack of help from medical professionals. Those who do not have healthcare coverage, and/or live in remote areas may be worse off. They will be trapped in expensive doctors' visits, hospital procedures and other haphazard medical interventions, while enduring possibly life-threatening ailments. In sum, although knowing one has a serious chronic disease such as Mastocytosis is frightening, nothing is more frightening than being very sick but not knowing why. The lives of undiagnosed Mastocytosis patients exist in a state of suffering and lifestyle limitations.

To complicate matters, the responses of the medical professionals may be gendered. As in cases of heart disease, although men's symptoms often generate a quick and accurate diagnosis and intervention, women's symptoms may be interpreted in much more skeptical ways. Women with a plethora of Mastocytosis symptoms that mimic anxiety and depression often have a harder time convincing their doctors to think out of the gendered-box. It is possible that the seriousness of their condition may be overlooked, as physicians who are

² Please visit Canada Mastocytosis Support at <http://cmsadmin.proboards.com/> for up-to-date information on Mastocytosis.

unfamiliar with this rare disease brush them off, or shift them to yet another fruitless path of investigative exploration.

Manifestations of Mastocytosis

Mastocytosis is a rare and mostly unknown disorder, or more correctly, it is a group of diseases (Krishnan & Smith, 2008; Horney, Sotlar & Valent, 2007; Mastocytosis, ND.; Robyn & Metcalfe, 2006). The first pathologically documented case of Mastocytosis dates back to 1869, as discovered by Nettleship and Tay (cited in Tay & Giam, 1993). Mastocytosis is considered an orphan disease or rare disorder, as it is estimated that Mastocytosis afflicts about one in 500,000 people in the mostly developed countries probably because these cases have been identified. How frequently it manifests itself throughout the developing regions of the world is unknown. However, many patients believe it is much more common and the problem is that many people suffer without a definitive diagnosis. Interestingly, since 1994, medical research suggests that Mastocytosis has been disproportionately diagnosed in 'white' persons (Almahroos & Kurban, 2003; Medina et al., 1994). However, in 2009, it is not known whether people of colour are less likely to get the disease, or more likely, it is even harder to diagnose the disease in people of colour. Moreover, there are many varieties of Mastocytosis, which make it into a collection of mast cell disorders, and a nightmare to diagnose. Some cutaneous types manifest in skin lesions such as urticaria pigmentosa³, mastocytoma, or Telangiectasia Macularis Eruptiva Perstans (Hermine et al, 2008; Soter, 2000, 1991).

Urticaria pigmentosa presents as dark spots that are associated with hive like swelling, have an increased number of cutaneous mast cells, and release histamine readily from minor stimuli to create systemic flushing symptoms. The mastocytoma is a more localized solitary collection of increased mast cells in the skin that can swell and release histamine readily. Telangiectasia Macularis Eruptiva Perstans (TMEP) is a skin predominant form of mast cell disease with small blood vessel proliferation (a reactive phenomena from persistent redness) that leads to increasing flushing symptoms with time.

Systemic forms of Mastocytosis create health problems related to liver, spleen, gastrointestinal tract, respiratory system, lymph nodes, bone structure/density and cognitive functioning. For example, a basic review of PubMed online returns new research articles proving that osteoporosis is an additional concern for mastocytosis patients. The concerns about bone density and bone health in general were addressed during the 2005 TMS Panel Discussion by Drs. Castells, Theoharides, and

³ Urticaria (hives) are raised, often itchy, red welts on the surface of the skin. They are usually allergic reaction to food or medicine (Healthline/hives, ND).

Butterfield (2005 TMS California Conference). Moreover, some patients develop osteosclerosis (Johansson et al., 1996). Some cutaneous Mastocytosis subtypes do not manifest systemic ailments, while some systemic variants of Mastocytosis do not involve skin complications. But most Mastocytosis patients—at least, those who have succeeded in getting a correct diagnosis—suffer from numerous disabling experiences (Hermine et al., 2008). In severe cases, extreme fatigue, cognitive dysfunction, bone pain, bone degeneration and loss, severe flushing and anaphylaxis are just a few of the serious complications which interfere with patients' lives (2005 TMS California Conference; Hermine et al., 2008; Robyn & Metcalfe, 2006).

The World Health Organization (WHO) has classified Mastocytosis as follows:

- Cutaneous Mastocytosis (CM)
- Indolent Systemic Mastocytosis (ISM)
- Systemic Mastocytosis with an associated clonal hematologic non mast cell lineage disease (SM-AHNMD)
- Aggressive Systemic Mastocytosis (ASM)
- Mast Cell Leukemia (MCL)
- Mast Cell Sarcoma
- Extra-cutaneous Mastocytoma

In general indolent types of Mastocytosis remain indolent and aggressive types progress with increasing severity of symptoms. However, in rare cases, transition from milder forms to much more aggressive forms including mast cell leukemia have been recorded (Brockow et al., 2003; Krishnan & Smith, 2008; Medina et al., 1994; Metcalfe, 2008).

Those patients with visible rashes on the skin typically find the diagnostic process easier, while those who do not have visible signs outwardly, but have systemic manifestations have the greatest diagnostic difficulty. There are also many reports of patients who have coexisting cutaneous and Systemic Mastocytosis.

Mast cells, produced in the bone marrow, are an important and necessary product for the blood generation/renewal system. Every person has some mast cells in their blood, and it is the opinion of the medical community that they function as part of the immune system (2005 TMS California Conference; Hermine et al., 2008; Metcalfe, 2008). They are important as a defense against parasites and bacteria (Mediana et al., 1994). For example, an experimental study on mice has shown the importance of mast cells. A group of mice with mast cells in their bloodstream, and a control group without mast cells were injected with equal amounts of *E-Coli* bacteria. The group with mast cells got very sick,

but somehow survived. The group which had no mast cells to begin with all died (2005 TMS California Conference). This suggests that, by concentrating in the area of the bacterial insult, mast cells may trigger other positive immunological responses in the body. However, and unfortunately, in most (but not all) Mastocytosis patients, there is an over-production and concentrated presence of mast cells in the blood stream, in organ tissues and/or in the bones. Moreover, in Mastocytosis patients, the profusion of mast cells behaves in unpredictable and undesirable ways (2005 TMS California Conference; Krishnan & Smith, 2008; Van Auken, 2006). In addition, the mast cells in about 98% of the patients are mutated (2007 TMS Houston Conference). Dr. Cem Akin from the University of Michigan, who is a leading expert/researcher in mast cell diseases, suggests that over-production of mutated mast cells is a *cancer-like*, or a neoplastic condition (University of Michigan, 2004).

The worldwide medical community opinions differ about the etiology of the Mastocytosis symptoms. One North American theory postulates that an inordinate over-production of mast cells is the culprit. Medical research demonstrating the irregularly shaped mast cells in patients supports this theory. However, the French association for the Initiatives of Research on Mastocytosis (AFFIRM, 2008) posits that it is actually the amount and location of mast cell degranulation which causes the damaging symptoms of Mastocytosis. More research is needed to clarify this incongruence.

Everyone has mast cells and these cells play an important role in our immune systems. However, people who have Mastocytosis, experience health problems due to an undesirable behaviour of mast cells called 'degranulation.' Due to a known or unknown trigger, a profusion of mast cells simultaneously burst open in an effort to protect the body, dumping histamine and other chemicals in massive amounts. Mastocytosis patients' symptoms arise from this degranulation, which leaks fluid into the connective tissue spaces between cells (Van Auken, 2006; 2005 TMS California Conference), even when there is no legitimate external trauma or irritant/parasite in the body. In this regard, Mastocytosis resembles allergic reactions, but the triggers of degranulation are many and often ambiguous (Mastokids, 2007a). Culprits of degranulation can include food substances, exercise, heat, cold, friction, dyes, medications, moulds, odours, chemical substances and other, normally benign environmental prompts (Mastokids, 2007a). It is interesting to note that the vast majority of Mastocytosis patients do not show reactions to many routine allergy tests, until and unless they are also tested for an exaggerated response to histamine. Yet, like severe allergy sufferers, Mastocytosis patients often have high blood tryptase levels (over 20ng/ml), as if they are suffering from chronic allergies (Hermine et al., 2008; Payne & Kam, 2004; TMS, 2007). When

degranulation is concentrated in the skin, the post inflammatory stage results in hyperpigmented residual from the urticarial reactions, or the uncommon reactive small blood vessels (TMEP) as a result of persistent flushing.

