

EU survey and results about mastocytosis

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Participants

107 Questionnaires came back

Austria (A): 11

Germany (G): 47

Others (Czech Republic and Slovenia): 2

Spain (E): 14

The Netherlands (NL): 18

United Kingdom (UK): 15

Questionnaire

- A Symptoms and general problems
- B Laboratory investigations and other tests
- C Diagnostic problems
- D Therapy and physicians' recommendations

A: Symptoms and General Problems

1. What symptoms are relevant – what symptoms are particularly annoying/ difficult to tolerate?

A few patients listed more than one symptom of one discipline. Here comes the total number of symptoms assigned to the organ systems.

- 157 – Neuropsychology
- 117 – Dermatology
- 87 – Gastrointestinal tract
- 69 – Musculoskeletal system
- 52 – Cardiovascular system
- 17 – General symptoms
- 15 – Ear nose and throat and breathing organs
- 10 – Symptoms mentioned in the context of temperature (heat, cold, temp. changes)
- 9 – Neurology
- 6 – Urology
- 3 - Ophthalmology

The following evaluation shows the percentage of patients suffering from symptoms of different organ systems.

- 63% - Dermatology
- 54% - Gastrointestinal tract
- 51% - Neuropsychology
- 38% - Musculoskeletal system
- 35% - Cardiovascular system
- 12% - General symptoms
- 11% - Symptoms mentioned in the context of temperature
- 10% - Ear nose and throat and breathing organs
- 8% - Neurology
- 6% - Urology
- 3% - Ophthalmology

Neuropsychology:

Symptoms	Number of patients who mentioned the symptoms
Fatigue	35
Headache	23
Sleeping problems	17
Dizziness	16
Concentration problems	14
Memory problems	10
Drowsiness	10
Depression	7
Restlessness	6
Brain fog	6
Anxiety disorder	4
Erratic mood swings	3
Mental stress due to skin lesions	2
Irritation	2
Problems in finding the correct words	2

Dermatology:

Symptoms	Number of patients who mentioned the symptoms
Pruritus	38
Skin lesions	29
Flushing	19
Skin reddening	10
Wheals	7
Urticaria	3
Bruising	3
Oedema	3
Inflammation of the mucous membrane	2
Skin problems	2
Burning sensation of the skin	1

Gastrointestinal tract:

Symptoms	Number of patients who mentioned the symptoms
Diarrhoea	19
GI tract problems	14
Nausea	14
Abdominal pain	11
Stomach cramping	7
Intestinal cramping	6
Reflux esophagitis / heart burn	5
Food intolerance	4
Vomiting	2
Bloating	2
Burning pain	1
Weight loss	1
Swallowing problems	1

Musculoskeletal system:

Symptoms	Number of patients who mentioned the symptoms
Bone pain	24
Joint pain	20
Muscle pain	13
Osteoporosis	5
Vertebra fractures	2
Joint stiffness	1
Joint swelling	1
Muscle stiffness	1
Osteosclerosis	1
Back pain	1

Cardiovascular system:

Symptoms	Number of patients who mentioned the symptoms
Tachycardia	23

Shortness of breath	8
Anaphylaxis	7
High blood pressure	5
Circulatory problems	4
Fluctuation in blood pressure	4
Cardiovascular weakness	1

General symptoms:

Symptoms	Number of patients who mentioned the symptoms
Sweating	5
Malaise (flu like symptoms)	5
Asthenia	4
Night sweat	2
Meteor sensitivity (feeling not good around weather changes)	1

Ear nose and throat and breathing organs:

Symptoms	Number of patients who mentioned the symptoms
Enhanced sense of smell and sense of hearing	3
Rhinitis	2
Chronic sinusitis	2
Tinnitus	2
Breathing problems	2
Asthma	1
Bronchospasm	1
Severe mucus production	1
Nose bleeding	1

Symptoms mentioned in the context of temperature:

Symptoms	Number of patients who mentioned the symptoms
Problems with cold and heat	6
Problems with temperature changes	4

Neurology:

Symptoms	Number of patients who mentioned the symptoms
Nerve pain	3
Tingling sensations in arms and legs	3
Muscle twitching	2
Restless legs syndrome	1

Urology:

Symptoms	Number of patients who mentioned the symptoms
Urinating frequently	6

Ophthalmology:

Symptoms	Number of patients who mentioned the symptoms
Blurred vision	3

This is the table of the top 20 symptoms (symptoms which were mentioned most frequent)

1	Pruritus
2	Fatigue
3	Skin lesions
4	Bone pain
5	Headache
6	Tachycardia
7	Joint pain
8	Flushing
9	Diarrhoea
10	Sleeping problems
11	Dizziness
12	Concentration problems
13	GI tract problems
14	Nausea
15	Muscle pain
16	Abdominal pain
17	Memory problems
18	Drowsiness
19	Skin reddening
20	Shortness of breath

2. Hierarchy of symptoms according to frequency and clinical impact

This question is answered in the evaluation of question 1.

