Multiple Myeloma Early Detection, Diagnosis, and Staging

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 Multiple Myeloma Be Found Early?
- Signs and Symptoms of Multiple Myeloma
- Tests to Find Multiple Myeloma

Stages and Outlook (Prognosis)

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

- Multiple Myeloma Stages
- Survival Rates for Multiple Myeloma

Questions to Ask About Multiple Myeloma

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 Multiple Myeloma

Can Multiple Myeloma Be Found Early?

It's difficult to diagnose multiple myeloma early. Often, multiple myeloma causes no symptoms until it reaches an advanced stage. Sometimes, it might cause vague symptoms that at first seem to be caused by other diseases. Sometimes, multiple myeloma is found early when a routine blood test shows an abnormally high amount of protein in the blood.

People with MGUS (monoclonal gammopathy of unknown significance) or solitary plasmacytoma are at risk of developing multiple myeloma and have regular bloodwork to monitor for it. Multiple myeloma may be diagnosed sooner in those people than those who did not have MGUS or a solitary plasmacytoma.

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Signs and Symptoms of Multiple Myeloma

Some patients with multiple myeloma have no symptoms at all. Others can have common symptoms of the disease including:

Bone problems

- Bone pain, which can be in any bone, but is most often in the back, the hips, and skull
- Bone weakness, either all over (osteoporosis), or where there is a plasmacytoma
- Broken bones (fractures), sometimes from only a minor stress or injury

Low blood counts

Shortages of red blood cells, white blood cells, and blood platelets are common in multiple myeloma and might lead to other symptoms.

- Anemia: A reduced number of red blood cells that can cause weakness, a reduced ability to exercise, shortness of breath, and dizziness.
- Leukopenia: Too few white blood cells that can lower resistance to infections such as pneumonia.
- Thrombocytopenia: When blood platelet counts are low which may cause serious bleeding even with minor scrapes, cuts, or bruises. .

High blood levels of calcium

High levels of calcium in the blood (called **hypercalcemia**) can cause:

- Extreme thirst, leading to drinking a lot
- Urinating (peeing) a lot
- Dehydration
- Kidney problems and even kidney failure
- Severe constipation,
- Abdominal (belly) pain
- Loss of appetite
- Weakness
- Feeling drowsy
- Confusion

If the level of calcium gets high enough, you can even slip into a coma.

Nervous system symptoms

If myeloma weakens the bones in the spine, they can collapse and press on spinal nerves. This is called **spinal cord compression** and can cause

- Sudden severe back pain
- Numbness, most often in the legs
- Muscle weakness, most often in the legs.

This is a medical emergency and you should contact your doctor right away or go to the emergency room. If spinal cord compression is not treated right away, there is a possibility of permanent paralysis.

Nerve damage

Sometimes, the abnormal proteins produced by myeloma cells are toxic to nerves. This damage can lead to weakness and numbness and sometimes a “pins and needles” sensation. This is also called peripheral neuropathy.

Hyperviscosity

In some patients, large amounts of myeloma protein can cause the blood to “thicken.” This thickening is called **hyperviscosity**. It can slow blood flow to the brain and cause:

- Confusion
- Dizziness
- Symptoms of a stroke, like weakness on one side of the body and slurred speech

Patients with these symptoms should call their doctor. Removing the protein from the blood using a procedure called plasmapheresis can rapidly reverse this problem. (Note: This is not something that can be treated with drugs known as “blood thinners.”)

Kidney problems

Myeloma protein can damage the kidneys. Early on, this doesn’t cause any symptoms, but signs of kidney damage may be seen on a blood test or a urine test. As the kidneys

start to fail, they lose the ability to get rid of excess salt, fluid, and body waste products. This can lead to symptoms such as:

- Weakness
- Shortness of breath
- Itching
- Leg swelling.

Infections

Myeloma patients are much more likely to get infections. When someone with myeloma gets an infection, they may be slow to respond to treatment. That person may stay sick for a long time. Pneumonia is a common and serious infection seen in myeloma patients.