Urticaria pigmentosa (UP) can range from slightly brownish spots flush on the skin to angry red and garnet-coloured welts that are scattered or raised wheal on the skin. If these lesions are scratched, they bloom (elevate) and become angrier, justifying the Latin name they have been given (urticaria = itchy/scratchy). This reaction is called Darier's Sign, as it was discovered and named by a French dermatologist Ferdinand-Jean Darier. Once these lesions appear in adults, there is only a 10% chance that they will ever go away (Brockow et al., 2002; Medina et al., 1994). So, over time, urticaria has a tendency to multiply and spread into different parts of the body, and it is suggested that the profusion of UP is correlated with the clinical patterns of the disease (Brockow et al., 2002). It is rare, but not impossible that the skin lesions reach the visible parts of the body, such as the hands and the face. If and when they do, patients, especially women, become highly self-conscious. Unlike adults, urticaria in young children has a 50% chance of regression or spontaneous recovery (Brockow et al., 2002; 2003; Hermine et al., 2008). The TMEP lesions range in colour from tan to red or brown and they are splotchy in appearance. These lesions darken over time, becoming more unsightly than when they first appeared. As with UP, scratching when the lesions itch can cause further degranulation, resulting in even more lesions. Rarely, TMEP lesions will produce elevated urticarial wheals and flat red flares. Darier's sign is a common secondary presentation amongst all forms of cutaneous Mastocytosis. As TMEP is the rarest cutaneous form of mastocytosis, less is known about it. However, in recent years, it has been confirmed that TMEP can, on occasion, present with or lead to development of Systemic Mastocytosis (Nguyen, 2004).

In very severe cases of degranulation, the chemical soup generated by degranulating mast cells may lead to flushing of the body and the face, swelling of the eyes, nose and throat (angioedema),⁴ choking responses in the throat and loss of consciousness (anaphylaxis). In healthy persons' bodies, there is a balance (homeostasis) in intra and extracellular amounts of fluids, and this balance is more or less constant (except for accidents or trauma that may lead to hemorrhaging). In Mastocytosis induced anaphylaxis, the balance of fluids is drastically altered by the leakage of fluids from inside the tissue cells (intracellular

⁴ Angioedema is a swelling similar to hives, but the swelling is deeper or beneath the skin as well as potentially on the surface (modified from Healthline/angioedema, ND).

fluid) to between tissue areas (interstitial fluid). The leakage forces so much fluid outside of the cells as well as the circulatory system that the patient experiences a sudden drop in blood pressure (hypotension). More fluid loss may also take place through severe vomiting and diarrhea that often accompanies anaphylaxis (Mediana et al., 1994; Van Auken, 2006). Moreover, because erupting (degranulating) mast cells dump high levels of histamines, prostaglandins, heparin, neutral proteases, acid hydrolases, chemokines, cytokines, etc. into the interstitial areas between cells, the body also experiences a form of toxic shock (Hermine et al., 2008). In some cases, the toxic shock is fatal (Strober & Orlow, 2001).

In the long run, and in very aggressive cases of Mastocytosis, there is the danger of severe osteoporoses, other types of bone loss, bone calcification, and/or internal organ damage (Johansson et al., 1996). The internal organs most vulnerable to this disease are the lymph nodes, liver and the spleen. There may also be a slightly elevated propensity for development of blood or lymph related cancers in Mastocytosis patients, but fortunately, this correlation remains low. Moreover, only a small proportion of Mastocytosis patients suffer from the most aggressive forms of the disease, whereas 90% of cases are indolent (Hermine et al., 2008). The majority of patients suffer from a variety of discomforts/ailments, ranging from breathing problems, digestive (gas, acid reflex, indigestion, vomiting, etc.), and excretory (diarrhea) problems, flushing, light-headedness, cognitive dysfunction, hives and other allergic reactions. More recent work also delineated additional manifestations of the disease including sexual performance problems, clinical forms of depression, anger, and problems in social relations. Although not many patients experience organ damage or failure, most patients have to be regularly monitored for the possibility of such negative outcomes. The risk of anaphylaxis was already discussed. There is little doubt amongst patients that Mastocytosis is closely related to auto-immunity, but so far, the medical profession has not reached a consensus to classify Mastocytosis as an auto-immune disease (2005 TMS California Conference). Auto-immune diseases are those where the normal functioning of the body is so distorted that it ravages itself (like Systemic Lupus). Some branches of Medicine classifies Mastocytosis as an inflammatory or neoplastic disorder. However, the majority of Mastocytosis patients suffer symptoms similar to other auto-immune disorders.

Causes & Triggers

The causes of Mastocytosis are not known (2007 TMS Houston Conference; Krishnan & Smith, 2008; TMS, 2007). Some findings suggest

that exposure to physical or emotional trauma may trigger the development of Mastocytosis in an otherwise healthy person.

Triggers of attacks are exceptionally varied but better known. In Table I, we list some of the most common food related, physical, environmental and chemical triggers. Not all Mastocytosis patients react to all triggers, and a very severe trigger to one person may be a safe product for another. However, it is advisable that the listed triggers are approached with caution.

Table I. MOST COMMON MASTOCYTOSIS & UP TRIGGERS

FOOD-BASED	PHYSICAL & ENVIRONMENTAL	CHEMICALS
-Alcohol, especially malt-based, fermented drinks -Chocolate -Foods with high histamines tomatoes spinach grapes fresh and fermented cheeses non-pasteurized milk yogurt -Berries** -Bananas -Pitted fruits plums, cherries, peaches, mangoes, avocados -Shell-fish and some fin-fish crabs, lobsters, shrimp crayfish, jellyfish (contact) -Eggs -Pickled foods pickles of any kind sauerkraut olives -Fermented soy products -Gluten -Nuts -Spices, especially hot spices -Food preservatives/additives	-Exercise -Stress -Exposure to sun -Heat -Cold -Friction -Bites from venomous species (snakes, spiders, insects, etc.) -Smells from over-ripe foods -Wools, animal pelts, etc. -Moulds and spores** -Metals/alloys (contact) -Flashing lights	-Cleaning products/detergents -Make-up, soaps, shampoos -Creams, lotions -Perfumes -Medications pain-killers aspirin type head-ache pills antibiotics tranquilizers narcotics (codeine, morphine) anesthetics iodine quinine pills that contain artificial dyes eye and ear drops laxatives vitamins
**Blueberries seem to have a natural mast cell regulator property. Patients who can tolerate blueberries may benefit from consuming small amounts every day.	**Including moulds in foods such as blue-cheese.	

Note: for additional details, visit Mastokids, 2007a/b, and TMS, 2007. Also, for more information, please visit www.chronichives.com

Patients and if children, their caregivers must realize that what may be safe one day may not be safe on another day, and groups of foods which may have been alright at one time may start causing reactions over time. Combinations of histamine releasing foods, physical and environmental along with chemical triggers may cause reactions where the same substances alone may be lower than the threshold required for reactions.

Mastocytosis patients universally tend to follow a special histamine-free diet in an effort to alleviate or prevent symptoms from occurring. Many patients use the book, *Dealing with Food Allergies*, by Janice Vickerstaff Joneja (2003) as a resource for managing trigger foods.