3. Classification and Grading of Symptoms: which symptoms can be graded and how could such classification look like?

Symptoms can be graded in severity and frequency:

Severity: 1 - 10

Frequency: always – sometimes - rare

4. What symptoms respond well to therapy / drugs?

- Skin problems
- GI tract problems

5. What symptoms respond well to histamine receptor blockers?

- Skin problems
- GI tract problems

6. Which symptoms respond well to other drugs – and to which drugs?

Pain	Paracetamol
Stomach problems	Proton pump inhibitor
GI tract problems	Cromolyn

7. Which drugs are usually well tolerated and which drugs may be less well tolerated by mastocytosis patients?

Well tolerated are:	Less well tolerated are:
Antihistamines	Aspirin
Paracetamol	NSAID (Ibuprofen)
Proton pump inhibitor	Antibiotics
Cromolyn	Codeine
---	Novalgin

8. How often is an accompanying allergy diagnosed?

Frequency: 32% of patients suffer from one or more allergies

9. Which therapy and management is most helpful in case of a known allergy?

Helpful are:

- Antihistamines
- Avoiding of triggers
- Emergency equipment (Epipen)
- Desensitization

10. Which kind of situations can produce a particular discomfort / insecurity?

- Fear of GI tract reactions (especially if one is not at home or goes out for a meal)
- Fear of reactions which might end up in anaphylaxis
- Uncertainty in regard of cold / heat / temperature changes (sunbathing, fevers, freezer cabinets in supermarkets)
- Fear of facing physicians, paramedics and dentists who do not know anything about mastocytosis
- Fear of treatment errors in emergency rooms and hospitals
- Uncertainty in stressful situations
- Uncertainty due to the cosmetic aspect of the skin spots (especially in summer if one wears swimwear or shorts and a shirt with short sleeves)
- Fear of reactions against medication, vaccinations, local anaesthesia, general anaesthesia, contrast media and prescription of new medication.
- Uncertainty on travels
- Uncertainty of being in community

11. Which symptoms are rare in mastocytosis and which symptoms may not at all be associated with mastocytosis?

It was not possible to evaluate the answers of this question, because so many different answers were given. Many people noted down the symptoms and listed the above as masto symptoms.

<p>Muscle pain, joint pain, bone pain, headache, fatigue, GI tract problems, sinusitis, frequently getting colds, tooth pain, anxiety disorder, depression, aggression, problems of wound healing, muscle twitching, circulatory problems, hypothyroidism, pleural effusion, uterine fibroids, periodontitis, coronary heart disease, heart disease, adrenal insufficiency, sleep problems, restless-legs-syndrome, trigeminal neuralgia, hair loss, tinnitus, hyperhidrosis, sicca-syndrome, temperature discomfort, allergies, skin rash, breathing problems, AML, GIST</p>

B: Laboratory investigations and other tests

1. Are repeated laboratory investigations performed and recommended by the treating physician? Are these tests helpful?

Laboratory investigations on a regular basis: 82.9%

No laboratory investigations: 17.1%

21 Patients say that laboratory investigations are meaningful.

Ultrasound of the abdomen and endoscopies are two investigations which appear to be meaningful to some patients.

2. Which investigations appear to be particularly stressing and/or unjustified?

Investigations which are stressing :	Numbers of patients
No one	29
Bone marrow biopsy	29
Endoscopies	11
Investigations with contrast media	2
Every investigation	2
Skin examination	1
Skin biopsy	1

Investigations which are unjustified :	Numbers of patients
Bone marrow biopsy and endoscopies in skin mastocytosis because there is no change of treatment	2
Monitoring of the skin	1

Comment:

“... the travel to the hospital / health centre is already stressing ...” (NL)

3. How often are serum tryptase levels determined in a patient with mastocytosis?

Once a year: 41.0%
Several times a year: 39.7%
Rarely: 16.7%
Never: 2.6%

4. Are serum tryptase levels usually measured in a certain clinical situation at the time of maximum symptoms? Or at a symptom free interval? Or in both the interval and when symptoms occur?