Signs and symptoms of light chain amyloidosis

Patients with amyloidosis (discussed in What Is Multiple Myeloma?[1]) can have some of the same problems as patients with myeloma, such as kidney problems and nerve damage. They can also have other problems, such as:

- **Heart problems**: The heart may enlarge and become weaker. In some people, the heart becomes so weak that fluid builds up in the lungs, making them feel short of breath. Fluid may also build up in the legs and feet (edema). This is called congestive heart failure.
- **Enlarged liver**: The person may feel the liver below the right ribs. When this gets large it can press on the stomach so the person feels full after eating only a small amount of food.
- **Enlarged tongue**: When amyloid builds up in the tongue it can get larger. This can lead to problems swallowing and problems breathing during sleep (sleep apnea).
- **Skin changes**: Changes in the color or texture, easy bruising, and bleeding into the skin around the eyes (“raccoon eyes”)
- **Kidney problems**
- **Carpal tunnel syndrome**: Which causes numbness and weakness in the hands.

Hyperlinks

1. www.cancer.org/cancer/multiple-myeloma/about/what-is-multiple-myeloma.html

References

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Tests to Find Multiple Myeloma

If symptoms suggest that a person might have multiple myeloma, more tests are done.

Lab tests

Blood counts

The complete blood count[1] (CBC) is a test that measures the levels of red cells, white cells, and platelets in the blood. If there are too many myeloma cells in the bone marrow, some of these blood cell levels can be low. The most common finding is a low red blood cell count (anemia[2]).

Blood chemistry tests

Levels of blood creatinine, albumin, calcium, and other electrolytes will be checked.

- Creatinine levels show how well your kidneys are working. High levels mean that the kidneys are not functioning well. This is common in people with myeloma.
- Albumin is a protein found in the blood. Low levels can be seen in myeloma.

- Calcium levels may be high in people with advanced myeloma. High calcium levels (hypercalcemia) can cause symptoms of fatigue, weakness, and confusion.

A blood test to measure lactic dehydrogenase (LDH) levels might also be done. It can be a useful indicator of a patient's prognosis (outlook). High levels mean the disease is more advanced and may have a worse prognosis.

Urine tests

A routine urine sample is typically taken to look for myeloma protein that has filtered through the kidney. You most likely also will be asked to give a sample of urine that has been collected over a 24-hour period, so it can measure how much myeloma protein is present. These tests are called urine protein electrophoresis (UPEP) and urine immunofixation.

Quantitative immunoglobulins

This test measures the blood levels of the different antibodies (also called immunoglobulins). There are several different types of antibodies in the blood: IgA, IgD, IgE, IgG, and IgM. The levels of these immunoglobulins are measured to see if any are abnormally high or low. In multiple myeloma, the level of one type may be high while the others are low.

Electrophoresis

The antibody produced by myeloma cells is abnormal because it is monoclonal (all the exact same). Serum protein electrophoresis (SPEP) is a test that measures the antibodies in the blood and can find a monoclonal antibody. Another test, called immunofixation or immunoelectrophoresis, is used to determine the exact type of abnormal antibody (IgG. IgA or some other type). Finding a monoclonal antibody in the blood may be the first step in diagnosing multiple myeloma. This abnormal protein is known by several different names, including **monoclonal immunoglobulin**, **monoclonal protein (M protein*)***, **M spike**, or **paraprotein**.

Antibodies are made up of chains of protein : 2 long (heavy) chains and 2 shorter (light) chains. Sometimes pieces of the abnormal myeloma protein are filtered through the kidney into the urine. This urine protein, known as **Bence Jones protein**, is the part of the antibody called the light chain. The tests used for finding a monoclonal antibody in urine are called urine protein electrophoresis (UPEP) and urine immunofixation. These are done most often on urine that has been collected over a 24-hour period, not just on

a routine urine sample.

Serum free light chains

This blood test can measure the light chain levels in the blood and is done when looking for myeloma or light chain amyloidosis.

This is most helpful in the rare cases of myeloma in which no M protein is found by SPEP. Since the SPEP measures the levels of intact (whole) antibodies, it cannot measure the amount of light chains only.