Increasingly, Mastocytosis patients worldwide are starting to communicate with each other on coping mechanisms to manage their disorder. Fellow patients often are the best avenue of information for good care. Over time, most patients create a record of triggers they found bothersome or which made them feel ill. This personal record is their guide to help them keep feeling well. It includes everything they know they have reacted to in the past, as well as tracking/proving whether a suspected substance is a trigger for them. Many patients, upon receiving a diagnosis of Mastocytosis, can go back and connect the dots to answer ongoing and puzzling health sensitivities. *Physicians are encouraged to listen to patients and support their efforts to minimize symptoms.*

Diagnosis

From the beginning of this manuscript, we have tried to underscore the fact that Mastocytosis symptoms can masquerade as so many other diseases (TMS, 2007). The WHO criteria states that “multifocal dense infiltrates of mast cells (with more than 15 mast cells aggregating) detected in sections of bone marrow and/or other extracutaneous organ(s) by tryptase immunohistochemistry or other stains is the major criterion, for tissue from the bone marrow, from the GI tract, and other internal organs” (cited in 2007 TMS Houston Conference). Yet, someone has to suspect the disease before any of these tests can be done. Since so few physicians are familiar with the disease, it remains very difficult to diagnose. However, if the physicians are capable of recognizing the skin lesions, chronic tiredness, fever, flushing, anxiety, tachycardia, unintentional weight loss, trouble with concentration and other cognitive changes, anaphylaxis, etc., there are numerous options for a possible diagnosis to follow up with the WHO criterion such as:

- Blood tryptase levels
- 24-hr urine histamine
- Skin, organ and/or bone marrow biopsy (Soter, 2000, 1991).

The consensus criteria suggested by Gould and Park (2003) are divided into major and minor categories. The major criteria are multiple and dense accumulations of mast cells in bone marrow. Minor criteria are: more than 25% of mast cells in bone marrow are either elongated or atypical; there is mutation of the tyrosine kinase KIT at codon 816; mast cells in bone marrow, blood or other organs have CD2 or CD25 on their surface molecules; serum total tryptase levels are greater than 20ng/ml. If one major and one minor, or if three minor criteria are found, the diagnosis is Mastocytosis (Gould & Park, 2003; Hermine, 2008; 2007 TMS Houston Conference).

Notwithstanding the above, it is vitally important to note that the current diagnostic tests for Mastocytosis (with the exception of the skin biopsy) do not consistently return accurate results for all patients. There are differing thoughts and experiences with these tests. As if to prove the problem, there are many patients who suffer all the symptoms of Mastocytosis despite receiving perfectly normal results on the diagnostic tests. That prompted a small group of doctors in the US to diagnose those patients with 'Mast Cell Activation Disorder' (MCAD) so that they could proceed with much needed treatment. The patients benefited from the same treatment given to Mastocytosis patients, despite not meeting the diagnostic criteria.

Additionally, it is believed by some patients that the bone marrow biopsy can worsen the disorder. As well, they believe it is pointless to perform a bone marrow biopsy when the patient is not symptomatic. These differing thoughts versus experience represent the dilemmas of diagnosing Mastocytosis today. In the meantime, patients need to be treated on the basis of their symptoms, to alleviate their suffering and hopefully slow down the disease progression, whether a diagnosis exists or not.

Treatment

There is no known cure for Mastocytosis. What little treatment exists is directed to the symptomatic relief of patients (Strober & Orlow, 2001; Soter, 2000). First line therapies include H1 antihistamines (Reactine, Benadryl, Claritin, Allegra, Atarax), and H2 antihistamines (Zantac, Pepcid, Axid, Tagamet). The H1 type is to reduce skin sensitivity and flushing symptoms. The H2 type is to reduce digestive problems, acid reflux and vomiting/diarrhea. Ketotifen (Zaditen) which is a mast cell stabilizer also has been shown to offer one of the best treatments, bringing mast cell degranulation under some control. Finally, low doses of Doxepin on a daily basis have been found to work extremely well amongst patients, when used for its powerful antihistamine properties.

Second line therapies are variations of photo-chemotology, including Oral PUVA (Psoralen baths plus Ultra Violet A), and UVA1 phototherapies (Soter, 2000). These therapies regress or eliminate manifestations of urticaria and their related symptoms (itching) for between 12-18 months. The unfortunate side effect relates to the repeated damage from cumulative UV exposure. Also, in almost all clinical studies, symptoms have reappeared with time (Soter,2000).

There are also third line therapies for particularly aggressive cases, which include interferon, surgical excision (the example was removal of throat tissue), electron beam radiation, flash lamp-pumped pulsed dye laser, and even chemotherapy (Soter, 2000). Some patients have been receiving interferon-Alfa on a long term basis (5+ years), with some relief and little or no side effects (2005 TMS California Conference). The ultimate goal is to develop 'targeted agents' which will neutralize or eliminate the 'bad' mast cells. Otherwise, chemotherapy types of drugs are killing the 'good' with the 'bad', and might not be good for patients whose immune systems are already compromised due to Mastocytosis (2007 TMS Houston Conference). Some experts have even suggested bone marrow transplants (University of Michigan, 2004). Moreover, in dire cases of anaphylaxis or persistent tachycardia, patients use epinephrine subcutaneous injection (eg. Epi-pen). Epinephrine does not block mast cells, but it neutralizes some of the reactions to their degranulation (2007 TMS Houston Conference).

Disability & Perceptions of Disability

By this point, it should be crystal clear that Mastocytosis can manifest itself in a myriad of symptoms, ranging from mostly inconvenient, to seriously affecting quality of life, to possibly fatal. A large study carried out in France (Hermine et al., 2008), compared the perceptions of disability of cutaneous, indolent and aggressive Mastocytosis (363 patients) with those who did not have the disease (90 controls). The study did not include patients with leukemia. 'Disability' was measured through seven measurable parameters: existence of life-threatening anaphylaxis, number of flushing episodes/week, number of stools/day, number of micturitions/day, pruritus score, depression, and quality of life score (QL). At the 'objective' level, researchers defined disability as the existence of recurring anaphylactic episodes, seven or more flushings/week, four or more stools/day, eight or more micturitions/day, pruritus score of six or more, depression score of 10 or more, and QL score of 60 or more. Researchers also gathered a complex perceptual measure consisting of patient experiences on 38 distinct Mastocytosis symptoms. Moreover, each of the ratings (0-4) on the 38 symptoms was assigned a weight of severity (1-5) by the patients. Researchers called this composite scale the AFIRMM score where the

ratings could range from 0 (least severe) to 760 (most severe). We will now highlight some of the fascinating findings from this study.

1. Overall, in all seven objective parameters of disability, Mastocytosis patients scored significantly higher (worse) than controls. Yet, there were either exceptionally few or no statistically significant differences in the reported disability symptoms amongst patients with cutaneous, indolent or aggressive types.
2. With very few exceptions, the level of mast cell mutations (D816V) or the elevated levels of blood tryptase were *not* related to levels of objective disability.
3. In terms of the composite measure (AFIRMM score), findings were similar. Patients showed significantly higher perceptions of disability than controls ($p < .0001$). However, the differences between cutaneous, indolent or aggressive Mastocytosis patients were either very few or non-existent.
4. Again, with very few exceptions, neither the level of mast cell mutations (D816V) nor the blood tryptase elevations predicted the perceived level of disability or impact on quality of life (AFIRMM).

There is another important finding which requires emphasis (Hermine et al., 2008). Although none of the individual symptoms Mastocytosis patients experience/suffer from is exclusive to this disease (other illnesses also show such symptoms), what is unique is the exceptionally varied number of symptoms that seem to disable Mastocytosis patients. Moreover, despite their major impact on Mastocytosis patients' lives, some of these symptoms have been largely ignored by the medical community. For example, especially male Mastocytosis patients seem to feel much angst about sexual performance Mastocytosis seems to degrade, and both male and female patients seem to be tormented by the appearance of skin welts, lesions and overall appearance. The authors also caution the medical community to be better prepared for the plethora of symptoms for avoiding misdiagnoses. Moreover, they suggest, medical professionals should also respond to the feelings and perceptions of Mastocytosis patients in areas where the disease affects their quality of life (Hermine et al., 2008).

Methods

In this qualitative study, we will relay 1st hand stories from 12 long-term Mastocytosis sufferers. All stories were recruited from members of Canada Mastocytosis Support group (footnote #1). With the exception of the group administrator and a few others, almost all

members use pseudonyms in communications. Since 2008, a few members of this electronic support group have been meeting and sharing their personal experiences. In December, 2008, an electronic call was placed on the support site by the site administrator, informing the members about the current study. The call asked members to volunteer their stories about the difficulties they may have experienced in the diagnosis of their Mastocytosis. Participants were asked to include their (current) age and sex, but no other identifying characteristics were asked. With the exception of age/sex, anonymity in all other aspects was assured. No methodological efforts to match, stratify or randomize the sample were undertaken. Participants were not promised any benefits for participation. Thus, in this qualitative study, we intend to make *no generalizations*. Each story is as individual as the Mastocytosis sufferer who has provided it. Neither do we put words in our participants' mouths. With the exception of shortening very long submissions (ranging from one paragraph to 17, single-spaced pages), all submissions are included, and all are quoted verbatim, in part or in full. However, it is our contention that many insights can be gained from the many years of struggle of these patients. We thank each of them for sharing their difficult experiences with all concerned, with the single hope of making the road to diagnosis a little smoother for both patients and physicians.

