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Lymphoma of the Skin Early Detection, Diagnosis, and Staging

Know the signs and symptoms of lymphoma of the skin. Find out how lymphoma of the skin is tested for, diagnosed, and staged.

Detection and Diagnosis

Catching cancer early often allows for more treatment options. Some early cancers may have signs and symptoms that can be noticed, but that is not always the case.

- Can Lymphoma of the Skin Be Found Early?
- Signs and Symptoms of Skin Lymphoma
- Tests for Lymphoma of the Skin

Stages of Skin Lymphoma

After a cancer diagnosis, staging provides important information about the extent of cancer in the body and anticipated response to treatment.

Lymphoma of the Skin Stages

Questions to Ask About Skin Lymphoma

Here are some questions you can ask your cancer care team to help you better understand your diagnosis and treatment options.

Questions to Ask About Lymphoma of the Skin

Can Lymphoma of the Skin Be Found Early?

This type of lymphoma first appears in the skin, so it is usually found earlier in the course of the disease than many other types of cancer. Unfortunately, it is sometimes hard even for experienced doctors to diagnose skin lymphomas right away because they often look like other, more common skin problems such as infections or eczema.

The best approach is to see a doctor if you notice symptoms that might be from a skin lymphoma (or another type of skin cancer). This includes any new lesion (abnormal

Signs and Symptoms of Skin Lymphoma

Lymphomas of the skin can be seen and felt. They can appear as:

- Papules (small, pimple-like lesions)
- Patches (flat lesions)
- Plaques (thick, raised or lowered lesions)
- Nodules or tumors (larger lumps or bumps under the skin)

The lesions are often itchy, scaly, and red to purple. The lymphoma might show up as more than one type of lesion and on different parts of the skin (often in areas not exposed to the sun). Some skin lymphomas appear as a rash over some or most of the body (known as **erythroderma**). Sometimes larger lesions can break open (ulcerate).

Along with skin problems, in rare cases lymphoma of the skin can cause general symptoms, such as:

- Unexplained weight loss
- Fever
- Profuse sweating (enough to soak clothing), particularly at night
- Severe itchiness

Sometimes a skin lymphoma can reach the lymph nodes (small, bean-sized collections of immune cells), which can make them bigger. An enlarged lymph node might be felt as a lump under the skin in the neck, underarm, or groin area.

Most of these symptoms are more likely to be caused by other, less serious conditions. Still, if you have any of them it's important to have them checked by a doctor so that the cause can be found and treated, if needed.

References

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Tests for Lymphoma of the Skin

Because this type of lymphoma affects the skin, it is often noticed fairly quickly. But the actual diagnosis of skin lymphoma might be delayed because the symptoms often resemble other, more common skin problems. The diagnosis of skin lymphoma can only be confirmed with a skin biopsy (described below). Other tests might be needed as well.

- Medical history and physical exam
- Skin biopsies
- Lymph node biopsies
- Other types of biopsies
- Lab tests of biopsy or blood samples
- Blood tests
- Imaging tests

Medical history and physical exam

When a doctor takes your **medical history**, you will be asked about your symptoms, possible <u>risk factors</u>¹, family history, and other medical conditions. The doctor will ask when you first noticed the changes in your skin, if they have changed in size or appearance, and if they are itchy or painful. You may be asked if you have any other symptoms, like fever or weight loss. Because skin lymphomas can be hard to tell apart from allergies and other causes of rashes, you might also be asked if you have any allergies or have recently been exposed to something that could be causing your skin problems, such as a new medicine or a new laundry detergent or any new creams or lotions.

During the **physical exam**, your doctor will note the size, shape, color, and texture of any area(s) of skin in question. Your body will be checked all over for any other abnormal areas on your skin.

The doctor might also feel the lymph nodes (small, bean-sized collections of immune cells) under the skin in your neck, underarms, or groin, as lymphomas can to seg 1 0 0 1 721 0 0 1s.

A <u>biopsy</u>² is a procedure in which a doctor removes a sample of body tissue for viewing under a microscope or other lab tests. A biopsy is needed to diagnose lymphoma of the skin.