Routine measurement: 64 persons
Routine and after an episode: 9 persons
I don't know 2 persons
Never 1 person

5. Are other laboratory tests performed to measure mast cell activation?

Laboratory parameter	Numbers of patients
None	54
N-Methyl histamine in urine	2
Histamine in urine	1
Serotonin in blood serum	2
Histamine in blood serum	1

6. Which other laboratory values are recorded?

- Routine laboratory investigation
- Vitamin B12

7. How often is osteoporosis diagnosed and how often are investigations performed to diagnose or exclude osteopathy?

How often is osteoporosis diagnosed?

No Osteoporosis	81.4%
Osteopenia	4.1%
Osteoporosis	10.4%
Osteoporosis with fracture	4.1%

How often are investigations done regarding osteopathy?

Never	41.7%
Just when I ask for them	10.0%
Regular	13.3%
Irregular	35.0%

8. What investigations are recommended to screen for and diagnose osteoporosis?

Examinations	Number of patients
Bone densitometry	28
DEXA	12
qCT	2
Alkaline phosphatase in blood	1
Calcium in urine	1

9. What investigations are required to investigate the GI tract in patients with suspected or known mastocytosis – when are these investigations recommended?

Examinations	Number of patients
Endoscopies	35
Endoscopies are recommended due to GI tract problems	15
No endoscopies recommended	37
Ultrasound	10
MRI	2

10. Is it justified to test all patients for the presence of allergy?

Reasonable	62.7%
Not reasonable	25.3%
I do not know	12.0%

11. What investigations are meaningful in the case of skin involvement? Is photo documentation necessary or justified and are photos taken regularly in practice?

- Photo documentation of the involved skin (done in the majority of patients at least once; Most patients consider this examination as important)
- Skin biopsy
- Darier sign
- Examination of the skin

Comments:

“The skin is not the problem in this disease.” (G)

“Every second year I have a follow up with my dermatologist. He says that the examinations of internal organs are much more important. You ask if the photo documentation is necessary? What do these brownish spots say about the disease?” (NL)

12. Role and importance of follow up investigations?

Follow up investigations are important.

C: Diagnostic problems

1. What are the major diagnostic challenges and problems in mastocytosis?

Problems of the physicians:

- Ignorance of the disease
- Physicians do not look closely enough
- Lack of interdisciplinary cooperation
- False and worthless histopathological examinations of biopsies

Comment:

“... it took 18.5 years until I got the diagnosis. Several disciplines come together in this disease. The specialization of the medical world makes it complicated obtaining a diagnosis because the treating Physician has problems looking closely enough.” (NL)

Problems of the doctor patient relationship

- Patients and their symptoms are not taken seriously
- Symptoms are not provable in most cases
- It is important that Physicians listen

Comment:

“Physicians behave as if they know everything. As soon as the opposite is revealed a person can go from one Physician to another before a diagnosis is reached.” (E)

Problems which are caused by the disease itself

- Rarity
- Diversity (classification, symptoms, organ involvement)
- Lack of a specific marker
- Special problem: no skin lesions

2. Is it justified to define a mast cell activation disease in the absence of classical mastocytosis criteria especially when typical symptoms are present?

Yes	66.7%
I do not know	23.2%
No	10.1%

Comment:

“... Mastocytosis and Mast Cell Activation Disorder are different diseases ...” (G)

3. Should mastocytosis patients always be seen by a physician trained in mastocytosis – or is it sufficient when the treating physician makes contact with a centre of excellence in mastocytosis?

	Number of patients
Experts are important	72
Problem: Consultant never contacts the expert	11
Both the local Physician and the expert are important in treatment	9

Comments:

“Experts cannot perform miracles but they provide clarity.” (NL)

“The expert should be a Haematologist and not a Dermatologist as it is the case currently.”

(E)

“It is important that the disease is not seen as a skin disease.” (UK)

4. Is the current classification sufficient or should the classification be adapted - and if yes should mast cell activation disorders be regarded as a separate entity?