Erroneous Diagnoses: Patient (P) Stories (verbatim)

P01 (female, current age 61):

The first time I passed out was in the winter of 1996. I was alone at home, with the exception of my pets (dogs/cats). I had just made myself an ethnic dish I love, which consisted of poached eggs, generous yogurt sauce with crushed (raw) garlic, all dressed with melted butter mixed with hot chilly peppers (believe me, it is delicious). Because of the raw garlic, I never served this food when my partner was home, but often consumed it on nights he was out of town. On this occasion, shortly after shining my plate with great zest, I felt a burning heat, and a strong tingling in my body. I think, burning started on my face, especially in my ears and cheeks. My eyes felt like they were bulging out of their sockets. Not knowing what hit me, and suspecting the garlic, I started moving around, and trying to do things to distract myself (oddly enough, I went to the basement to clean cat boxes). Rather than subsiding, the flushing and burning of my body increased to the degree that I opened the front door and flung myself on the icy porch. I passed out. When I woke up, I was lying sideways on the ice. I couldn't stand up, but dragged myself inside the door. I had the worst heart palpitations one can ever imagine. I was shivering uncontrollably, but could not move away from the cold floor. My bladder felt so full that I thought I was going to wet myself. My dogs were frantic, barking and trying to lick my face. I thought I was dying, thinking this was a heart attack like the one that killed my father. After a while (which seemed like a lifetime), I

crawled to the washroom. I felt exhausted! In this first attack, I did not call an ambulance because I was ashamed of my 'garlic-breath'. The next day, my GP ordered an EKG, and found it to be normal. She concluded it must have been indigestion.

P02 (female, current age 44):

When I first found symptoms unmanageable and interfering with my work and life, my family doctor referred me to an Internist, Allergist and a Cardiologist. I had extensive blood work, allergy tests, EKG and X-rays. On my own, I visited a physiotherapy clinic for seized joints and extreme body pain. I tried everything and kept working. All test results came back glowing and in fact, I appeared to be the picture of health on paper. In reality, I felt like I was 80 when I was only in my early to mid 30s.

In those days (1996/97), I began to experience difficulties with hot baths and showers, and with wine. In my work, there were a lot of dinners and usually, everyone drank wine or something stronger. I began to find that even one glass of wine made me feel horrible.... I just became so sick. Hot water made me itch and feel like I couldn't breathe. My skin began to itch a lot without any apparent reason or pattern. Also, my nose was constantly stuffy. Episodes of extreme fatigue came and went, and I suddenly dropped weight without trying. Bike riding and hiking brought on severe allergy attacks and drops in blood pressure for no apparent reason. I decided to eat only very healthy foods, which included spinach. The more I exercised and ate better foods, the worse I felt. I became increasingly weak and slow. The best description I could give for how I felt at the time was this: 'it feels like I'm dying standing up'. Eventually, it was nearly impossible to think straight and to make the smallest decisions at the office. Allergy tests came back almost completely clear, which was not surprising because I've never had allergies to anything. The allergist suggested I flush a saline solution periodically up my nose to help with the stuffiness. I tried to put weight on but could not. My weight dropped to 98 pounds and stayed there until years later when the stress was gone. Finally, between 1998/2000, I experienced rapid heart beating (tachycardia), just while sitting at my desk. My heart raced non-stop night and day for almost two years. EKG and doctors all said I was fine and it was stress. The stress diagnosis did not make sense because I've had a lot of stress over my lifetime and never felt or suffered this way. It had to be something else, but my doctors all persisted in diagnosing stress overload. They wanted me to try anti-depressants and sedatives. Both drugs did not help at all and ended up making me feel worse.

In 2000, my eldest sister passed away and that, coupled with incredible stress from work and my ongoing symptom escalation, made it impossible to continue working. I was already having difficulty thinking clearly. Things which had taken no time at all before were now taking hours.... I was worried about making a serious mistake in my work. It was impossible to stay awake for a full day and I was starting work days on the bathroom floor.

I had to leave my career behind and begin my life on disability. At this time, I finally asked to see a dermatologist for some spots which had appeared on my arms. They had started as a few red blotches in the summer of 1997.... By 2000, the spots were down both my arms and never faded. It took months to get an appointment.... When I did finally see her, I only wanted to see if we could clear up these spots. She took one look at them and declared it to be either lupus or some other strange name.... She took a biopsy, and diagnosed TMEP Mastocytosis. She gave me a piece of paper with the name of the disorder written down and a prescription for an H1 antihistamine. That was it. I was sent home and had no idea what I had or what was wrong or how serious it was. The doctor didn't tell me anything about it really other than it was the rarest form of a rare disorder. When I returned home, I began searching online for answers. That's where I found the best answers and advice for this disorder. But online reading of patient experiences also was overwhelming and terrifying, sometimes adding great stress. It was all too much for me to process or make sense of by myself. I hope that doctors make an effort to learn about this disorder so that they can advise patients, so that we're not left on our own. I don't know what was worse – the years I didn't know what was wrong, or knowing what was wrong and having to wade through other patient experiences to find something matching me for help and treatment.

P03 (male/child, current age 8):

We started seeing our family doctor about our son's rash during his 1st year. It was diagnosed as 'seb'. When treatment didn't work, the doctor decided that it was fungal, and we tried new medication which also didn't work. The rash was all over his scalp and was very itchy. We never were able to make any headway with our family doctor....When our son needed dental work done when he was four, he had a reaction to anesthesia and broke out in massive blisters all over his head, which they treated as a Staph infection. The blistering reoccurred over the next three years, and every time we took him to the doctor, they said it was a Staph infection. That combined with the itchiness, the spread of the rash down his neck and forehead and the discomfort it caused him on a day-to-day basis made us continue to pressure our doctor. We also were concerned that he wasn't eating well, was skinny and seemed to lack energy. We finally got really upset [and got referred to] a dermatologist who did the biopsy. She then... told us that he had Mastocytosis, showed us a page in a medical book with a list of medications he wasn't to have, and then, she told us to look it up online....Needless to say, we had no clue what Mastocytosis was and were upset with the dermatologist....We went back to the family doctor, who referred us to a pediatrician, who referred us to an immunologist and allergist....None of the doctors we have dealt with have experience managing Mastocytosis, and we have found the entire experience to be frustrating to say the least....Our son is now eight.

P04 (female, current age 60):

1. 1997: spleen removed due to illness and enlarged spleen, plus what was then thought to be a tumour. Many years later, it appears it was due to Mastocytosis.
2. 2007: dermatologist diagnosed urticaria pigmentosa. Covers me from clavicle to mid thigh....Until this point, [I] didn't know why I'd occasionally faint, get hives, experience plummeting blood pressure and chills and sweats.
3. 2008: diagnosed with Mastocytosis. Bone marrow biopsy and endoscopy.
4. ...Worst problems continue: apparently (according to gastroenterologist, I have far too many cells in the gut). That's as sophisticated as the doctors seem to get. I have major problems keeping food down.
5. Dermatologist is most competent, but he can't assist with tummy problems.
6. Clinical hematologist no help beyond saying "you have it, we can't really help you, here's some drugs that may or may not help."
7. Gastroenterologist confirms and suggests drugs that aren't related to Mastocytosis, and doesn't seem to understand Mastocytosis.