There are several types of skin biopsies, and the doctor's choice of which one to use is based on each person's situation. Usually a skin biopsy is done by a dermatologist.

Punch biopsy

For a punch biopsy³, the doctor uses a tool that looks like a tiny round cookie cutter.

Lymph node biopsies

Bone marrow aspiration and biopsy

These tests are sometimes done after lymphoma has been diagnosed to help figure out if it has spread to the bone marrow (the soft, inner part of certain bones). The two tests are often done at the same time. The samples are usually taken from the back of the pelvic (hip) bone, but sometimes they may be taken from other bones.

In **bone marrow aspiration**, you lie on a table (either on your side or on your belly). The doctor cleans the skin over the hip and then numbs the area and the surface of the bone by injecting a local anesthetic. This may cause a brief stinging or burning sensation. A thin, hollow needle is then inserted into the bone, and a syringe is used to suck out a small amount of liquid bone marrow. Even with the anesthetic, most people still have some brief pain when the marrow is removed.

A **bone marrowbiopsy**is usually done just after the aspiration. A small piece of bone and marrow is removed with a slightly larger needle that is pushed down into the bone. This may also cause some brief pain. Once the biopsy is done, pressure will be applied to the site to help stop any bleeding.

Lumbar puncture (spinal tap)

This test looks for lymphoma cells in the cerebrospinal fluid (CSF), which is the liquid that bathes the brain and spinal cord. Most people with skin lymphoma will not need this test. But doctors may order it if a person has symptoms that suggest the lymphoma might have reached the brain.

For this test, you may be asked to lie on your side or sit up. The doctor first numbs an area in the lower part of the back over the spine. A small, hollow needle is then inserted between the bones of the spine to withdraw some of the fluid.

Lab tests of biopsy or blood samples

Lab tests are done on the biopsy samples (and in some cases, blood samples) to help diagnose lymphoma and determine what type it is. Pathologists can sometimes tell which kind of lymphoma a person has by just looking at the cells under a microscope, but usually these other types of tests are needed to confirm the diagnosis.

Flow cytometry and immunohistochemistry

Cells from the biopsy samples are treated with special antibodies that stick to certain proteins on the cells. For immunohistochemistry, the cells are then looked at with a

microscope to see if the antibodies stuck to them (meaning they have these proteins). A special machine (flow cytometer) is used to analyze the cells for a flow cytometry test.

These tests can help tell whether a lymph node is swollen because of lymphoma, some other cancer, or a non-cancerous disease. The tests can also be used for **immunophenotyping** – determining which type of lymphoma a person has, based on certain proteins in or on the cells. Different types of lymphoma cells have different proteins on their surface.

Chromosome and gene tests

Normal human cells have 23 pairs of chromosomes, which are long strands of DNA that contain our genes. Each chromosome is normally a certain size and looks a certain way . But in some types of lymphoma, the cells have changes in their chromosomes, such as having too many, too few, or abnormal chromosomes. These changes can often help identify the type of lymphoma.

Cytogenetics (karyotyping): Cells are looked at with a microscope to see if the chromosomes have any abnormalities. Getting the results usually takes about 2 to 3 weeks because the cells must grow in lab dishes for a couple of weeks before they can be looked at.

Fluorescent in situ hybridization (FISH): This test looks more closely at lymphoma cell DNA using special fluorescent dyes that only attach to specific genes or parts of chromosomes. FISH can find most chromosome changes that can be seen in standard cytogenetic tests, as well as some gene changes too small to be seen with cytogenetic testing. FISH is very accurate and can usually provide results within a couple of days.

Polymerase chain reaction (PCR): PCR is a very sensitive DNA test that can find gene changes and certain chromosome changes too small to be seen with a microscope, even if very few lymphoma cells are present in a sample.

Molecular tests: Some newer types of sensitive lab tests, which can find changes in the DNA, RNA, or proteins in cancer cells, might also be helpful in some situations.

To learn more about these tests, see <u>Tests Used on Biopsy and Cytology Samples to Diagnose and Classify Cancer</u>⁶.

Blood tests

Blood tests⁷ measure the amounts of certain types of cells and chemicals in the blood.