	Number of patients
Extension of the classification according the newest knowledge	30
No extension of the classification	21
Separation of mast cell activation disorder	16
No separation of mast cell activation disorder	5

Comment:

“Each patient is different and everyone should be classified. As soon as every patient is classified, we shall have as many forms of mastocytosis as we have patients.” (E)

5. Should organ involvement be diagnosed and classified separately?

Yes	56.1%
I do not know	7.0%
No	36.9%

Comments:

“... so that the treatment is becoming more specific ...” (E)

“... it depends on the treatment possibility of the different organs ...” (G)

“... it is important, that the synopsis remains in one hand otherwise too many people are involved ...” (A)

6. Is it meaningful to define and to classify atypical symptoms?

Yes	84.0%
I do not know	9.4%
No	5.8%

Comments:

“... yes, because the classification of atypical symptoms makes them less atypical ...” (NL)

“... yes, because the atypical of a rare disease is important to be recognized ...” (E)

7. How could the diagnostics be improved in clinical practice?


- More information for Physicians. (Leaflets, Publications, Databases and improvement of education)
- Patients have to be taken more seriously; improvement of the knowledge of symptoms
- Transfers of patients to experts
- Shipping of biopsies to reference centres in order to have exact examinations and diagnoses
- Improvement of co-operation and communication between physicians (networks)
- It is important that physicians look look more closely
- Less time to diagnosis
- Guidelines for diagnostics
- Find a marker for mastocytosis

Comment:

“... before making the statement ‘no, this does absolutely not belong to mastocytosis’, find out first, if this is true.” (NL)

D: Therapy and Physician’s recommendations

1. How sufficient is patient information regarding: diagnostic procedures, required follow up investigations, prognosis, and therapy options?

	Total result	German result 
Good	48.3%	24.4%
Moderate	4.6%	8.9%
Bad	47.1%	66.7%

“... masto experts do not get out of their limited knowledge of their own discipline...” (G)

“... the treatment is guided by the patient ...” (UK)

“... the information I got from the Dermatologist between 1999 and 2006 was completely useless until the first visit at the Centre of Excellence ...” (E)

2. Are the treating physicians sometimes unable to manage patients with mastocytosis – if yes: how could the situation be improved?

Overwhelmed	78.8%
Sometimes overwhelmed	7.1%
Not overwhelmed	14.4%

Comments:

“... some Physicians pretend to have knowledge albeit they know very little ...” (UK)

“... even those who are knowledgeable do not know the basics i.e. that one can suffer from fatigue ...” (UK)

“... Dermatologists underestimate my disease and are not knowledgeable ...” (E)

“... Staff in emergency rooms are not knowledgeable ...” (E)

“... several times I have experienced that departments in hospitals did not want to treat me because they feared that I could have anaphylaxis.” (NL)

How can the situation be improved?

- Establishing of centres
- Establishing of networks
- Patient transfers to masto experts
- Improvement of education
- Awareness through information: Publications, Leaflets, TV, Internet, Databases, ID card for patients

3. Would a regional or even global patient ID-card be helpful?

Important	88.3%
Unimportant	11.7%

“... I had a bad experience in an emergency room in Spain, because no one spoke English.” (NL)

“... one has to teach the physician in the emergency room which meds can be administered and which ones cannot be administered. It is difficult if Physicians do not have a clue but think they know everything better and, therefore, the situation deteriorates ...” (E)

“... links to good websites would be important ...” (UK)

“... the number of a phone hotline would be important ...” (UK)

“... it would be good if an anaesthesia protocol was added as well as some information about drug and food intolerances ...” (UK)

“... it would be good if information about symptoms and treatment recommendations were included ...” (UK)

4. Is the number of specialized centres in Europe sufficient?

Not sufficient	68.7%
I do not know	26.5%
Sufficient	4.8%

“... some of the so called Centres of Excellence prove being incompetent during visits ...” (G)

5. Is the local medical care for patients with mastocytosis in Europe sufficient?

Bad	55.3%
Good	26.3%
I do not know	18.4%

6. How often is a histamine-poor/free diet recommended?

Not recommended	53.8%
Sometimes recommended	17.9%
Always recommended	28.3%

“... some physicians state that such a diet did not exist ...” (NL)

“... one should just avoid what is not tolerated ...” (A)

7. How important and how effective is diet in mastocytosis/allergy?

Important	67.0 %
I do not know	20.0%
Unimportant	12.3%

“... if I do not keep to the diet my symptoms will increase and so does my bone pain...”(UK)

“... it depends on the amount of histamine containing food one eats ...” (UK)

Conclusions

The evaluation shows the top 10 concerns the patients have. These concerns are compiled in the table below.

Top 10 Issues

1. Improved knowledge of all Physicians and disciplines on mastocytosis
2. ID Card for mastocytosis patients in Europe
3. Better medications for mastocytosis patients
4. Establishing of more Centres of Excellence in Europe
5. Improved knowledge and definition of mediator associated symptoms
6. More mastocytosis experts
7. Better diagnostics
8. More information for patients
9. Extension of the classification
10. Raising awareness via media