P05 (female, current age 40):

I have Urticaria Pigmentosa. I first noticed the spots when I was 27 (I am now 40). Actually to be really truthful, I always got the spots when I was younger but they would always go away. I got them when I came in from the cold on my legs. I never really worried about them because they always went away. But at 27, they started staying. I went to a dermatologist who took a biopsy and told me they were 'hives'. She seemed to think insect bites, but I knew better. She pretty much did not know what to do from there so I took over. Googling (or rather Yahooing back then) 'hives, spots, cold' etc. At about the age of 30, I came upon a website hosted by Jackie Vaughn. From a question I posted describing my spots she told me it was probably Urticaria Pigmentosa and sent me photos. Once I got the name, I learned about Mastocytosis and the types. I have no other symptoms other than the skin. I decided not to worry too much (it really is a good philosophy). When I was 39, my spots had increased (and still do) so now am constantly looking for a way to get rid of or hide them. I went to my general practitioner out here in BC. And she knew it was Mastocytosis. She sent me to a dermatologist. The dermo [sic] took another biopsy and asked it to be tested for masto and it came back negative. However, she decided to diagnose me by clinical analyses (as I have spots and Darier's sign). She basically has told me there is nothing she can do except PUVA and as a dermatologist she cannot recommend it due to the cancer risk. I know there are other options. Perhaps even laser. I asked her if gastrocom would help with the spot symptoms but she said no (but I read somewhere that it could). I am

discouraged at this point, now that I have a diagnosis, no one is willing to look at what options there are for me. To help me manage this [sic]. This is where I am at.

P06 (male, current age 75):

My husband is currently battling Systemic Aggressive Mastocytosis and has been for about seven years. He is currently 75 years old. He was diagnosed after much confusion surrounding a skin rash. Eventually after much discomfort with itching and flushing, a skin biopsy and bone marrow biopsy were conducted to provide us a conclusive diagnosis.

His disease has progressed severely and we continue to receive little if any help/treatment from the medical community. Any help from your organization would be most appreciated. Is there much research going on in the treatment of this disease? We feel quite alone against this overwhelming yet rare condition.

P07 (male, current age 49):

...One morning I was eating a bagel at work, and started feeling faint. My hands felt swollen, as did my feet. My ears were burning too, and I also had a dry scratchy feeling in my throat. I had never felt this before. I got up from where I was eating, and while en-route to my office, I passed out in the company boardroom. I woke up with my head throbbing and my receptionist looking at me, with a very concerned look on her face. I was red all over and my eyes were completely bloodshot. I was rushed to the hospital. They released [me] an hour later and told me to see my Doctor.

...Two weeks later while having breakfast at a diner near work, I felt it again – swelling feet, hands, burning ears, and a strange scratchy feeling in my throat. I left my food on the table, paid my bill, went outside to unlock my bike, then my head began to throb. The next thing I know, a pedestrian is standing over top of me, asking me what my name was? I was again rushed to the hospital, and given an IV of antihistamine. “You must have an allergy to something,” I was told.

...I was referred to a gastro specialist who proclaimed I had de-glutenal syncope (SP?) – meaning that when I swallow – I go into syncope. He surmised that I had a pocket in my throat, and when I ate (sometimes) food settled into the pocket, and once filled, it pressed against the sciatic nerve, and I go into syncope. Strange, rare, but treatable; confirm there is a pocket, and sew it up. To confirm this diagnosis I was sent to radiology to drink 14 gallons of radium and was bombarded with x-rays. I was told one of the heads of radiology [will] oversee the procedure. Afterwards, he came out to see me and said “You are disgustingly and absolutely normal!” and walked away annoyed.

P08 (female)

I was fourteen when my mother went with me to our family practitioner to see about the raised red spots that had first appeared on my thighs every time I played soccer in the cold. For a few months, I had resisted going to the doctor. But the number of spots had increased; they were spreading to my trunk and no longer fading entirely after exercise, and if I followed soccer practice with a hot shower, they would itch so badly that I would scratch until I drew blood. I was fortunate in that my doctor suspected mastocytosis right away, but her bedside manner left much to be desired: "It's ugly, but it's nothing to worry about," was how she prefaced her diagnosis. She then went on to tell me that I could try taking an antihistamine to alleviate the itching, but that it might be a long process to find one that would help, and that it would probably make me sleepy (this was in the early '90s, before the explosion of non-drowsy H1 and H2 inhibitors). My reaction was not to bother with medication. I was embarrassed by my doctor's comment about the appearance of the urticaria pigmentosa and deeply resistant to the idea of experimenting with medications that could make me tired. In retrospect, I realize that this was because I was already exhausted—a symptom (one of many) that I would not link to my illness for almost ten years. In part, this is because the various specialists that I saw over the years never clarified to me the likelihood that I might experience symptoms beyond the itchiness of the urticaria pigmentosa. But it is also because, having gotten mastocytosis at such a young age, it took me a long time to realize that the levels of tiredness I was experiencing were not normal. Doctors, I think, need to take extra care to determine whether children and adolescents with mastocytosis are indeed feeling symptomatic since, in at least some cases, exhaustion and other symptoms may be present despite all signs to the contrary (in my case, participation in after-school sports and excellent grades). Doctors also need to be informed and take seriously such gender specific symptoms as an increase in mast cell degranulation pre-menstruation. So although, thankfully, I didn't struggle to get a diagnosis, once I finally began to realize that, beyond itching, I wasn't feeling well, I was convinced that my symptoms were psycho-somatic.

Gendered Stereotypes

Mastocytosis, both in its systemic and its cutaneous forms, is an equal-opportunity abuser. It can hit young and old, men and women⁵ (Almahroos & Kurban, 2003; Medina, 1994). Both men and women may face mammoth difficulties in managing their symptoms, dealing with health complications, and getting a correct diagnosis. The fear of the unknown may equally impact them since, as we discussed, some of the

⁵ Almahroos & Kurban (2003) suggest that the sex ratio in pediatric cases is one to one. However, in adult cases of Mastocytosis, the ratio may be 1.5 (males) to one (female).

symptoms of the disease are exceptionally severe and disabling. Female patients may experience an exacerbation of their symptoms if and when they get pregnant, but most pregnancies end without too many complications, and with the birth of healthy infants (Worobec et al., 2000). However, despite similarities in patient experience, there may be gendered differences towards women in the reactions of the immediate family, friends and work-mates. The symptoms of this thousand-faced disease may be taken more seriously when they manifest in men than when they afflict women. As a traditionally male-dominated area of the sciences, medical professions may not be totally immune to these ingrained gender stereotypes either (Khoury & Weisman, 2002; Plechner, 2000). Like their Freudian predecessors, at least some medical professionals may see the symptoms through the lens of feminine hypersensitivities, anxieties, possible hypochondria or neurosis (McCracken, 1997). The already established connection between stress and the onset of Mastocytosis will only strengthen the overgeneralization of gendered expectations. In this regard, the following recollections from women patients will speak for themselves.

P01 (female, current age 61)

We were in the middle of a move. Most of our furniture was already in the new house, including my partner and our pets. However, I was still sleeping in the old house, since it was closer to my work, and since we still had some valuable possessions to be moved. One evening, I had a single glass of wine at a work-related reception, felt a bit dizzy, and came back to my almost empty house. It was about 6:30pm. I warmed up some soup, but felt worse. Since by that time, I was able to recognize the onset of an attack, I managed to call my partner just before I passed out. When I regained consciousness, I was lying on the floor, with the phone still in my hand. There were paramedics, police and firefighters all around. Obviously, before rushing to my aid, my partner had called 911. What was strange was that rather than helping me, the police were interviewing my partner. Looking at my beet-red and swollen face, they must have erroneously deduced that he must have hit me. Or else, why would a woman be lying on the floor, in a mostly-empty house, clutching a phone? Naively, and worrying about my health, my partner was inadvertently feeding into their suspicions. He was 'confessing' that this was not the first time this happened, and each time, it seems to be more serious than the previous. In order to re-focus the attention upon my self, I said I was at a work-related reception, and had a single glass of wine. Upon my revelation, the police circle around my partner immediately loosened, and I swear that I saw some fleeting winks. In the minds of the police and the paramedics, the mention of 'wine' instantly elevated me from an 'abused wife' to a 'falling drunk'. The paramedics must have passed along the 'drunk' diagnosis to the emergency doctors as well. After yet another clean EKG, the doctor (male) lectured me about the perils of drinking too much.