They are not used to diagnose lymphoma usually, but they can sometimes help determine how advanced the lymphoma is. They may also be used during certain types of treatment (such as chemotherapy) to monitor how well the bone marrow and other organs are functioning.

- Complete blood count (CBC): This test measures the levels of different cells in the blood, such as red blood cells, white blood cells, and platelets. The CBC is often done with a differential ("diff"), which counts the numbers of different types of white blood cells. If a person's blood counts are low, it might mean that the lymphoma is growing in the bone marrow and slowing normal blood cell production. People with Sezary syndrome will have Sezary cells in the blood, which can be found on the differential. People getting chemo will have their blood counts checked regularly to see if the treatment is affecting their bone marrow.
- **Blood chemistry tests:** These tests look at how well organs such as the kidneys and liver are working. These tests are also done regularly in people getting chemo.
- If you have been diagnosed with lymphoma, blood levels of lactate dehydrogenase (LDH) may be checked. LDH levels are often abnormally high in people with widespread lymphoma.
- For some types of lymphoma or if certain treatments might be used, your doctor
 may also advise you to have tests to see if you've been infected with certain
 viruses, such as hepatitis B virus (HBV), hepatitis C virus (HCV), human T-cell
 lymphotropic virus (HTLV-1), or human immunodeficiency virus (HIV).
 Infections with these viruses might affect your treatment.

Imaging tests

Imaging tests use x-rays, sound waves, magnetic fields, or radioactive particles to make pictures of the inside of the body. In someone with known or suspected lymphoma, these tests might be done for a number of reasons, including:

- To help find suspicious areas that might be cancer
- To learn how far the lymphoma has spread
- To find out if treatment is working
- To look for possible signs of the lymphoma coming back after treatment

Imaging tests aren't always needed for people with skin lymphomas who have only a few skin lesions, but they are often done if a lot of the skin is affected, or if lymphoma cells are found in the lymph nodes or blood.

To learn more about any of the imaging tests discussed here, see <u>Imaging (Radiology)</u> Tests⁹.

Chest x-ray

An x-ray of the chest may be done to look for enlarged lymph nodes in this area.

Computed tomography (CT) scan

The <u>CT scan</u>¹⁰ uses x-rays to make detailed, cross-sectional images of your body. Unlike a regular x-ray, CT scans can show the detail in soft tissues (such as internal organs). This scan can help tell if any lymph nodes or organs in your body are enlarged.

CT-guided needle biopsy: ACT scan can also be used to guide a biopsy needle into a suspicious area. For this procedure, you lie on the CT scanning table while the doctor advances the needle through the skin and toward the area. The scans are repeated until the needle is in the right place. A biopsy sample is then removed and sent to the lab to be looked at under a microscope.

Magnetic resonance imaging (MRI) scan

Like CT scans, MRI scans¹¹ show detailed images of soft tissues in the body. But MRI scans use radio waves and strong magnets instead of x-rays. MRI scans are very helpful in looking at the brain and spinal cord, but they are not often used to evaluate skin lymphomas unless a CT scan can't be done for some reason.

Ultrasound

<u>Ultrasound</u>¹² can be used to look at lymph nodes near the surface of the body or to look inside your abdomen for enlarged lymph nodes or organs such as the liver and spleen. (It's harder to use it to look at organs or lymph nodes in the chest because the ribs block the sound waves.)

This test is easy to have, and it uses no radiation. You simply lie on a table, and a

For a <u>PET scan</u>¹³, you are injected with a slightly radioactive form of sugar, which collects mainly in cancer cells. A special camera is then used to create a picture of areas of radioactivity in the body. The picture isn't detailed like a CT or MRI scan, but it can show possible areas of lymphoma in all areas of the body at once.

A PET scan can help tell if an enlarged lymph node contains lymphoma or is benign. It can also help spot small areas that might be lymphoma, even if the area looks normal on a CT or MRI scan.

PET scans can also be used to tell if an advanced skin lymphoma is responding to treatment. Some doctors will repeat the PET scan after a few courses of chemotherapy. If the chemo is working, the abnormal areas will no longer take up the radioactive sugar.