I am sure, he never believed my insistence on having had a single glass of wine. Come to think of it, I might not have finished it all.

Between 1996 and 2002, I lived through seven other serious attacks, all of which ended in the emergency rooms of various hospitals. All attacks came after a dinner. Although triggers were never the same (I eliminated foods from my diet after each attack, and the 1st ones to go were garlic and alcohol), the order of symptoms were identical (flushing, swelling of my face, extreme palpitations, passing out, strong shivers, pressure in the bladder, listlessness). Each time, I got shuffled between my GP and heart specialists, lung specialists, brain specialists, internal medicine specialists, endocrinologists and gynecologists. I went through repeated EEGs, EKGs, MRIs, CT scans, 48-hour heart monitors, pap-smears, blood tests, 24-hour urine tests, and any other tests the specialists plucked out at random from their medical books. Although no one believed me because I did not seem to have allergies, I became so afraid of my food that I lost 27 pounds. Although I lived in an abyss, people congratulated me for my weight-loss and told me I looked great! I heard erroneous diagnoses of menopause, anxiety attacks, dumping syndrome, hidden epilepsy and lupus. Although nobody admitted it, I am sure they also tested me for AIDS. One doctor (male) even had the nerve to suggest that maybe it was time I visited a psychiatrist. A dermatologist (male) totally missed my urticaria and offered me botox injections to remove 'the 11' (wrinkles) between my eye-brows. My relationship which was the envy of many, irreversibly crumbled under the stress of my health ordeals. Only after 10+ years, I was diagnosed in the winter of 2007, by a brilliant hematologist (male).

P08 (female):

One episode stands out in my mind, both because it led up to finally getting onto an effective medication regime, and because I had a decidedly gendered impression of my own health crisis. In the midst of an emotional conversation with an ex-boyfriend, I took one sip of wine and fainted. Both of us assumed I had experienced some kind of swoon. Mortified and baffled, I went home to bed. Only after I kept having episodes of near-fainting, daily vomiting, and incapacitating exhaustion did I start researching Mastocytosis online.

P09 (female/child):

*[After many tries to find an answer] I made an executive decision to return to [pediatrician's name] office, and refused to take no for an answer. He finally looked at me and said (I swear on my life, this is true) [parenthesis in original]: "You know Ms [name], I must tell you a story about my professor [name]." He continued to tell me a useless story [when] his professor, apparently told him that writing out prescriptions and referrals to **panicked mothers** [emphasis added], [was] one of his functions. This was an obvious insult to my intelligence, and I was hurt....But, he was in the process of writing the referral, so I [did not reply].*

...and [daughter's name] father gave me absolutely no support whatsoever...thinking like Dr [name], and I was wasting everyone's time...of course [daughter's] dad was not living with us, so how would he know the agony his daughter was in? [After a long struggle and numerous other referrals, Mastocytosis diagnosis]. I went back to Dr [name] and told him the diagnosis, where he admitted he had never heard of this. He didn't give me the apology I deserved, nor have I brought [daughter] back to him.

P10 (female):

*I feel really angry that specialists that I went to see about my severe anaphylaxis did not diagnose me. If you google 'bone pain' and 'anaphylaxis', you only get one hit: Mastocytosis. I should have done some research and diagnosed myself. Now, I deeply distrust doctors since so many of them have told me that **I was imagining all my health problems** [emphasis added].*

When doctors are baffled by the symptoms of a patient, they often react with anger. They accuse the patient of imagining [her] problems. If only they could be a bit more humble, and simply say that they have no idea what is wrong. Please, if any doctor is reading this, do try to be kinder and to really listen to your patients!

P11 (female, current age 48):⁶

[Summary of previous pages of the narrative: Patient 11 has a very rare form of Systemic Mastocytosis which has remained undiagnosed for a long time. When she goes through a hysterectomy to correct profuse bleeding and to remove fibroids, her Masto symptoms escalate. Most of the 35+ experts she sees interpret her symptoms in erroneous and maddeningly gendered ways. No one (except her gynecologist) believes her when she claims the hysterectomy decision for her was an easy one since she has three children, and a very supportive husband].

...After being released from the hospital for the 2nd time, I again had another episode of this dyspnea 2 weeks following this and again my doctor hospitalized me for the 3rd time and tested me for levels of anemia or infection. Again, nothing. This time he called in a GP to go over me. Again this doctor could not find anything to explain the dyspnea. In conference with my doctor, the suspicion of psychosomatic or emotional difficulties due to either surgery itself or the loss of my uterus were raised for the first time. My gynecologist defended me for he had already done an evaluation of me and did not feel that this was my case. He told the GP that I was not the kind of woman who presented psychosomatic issues and that my behavior gave him no reason to

⁶ Patient 11's experiences with the medical system are so long, so misleading and so negative that she replied to our call for Masto experiences with a 16 page (single-spaced) narrative. Here, we are only able to include a small part of her long, discouraging, terrifying and gender-based journey.

suspect an emotional difficulty with the hysterectomy. The two doctors disagreed.

*...As the time of my recovery wore on, more symptoms began to rise. I began having bouts of diarrhea, abdominal pain and flushing. In the search for answers, my gynecologist began referring me to colleagues who were GPs in hopes of finding some answers. He also asked me to perform various tests in hopes that we could find answers to what was causing the dyspnea. Each and every doctor that I saw came to the very same conclusion, psychosomatic! One doctor, a GP and pneumologist [sic] specialist, saw the flush and said that this was a sign of anxiety and that he had seen other women with this same reaction. He told me that my dyspnea was likely due to the abdominal pain that I was having. That my brain had somehow identified this and whenever I had the pain that it would trigger a response of dyspnea, in other words, psychosomatic. He said, resolve the pain and the dyspnea would also be resolved! ...Due to the results of these exams, my doctor sent me to a trusted gastric [sic] surgeon for his opinion. Just moments before going into his office, I had gone through a very strong episode of dyspnea. I went into this doctor's office breathless, flushed and trying to recover. He at first was very sympathetic with me and asked me what was the matter and why was I like this. I told him what had happened and that I was going through this ever since my surgery a few months before. He asked me what the surgery was. The moment I said 'hysterectomy' his whole demeanor changed. He went from being in a physically sympathetic position to that of leaning back in his chair, folding his arms and with an ironic smile on his face said, "Hysterectomy, eh? Ah ha! I understand!" and then proceeded to let me talk on, telling my story. It became obvious that he had already made his diagnosis, but allowed me to talk on. He examined me and even though he provoked a small reaction in touching upon my abdomen, after my returning to my seat, he told me that what I needed was a psychiatrist because I was obviously **mourning for my uterus!** [emphasis added]*

*...The neurologist listened only slightly to my story and when he heard what I had to say about this semi-conscious faint, he immediately stopped me and said that it was not a faint and then also proceeded to tell me that the redness I had was not a true flush, for he had seen plenty of flushing and mine was not the flush of a carcinoid, and indeed it was not a flush at all. He sent me back to the oncologist and then conferred with him. This doctor, the next day, then gave to me their official diagnosis, '**Hysteria!**' [emphasis added]*

Patient 12 (female, current age: 49)⁷

Aug 19-29/03: sick due to attack – unable to attend my work shifts.

⁷ Patient 12 also has suffered years of terrifying symptoms and repeated misdiagnosis. She responded to our call with two separate narratives, one about her symptoms in her young adulthood (5, single-spaced pages), and another about her experiences in the last seven years (12, single-spaced pages). We include only a small portion from her exceptionally difficult experiences.

Sept/03: returned to work after recent bad spell, hands now had a numb/tingling sensation in them. Started to see a physiotherapist for cranial massage to relieve the intense pain in the back of my head. Helped a bit at first, but then had to stop as it seemed like the pressure of the massage caused me to feel sick later.

Sept/03: saw visiting neurologist regarding continuing severe headaches (back of head). CAT scan and MRI were ordered (to rule out MS). The neurologist noted I had high arches and was not interested to hear any of my general health complaints, only wanted to hear answers to his very specific questions. [parentheses in original]

Oct/03: saw my doctor and requested a leave of absence as I was unable to meet the obligations of my two separate employers. Employment Insurance (sick leave) had been used up so I was no longer eligible for continued EI including regular EI as I was not able to work. Applied to the local Social Assistance office for financial assistance. Was granted the minimum income for an individual (\$500/mo) and given a lengthy and complex application for disability status which would allow a larger financial support. [parentheses in original]

March 09/04: received Provincial Disability denial. My doctor had failed to prove that my illness was severe enough to warrant this designation. The lack of a firm diagnosis was not in my favour either. This was so discouraging at this point as my sickness continued to affect me in random and unpredictable ways. I had used up any tiny resources that I had, since the BC government was only paying me \$500 per month. I only managed to get through this period with the help of family.

Where should we go from here?

There is no doubt that Mastocytosis is a serious, and in rare occasions, a fatal disease. There is also no doubt that many dozens of dedicated specialists, including Drs. Cem Akin (Ann Arbor, Michigan), Joseph Butterfield (Rochester, Minn.), Marianna Castells (Boston, Mass.), Matthew Cheung (Toronto, ON.), Luis Escribano (Spain), Dean D. Metcalfe (NIH), Mary Messieh (Hamilton, ON.), Lawrence Schwartz (Richmond, Virginia), Gary Sibbald (Toronto, ON.), Theoharis Theoharides (Boston, Mass.), Peter Vadas (Toronto, ON.), Peter Valent (Vienna), are breaking new ground with their research and patient care. There are task forces working towards research promotion, public awareness and education in mast cell disorders (AAAAI Mast Cell Disorder, 2006). Patient supports have greatly expanded throughout the world, focusing on bringing patients together, linking physicians with patients, informing of government supports, and sharing treatment and research advances (eg. Canada Mastocytosis Support; UK Mastocytosis Support; German Internet Support Group). There is also a flurry of activity in Mastocytosis annual conferences, panel discussions, and

research centres (i.e., Initiatives of Research on Mastocyte and Mastocytosis, France; MastoKids Organization, USA; European Competency Network on Mastocytosis, Europe; TMS Annual Conferences, USA). Important research is being carried out on role of mast cells as defense and repair mechanisms, inhibitory receptors on mast cells and mast cells as regulators of the immune system (AAAAI Mast Cell Disorder, 2006). There is also research on the link between mast cells and estrogen and progesterone since two of the four receptors of the mast cells may be sensitive to these hormones (2005 TMS California Conference). But, as we have seen in the candidly written experiences of the participants in this study, there needs to be much more done to allow medical insights to trickle down into the daily lives of Mastocytosis patients.

So far, when patients are successfully linked with a true expert in Mastocytosis, and are provided with the correct and up-to-date information about this cruel disease, they seem to learn ways of monitoring their bodies, and they seem to re-establish some control and predictability over their much challenged lives. Where the disease/patient/doctor triangulation seems to be at its weakest point is the process of diagnosis. The almost absolute lack of preparedness towards recognition of the various symptoms patients may manifest, by many general practitioners/pediatricians and the emergency personnel, is a major stumbling block. We suggest that, starting from medical schools, and much before any kind of specialization is allowed to take place, medical curriculum *should* include thorough education and training on Mastocytosis, and mast cells' role in diseases and disorders. This early education *must* be refreshed during residency requirements, and possibly during periodic check-points in medical practitioners' careers. We live in a crowded and globalized world where new diseases, mutations of older diseases, and environmentally/biologically triggered immune problems are on the rise. Even in relatively predictable career paths of the general practitioners, vigilance about learning new developments should be a must (new ailments as well as new ways of dealing with them). We believe that patients do have the right to expect accuracy and professional accountability from their healthcare providers, whether they are GPs or renowned specialists. Currently, people with complex diseases such as Mastocytosis are often falling through the cracks.

Another important bottle neck area seems to be the segmentation and over-specialization in the medical care system. Of course, we are by no means trying to dispute the crucial importance of specialization, but flagging the issue in the diagnosis and treatment of multi-organ/multi-system diseases such as Mastocytosis. We are not nostalgically calling for the return of the 'good old days' either, where doctors (mostly men)

made house calls, and served one and all health issues from what was contained in their medical bags. We are fully aware that those 'good old days' may not have been so good, and even if they were, will no longer suffice. We are, however, recommending a better communication system, education, better cooperation, an easily accessible data-base of already collected information, a more efficient way of flagging serious symptoms, and a heightened awareness of diseases that straddle the whole body, rather than involving individual organs (be it brain, heart, lungs, etc.). Cooperation must include some sharing of information amongst specialists (of course, with patient's informed consent), to flag mutual areas of concern, as well as to reduce redundancy. An effort must be made to reduce test duplications, so that a patient is not subjected continually to the same tests by different doctors. There must be a consensus and trust built between physicians, which will allow them to approach this disorder as a team. Let alone beleaguering the already overloaded healthcare system, Mastocytosis patients who are already dealing with a long list of symptoms do not need more run-around, punctures, prods or radiation exposure. We suggest that physicians, nationwide and worldwide, should participate in periodic group meetings amongst different specialists to review particularly elusive cases, so they may generate new insights.

There also needs to be more cooperation between the patients (or caregivers of children/incapacitated adults) and physicians. Historically, the medical system has been rigidly hierarchical, where the doctors 'knew-it-all', and the patients were expected to be submissive and deferential (Plechner, 2000). In the old system, biases about gender, age and possibly other status characteristics (race, sexual orientation?) were also rampant, and unquestioned. Fortunately, we live in an era where much has changed. There is an unprecedented proliferation of information technologies, coupled with higher levels of educational attainment (at least, in developed countries). Patients, especially those who suffer from serious chronic conditions such as Mastocytosis, are more alert to what is happening in their bodies. They need to be heard, they need to be believed, and they need to be incorporated as *active agents* into their healthcare rather than as passive recipients of that care. Where applicable, physicians and other healthcare providers should also try to reflexively re-evaluate their own perceptions and attitudes about their patients, including questioning biases they may still hold. Of course, the success of the physician/patient interaction is contingent on physicians' willingness to 'learn' from their patients. Let us return to an excerpt from one of our contributors, and his opportunity to address a group of physicians. As he makes it clear, many were eager to learn from his experiences, whereas many others were dismissive, and closed to learning from a patient:

P07 (male, current age 49):

...In March 2003, I addressed a group of Canadian Allergists/Immunologists Teaching Doctors, and their residents in Halifax, Montreal, Hamilton, and Waterloo via video-conference about Mastocytosis.

The presentation was very well received. I hate to say it, but my personal story sounded like a bad episode of Seinfeld....particularly because of the Doctors who said to me..."Hmmm, yes. Very interesting....and good luck with all that..." Please know that I did not intend to entertain these doctors, but as they heard the [sic] all the weird misses that I had over the years, and how long it took to finally come up with a diagnosis, some of them laughed out loud – not out of disrespect to me – but out of embarrassment for their fellow doctors, who just didn't have a clue as to what they were looking at.

I also noted how once I was diagnosed, I went back to the doctors who had totally missed the Masto and explained to them what I had. Sadly, they all shrugged their shoulders and said... "oh you've been diagnosed, that's great, see ya" nor [sic] showed any interest in hearing about Mastocytosis, or how I was finally diagnosed.

Our readers should note that this patient is male and a business professional. Out of all our patient experiences, he was the only one invited to speak to a group of doctors. Females manifesting complicated cases, even more complicated than P07, were not invited to speak to groups of doctors, let alone to one doctor. A few of our patient contributors are or were business professionals also. At best, most patients experience their main medical specialist treating them with a few medical residents-in-training watching so they can learn. Their experiences with the disease are rarely asked. In light of the above discussion, we suggest the following best practices:

1. Patient specific, electronic medical records that would have all test results, and go with the patient.
2. Interprofessional team of experts that would develop a coordinated care plan for Mastocytosis patients. The team could include Dermatologist and Allergist along with the particular patient, and then could extend to Gastroenterologist, Pulmonary and Hematological expertise as needed. The team could also include a knowledgeable patient to speak to the patient-centered concerns.