Doctors often use a machine that does both a PET and CT scan at the same time (**PET/CT scan**). This lets the doctor compare areas of higher radioactivity on the PET scan with the more detailed appearance of that area on the CT scan.

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/skin-lymphoma/causes-risks-prevention/risk-factors.html</u>
- 2. www.cancer.org/cancer/diagnosis-staging/tests/biopsy-and-cytology-tests.html
- 3. <u>www.cancer.org/cancer/types/skin-cancer/skin-biopsy-treatment-procedures/punch-biopsy.html</u>
- 4. <u>www.cancer.org/cancer/types/skin-cancer/skin-biopsy-treatment-procedures/standard-local-excision.html</u>
- 5. www.cancer.org/cancer/types/skin-cancer.html
- 6. <u>www.cancer.org/cancer/diagnosis-staging/tests/biopsy-and-cytology-tests/testing-biopsy-and-cytology-samples-for-cancer/special-tests.html</u>
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- 8. www.cancer.org/cancer/types/skin-lymphoma/about/types-of-skin-lymphoma.html
- 9. <u>www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/imaging-radiology-tests-for-cancer.html</u>
- 10. www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/ct-scan-for-cancer.html
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How is the stage determined?

The tests used to gather information for staging include:

- Physical exam
- Biopsies
- Imaging tests, such as CT scans
- Blood tests

These tests are described in Tests for Lymphoma of the Skin.

The staging systems for skin lymphomas were developed by the International Society for Cutaneous Lymphomas (ISCL) and the European Organization for Research and Treatment of Cancer (EORTC). There are 2 different staging systems:

- One for mycosis fungoides and Sezary syndrome
- One for other skin lymphomas

These systems can be hard to understand. If you have questions about the stage of your lymphoma, ask your cancer care team to explain it to you in a way you understand. This can help you make choices about your treatment.

Staging for mycosis fungoides and Sezary syndrome

Mycosis fungoides (MF) and Sezary syndrome (SS) are staged based on 4 factors:

- T describes how much of the skin is affected by the lymphoma (tumor).
- N describes the extent of the lymphoma in the lymph **nodes** (bean-sized collections of immune cells).
- **M** is for the spread (**metastasis**) of the lymphoma to other organs.
- B is for lymphoma cells in the blood.

T categories

T1: Skin lesions can be small patches (flat lesions), papules (small bumps), and/or plaques (raised or lowered, flat lesions), but the lesions cover less than 10% of the skin surface.

T2: The patches, papules, and/or plaques cover 10% or more of the skin surface.

T3: At least one of the skin lesions is a tumor (a lesion growing deeper into the skin) that is at least 1 centimeter (cm) (a little less than 1/2 inch) across.

T4: The skin lesions have grown together to cover at least 80% of the skin surface.

N categories

N0: Lymph nodes are not enlarged and a lymph node biopsy is not needed.

N1: Lymph nodes are enlarged, but the patterns of cells look normal or close to normal under the microscope.

N2: Lymph nodes are enlarged, and the patterns of cells look more abnormal under the microscope.

N3: Lymph nodes are enlarged, and the patterns of cells look very abnormal under the microscope.

NX: Lymph nodes are enlarged but haven't been removed (biopsied) to be looked at under the microscope.

M categories

M0: The lymphoma cells have not spread to other organs.

M1: Lymphoma cells have spread to other organs, such as the liver or spleen.

B categories

B0: No more than 5% of lymphocytes in the blood are Sezary (lymphoma) cells.

B1: Low numbers of Sezary cells in the blood (more than in B0 but less than in B2).

B2: High number of Sezary cells in the blood.

Stage grouping

Once the values for T, N, M, and B are known, they are combined to determine the overall stage of the lymphoma. This process is called **stage grouping**.

Mycosis fungoides (MF) and Sezary syndrome (SS) stages range from I (1) through IV (4). As a rule, the lower the number, the less the cancer has spread. A higher number, such as stage IV, means cancer has spread more. And within a stage, an earlier letter means a lower stage. Although each person's cancer experience is unique, cancers with similar stages tend to have a similar outlook and are often treated in much the same way.

Stage IA: T1, N0, M0, B0 or B1

There are skin lesions but no tumors. Skin lesions cover less than 10% of the skin surface (T1), the lymph nodes are not enlarged (N0), lymphoma cells have not spread to other organs (M0), and the number of Sezary cells in the blood is not high (B0 or B1).

Stage IB: T2, N0, M0, B0 or B1

There are skin lesions but no tumors. Skin lesions cover at least 10% of the skin surface (T2), the lymph nodes are not enlarged (N0), lymphoma cells have not spread to other organs (M0), and the number of Sezary cells in the blood is not high (B0 or B1).

Stage IIA: T1 or T2, N1 or N2, M0, B0 or B1

There are skin lesions but no tumors. Skin lesions can cover up to 80% of the skin surface (T1 or T2). Lymph nodes are enlarged but the patterns of cells do not look very abnormal under the microscope (N1 or N2). Lymphoma cells have not spread to other organs (M0), and the number of Sezary cells in the blood is not high (B0 or B1).

Stage IIB: T3, N0 to N2, M0, B0 or B1

At least one of the skin lesions is a tumor that is 1 cm across or larger (T3). The lymph nodes are either normal (N0) or are enlarged but the patterns of cells do not look very abnormal under the microscope (N1 or N2). Lymphoma cells have not spread to other organs (M0), and the number of Sezary cells in the blood is not high (B0 or B1).

Stage IIIA: T4, N0 to N2, M0, B0

Skin lesions cover at least 80% of the skin surface (T4). The lymph nodes are either normal (N0) or are enlarged but the patterns of cells do not look very abnormal under the microscope (N1 or N2). Lymphoma cells have not spread to other organs or tissues (M0), and no more than 5% of the lymphocytes in the blood are Sezary cells (B0).

Stage IIIB: T4, N0 to N2, M0, B1

Skin lesions cover at least 80% of the skin surface (T4). The lymph nodes are either normal (N0) or are enlarged but the patterns of cells do not look very abnormal under the microscope (N1 or N2). Lymphoma cells have not spread to other organs (M0), and the number of Sezary cells in the blood is low (B1).

Stage IVA₁: Any T, N0 to N2, M0, B2

Skin lesions can cover any amount of the skin surface (any T). The lymph nodes are either normal (N0) or are enlarged but the patterns of cells do not look very abnormal under the microscope (N1 or N2). Lymphoma cells have not spread to other organs (M0), and the number of Sezary cells in the blood is high (B2).

Stage IVA2: Any T, N3, M0, any B

Skin lesions can cover any amount of the skin surface (any T). Some lymph nodes are enlarged and the patterns of cells look very abnormal under the microscope (N3). Lymphoma cells have not spread to other organs (M0). Sezary cells may or may not be in the blood (any B).

Stage IVB: Any T, any N, M1, any B

Skin lesions can cover any amount of the skin surface (any T). The lymph nodes may be normal or abnormal (any N), and Sezary cells may or may not be in the blood (any B). Lymphoma cells have spread to other organs, such as the liver or spleen (M1).

Staging for other skin lymphomas

The staging system for types of skin lymphoma other than mycosis fungoides and Sezary syndrome is still fairly new, and doctors are still trying to determine how useful it is. The system is based on 3 factors:

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lymphoma progresses (continues to grow) during treatment or comes back after treatment.

T categories

T1: There is only a single skin lesion.

- T1a: The skin lesion is less than 5 cm (about 2 inches) across.
- T1b: The skin lesion is at least 5 cm across.

T2: There are 2 or more lesions on the skin. These may be in a single body region or in 2 body regions that are next to each other.

- **T2a:** All of the skin lesions could be placed within a circle that is 15 cm (about 6 inches) across.
- **T2b:** The circle needed to surround all of the skin lesions is larger than 15 cm across, but smaller than 30 cm (about 1 foot) across.
- T2c: The circle needed to surround all of the skin lesions is larger than 30 cm across.

T3: There are skin lesions in body regions that aren't next to each other, or in at least 3 different body regions.