Last but not least, more action on the patients' part also comes with responsibilities. After all, patients have the 1st hand knowledge of what is happening to them. Without falling into long-winded stories their doctors may not have the time/patience to hear, they nevertheless must try to succinctly and accurately summarize their experiences. They must learn to ask relevant questions and seek clarification. They may start to

keep notes or diaries for themselves, to see if there are 'patterns' in the manifestation of their disease. For example, they may identify triggers which make them sick, and take measures to avoid them. This systemic rather than haphazard recollection of experiences may also help doctors to have a clearer picture of what they are dealing with. Good support groups such as the Canadian Mastocytosis Support, also provide invaluable information, so each patient does not have to invent the wheel for him/herself. Patients also must believe that they have the right to ask for a referral, if their current care provider is repeatedly failing to respond to their health concerns. The diagnosis and treatment of complex diseases such as Mastocytosis require nothing less than mutual responsibility, informed cooperation and open communication between those who suffer and those who are professionally and socially entrusted with the responsibility of providing help.

REFERENCES

- 2005 TMS California Conference. Panel discussion (Transcript by W. Hermann & V. Slee). *The Mastocytosis Chronicals*, 2006 (spring), 12-19.
- 2007 TMS Houston Conference (Transcript by M. Lamanna & V. Slee). *The Mastocytosis Chronicals*, 2008 (winter), 18-23.
- AAAAI Mast Cell Disorders, 2006. Update on the AAAAI (American Academy of Asthma, Allergy & Immunology) Mast Cell Disorder Task Force. *Mastocytosis Chronicals*, p. 20-21.
- AFFIRM, 2008. Association Francaise pour les Initiatives de Recherche sur le Mastocyte et les Mastocytoses. <http://www.afirmm.com/>
- Almahroos, M. & Kurban, A.K. 2003. Management of Mastocytosis. *Clinics in Dermatology*, 21(4), 274-277.
- Brockow, K., Akin, C., Huber, M. & Metcalfe, D.D. 2003. Assessment of the extent of cutaneous involvement in children and adults with Mastocytosis: relationship to symptomology, tryptase levels, and bone marrow pathology. *Journal of the American Academy of Dermatology*, 48(4), 508-516.
- Brockow, K. Scott, L.M., Worobec, A.S., Krishenbaum, A., Akin, C., Huber, M.M. & Metcalfe, D.D. 2002. Regression of urticaria pigmentosa in adult patients with systemic Mastocytosis: correlation with clinical patterns of disease. *Archives of Dermatology*, 138(6), 785-790.
- Gould, N. & Park, R. 2003. What you should know about anesthesia - It could save your life.
- The Mastocytosis Society of USA.
<http://tmsforacure.org/research/anesthesia.shtml>

- Healthline/hives(urticaria). ND.
<http://www.healthline.com/adamcontent/hives> (last visited, Dec. 2008).
- Healthline/angioedema. ND.
<http://www.healthline.com/adamcontent/angioedema> (last visited, Dec. 2008).
- Hermine, O., Lortholary, O., Leventhal, P.S., Catteau, A., Soppelsa, F., Baude, C. et al. 2008. Case-Control Cohort Study of Patients' Perceptions of Disability in Mastocytosis. *PLoS ONE*. 2008; 3(5): e2266. Published online 2008 May 28. doi: 10.1371/journal.pone.0002266.<http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2386235> (last visited, October, 2008).
- Horny, H.P., Sotlar, K. & Valent, P. (2007). Mastocytosis: State of the art. *Pathobiology*, 74 (2): 121-32.
- Johansson, C., Roupe, G., Lindstedt, G. & Mellstrom, D. 1996. Bone density, bone markers & bone radiological features in mastocytosis. *Age & Ageing*, 25, 1-7.
- Khoury, A.J. & Weisman, C.S. 2002. Thinking about women's health: The case for gender sensitivity. *Women's Health Issues*, 12(2), 61-65.
- TMS October 2005 Panel Discussion, National USA Mastocytosis Conference. Retrieved from: <http://www.tmsforacure.org/transcripts/expertpanel2005.shtml>
- Krishnan, K. & Smith, S.J. 2008. Mastocytosis, Systemic. E-medicine. Retrieved from: <http://emedicine.medspace.com/article203948-overview> (last visited, Dec. 2008)
- Mastocytosis. ND. Retrieved from: <http://en.wikipedia.org/wiki/Mastocytosis> (last visited Dec. 2008).
- Mastokids. 2007a. Nonimmunological mast cell degranulators. Retrieved from: <http://mastokids.org/index.php?x+degranlist.php> (last visited, Dec. 2008).
- Mastokids. 2007b. Important anesthesia information for patients with mastocytosis. Retrieved from: <http://mastokids.org/index.php?x+anesthesia.php> (last visited, Dec. 2008).
- McCracken, J. 1997. Sigmund Freud. In J. McCracken (Ed.). *Thinking About Gender: A Historical Anthology* (pp. 460-482). Philadelphia: Harcourt & Brace.
- Medina, R., Faecher, R.S., Stafford, D.S., Zander, D.S. & Baughman, R.A. 1994. Systemic mastocytosis involving the mandible. *Oral Surgery, Oral Medicine, Oral Pathology*, 78, 28-35.
- Medterms ND. *Pruritus*. Retrieved from: <http://www.medterms.com/script/main/art.asp?articlekey=5095> (last visited, Dec. 2008).
- Metcalf, D.D. 2008. *Mast cells & Mastocytosis*. *Blood*, 112(4), 946.

- Nguyen, N.Q. 2004. *Telangiectasia macularis eruptiva perstans*. *Dermatology Online Journal* 10(3):1
- Payne, V. & Kam, P.C.A. 2004. *Mast cell tryptase: A review of its physiology and clinical significance*. *Anaesthesia*, 59, 659-703.
- Plechner, D. 2000. *Women, medicine, and sociology: Thoughts on the need for a critical feminist perspective*. *Health, Illness & Use of Care: The Impact of Social Factors*, 18, 69-94.
- Robyn, J. & Metcalfe, D.D. 2006. *Systemic Mastocytosis*. *Advances in Immunology*, 89, 169-243.
- Soter, N.A. 2000. *Mastocytosis and the Skin*. In D.D. Metcalfe & N.A. Soter (eds). *Mast Cell Disorders*. *Hematology/Oncology Clinics of North America*, 14 (3):537-55.
- Soter, N.A. 1991. *The skin in Mastocytosis*. *Journal of Investigative Dermatology*, 96, 32S-39S. Retrieved from: <http://www.nature.com/jid/journal/v96/n3s/abs/5612611a.html> (last visited, January, 2009).
- Strober, B.E. & Orlow, S.J. 2001. *Diffuse cutaneous mastocytosis*. *Dermatology Online Journal*, 7(2), 15-21.
- Tay, Y.K. & Giam, Y.C. 1993. *Cutaneous Mastocytosis in Singapore*. *Singapore Medical Journal*, 34, 425-429. <http://smj.sma.org.sg/3405/3405a14.pdf> (last visited, February, 2009).
- TMS (The Mast Cell Activation Disorders) 2007. Retrieved from: <http://www.tmsforacure.org/patientinfo.shtml> (last visited Dec. 2008).
- Vickerstaff Joneja, J. 2003 (3rd Printing). *Dealing with Food Allergies: A Practical Guide to Detecting Culprit Foods & Eating a Healthy, Enjoyable Diet*. Boulder, Colorado: Bull Publishing.
- TMS attends AAAAI Conference Miami, Florida. *The Mastocytosis Chronicles*, 2006 (spring), 8-11.
- University of Michigan. 2004 (Aug. 18). *U-M Tackles Mysterious, Potentially Fatal Diseases Caused by Too Many Allergy Cells*. Retrieved from: <http://www.med.umich.edu/opm/newspage/2004/mastocytosis.htm> (last visited, Dec. 2008).
- Van Auken, C. 2006 (fall). *Understanding 'Third-spacing'*. *The Mastocytosis Chronicles*. 8-9.
- WHO (World Health Organization). 2007. Retrieved from: http://www.medicalcriteria.com/criteria/hem_mastocytosis_class.html (last visited January, 2009).
- Worobec, A.S., Akin, C., Scott, L.M. & Metcalfe, D.D. 2000. *Mastocytosis complicating pregnancy*. *Obstetrics & Gynecology*, 95(3), 391-395.