- T3a: There are skin lesions involving 2 body regions that aren't next to each other.
- T3b: There are skin lesions involving 3 or more body regions.

N categories

N0: No lymph nodes are enlarged or contain lymphoma cells.

N1: There are lymphoma cells in the lymph nodes that drain an area where skin contained lymphoma.

N2: One of the following is true:

- At least 2 sets of lymph nodes from different areas contain lymphoma cells
- There are lymphoma cells in lymph nodes that do not drain areas where the skin contained lymphoma.

N3: Lymph nodes deep inside the chest or abdomen contain lymphoma cells.

M categories

M0: No signs of lymphoma outside of the skin or lymph nodes.

M1: Lymphoma has spread to other organs or tissues.

This system does not assign an overall stage to the lymphoma, like the system for mycosis fungoides/Sezary syndrome does. Because this system is still fairly new, it's not yet clear how well it can help predict a person's prognosis (outlook).

Hyperlinks

- 1. www.cancer.org/cancer/types/skin-lymphoma/treating.html
- 2. www.cancer.org/cancer/types/non-hodgkin-lymphoma.html

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American Joint Committee on Cancer. Primary Cutaneous Lymphomas. In: *AJCC Cancer Staging Manual*. 8th ed. New York, NY: Springer; 2017: 967-972.

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Questions to Ask About Lymphoma of the Skin

It's important to have honest, open discussions with your cancer care team. They want to answer all of your questions, no matter how minor they might seem. For instance, consider asking these questions:

- When you're told you have lymphoma of the skin
- When deciding on a treatment plan
- During treatment
- After treatment

When you're told you have lymphoma of the skin

- What kind of skin lymphoma¹ do I have?
- Has my biopsy been reviewed by a pathologist who is an expert on skin lymphoma?
- How sure are you of my diagnosis?
- What is the stage (extent) of the lymphoma, and what does that mean in my case?
- Do I need any other tests before we can decide on treatment?
- Do I need to see any other types of doctors?
- If I'm concerned about the costs and insurance coverage for my diagnosis and treatment, who can help me?

When deciding on a treatment plan

- How much experience do you have treating this type of lymphoma?
- Should I get a <u>second opinion</u>² before starting treatment? Can you suggest a doctor or cancer center?
- What are my <u>treatment choices</u>³?
- What do you recommend and why?
- Do we need to treat the lymphoma right away?
- What is the goal of the treatment?
- What should I do to be ready for treatment?
- How long will treatment last? What will it be like? Where will it be done?
- What are the risks or side effects⁴ of the treatments you suggest?
- How will treatment affect my daily activities?
- What is my outlook for survival?
- What are the chances of the lymphoma coming back with these treatment plans?
- What would we do if the treatment doesn't work or <u>if the lymphoma recurs</u>⁵?

During treatment

Once treatment begins, you'll need to know what to expect and what to look for. Not all of these questions may apply to you, but getting answers to the ones that do may be helpful.

- How will we know if the treatment is working?
- Is there anything I can do to help manage side effects?
- What symptoms or side effects should I tell you about right away?
- How can I reach your office on nights, holidays, or weekends?
- Are there any limits on what I can do?
- Can you suggest a mental health professional I can see if I start to feel overwhelmed, depressed, or distressed?

After treatment

- What type of <u>follow-up</u>⁶ will I need after treatment?
- What symptoms should I watch for?
- How will we know if the lymphoma has come back? What would my options be if that happens?

Along with these sample questions, be sure to write down some of your own. For instance, you might want more information about recovery times so that you can plan your work or activity schedule. Or you might ask about <u>clinical trials</u>⁷.

Keep in mind that doctors aren't the only ones who can give you information. Other health care professionals, such as nurses and social workers, might be able to answer some of your questions. See The Doctor-Patient Relationship⁸.

Hyperlinks

- 1. www.cancer.org/cancer/types/skin-lymphoma/about/types-of-skin-lymphoma.html
- 2. <u>www.cancer.org/cancer/managing-cancer/finding-care/seeking-a-second-opinion.html</u>
- 3. www.cancer.org/cancer/types/skin-lymphoma/treating.html
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- 7. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>
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