This test also calculates thelight chain ratio which is used to see if there is one type of light chain more than the other. There are 2 kinds of light chains: kappa and lambda. Normally, they are present in equal amounts in the blood, giving a ratio of 1 to 1. If there is more of one type of light chain than the other, the ratio will be different, which can be a sign of myeloma.

Beta-2 microglobulin

This is another protein made by the myeloma cells. Although this protein itself doesn't cause problems, it can be a useful indicator of a patient's prognosis (outlook). High levels mean the disease is more advanced and may have a worse prognosis.

Types of Biopsies

Bone marrow biopsy

People with multiple myeloma have too many plasma cells in their bone marrow. The procedure used to check the bone marrow is called a **bone marrow biopsy** and **aspiration**. It can be done either at the doctor's office or at the hospital.

In bone marrow aspiration, the back of the pelvic bone is numbed with local anesthetic. Then, a needle is inserted into the bone, and a syringe is used to remove a small amount of liquid bone marrow. This causes a brief sharp pain. For the biopsy, a needle is used to remove a tiny splinter of bone and marrow. Patients may feel some pressure during the biopsy. There is some soreness in the biopsy area when the numbing medicine wears off. Most patients can go home immediately after the procedure.

The bone marrow tissue is examined in the lab to see the appearance, size, and shape of the cells, how the cells are arranged and to determine if there are myeloma cells in

the bone marrow and, if so, how many. The aspirate (the liquid part of the bone marrow) may also be sent for other tests, including immunohistochemistry and flow cytometry, and chromosome analyses, including karyotype and fluorescent in situ hybridization (also known as FISH).

- **Immunohistochemistry:** a part of the biopsy sample is treated with special proteins which cause color changes and help identify myeloma cells.
- **Flow cytometry:** A sample of bone marrow is treated with special proteins that stick only to certain cells. This can help determine if those cells are abnormal and if they are myeloma cells, lymphoma cells, some other cancer, or a non-cancerous disease.

- **Cytogenetics:** A test that evaluates chromosomes (long strands of DNA) in normal bone marrow cells and myeloma cells. Some myeloma cells may have too many chromosomes, too few chromosomes, or other chromosome abnormalities (such as translocations and deletions). Finding these changes can sometimes help in to predicting a person's prognosis (outlook). Cytogenetic testing usually takes about 2 to 3 weeks to get a result.

- **Fluorescent in situ hybridization (FISH):** It uses special fluorescent dyes that only attach to specific parts of chromosomes. It can find most chromosome changes (such as translocations and deletions) that can be seen in the lab in standard cytogenetic tests, as well as some changes too small to be seen with usual cytogenetic testing. It's very accurate and results are often available within a couple of days.

Fine needle aspiration biopsy

Fine needle aspiration (FNA) uses a very thin needle and a syringe to withdraw a small amount of tissue from a tumor or lymph node. The doctor can aim the needle while feeling an enlarged lymph node near the surface of the body. If the abnormal area (tumor) is deep in the body, the needle can be guided while it's watched on a computed tomography (CT) scan (see discussion of imaging tests later in this section). The main advantage of FNA is that it doesn't require surgery. The disadvantage is that in some cases the thin needle cannot remove enough tissue for a definite diagnosis.

Core needle biopsy

This test is similar to FNA, but a larger needle is used and a larger tissue sample is removed.

If an area looks abnormal on an x-ray, a biopsy may be needed to confirm that it's a plasmacytoma. Most often, a needle biopsy (fine or core) is used.

Imaging tests

Imaging tests[3] use sound waves, x-rays, magnetic fields, or radioactive substances to create pictures of the inside of your body. Imaging tests may be done for a number of reasons, such as:

- To look at suspicious areas that might be cancer
- To learn how far cancer has spread
- To help determine if treatment is working

Bone x-rays

X-rays can detect bone destruction caused by the myeloma cells. Often doctors will do a series of x-rays that includes most of the bones. This is called a **bone survey** or **skeletal survey**.

CT scan (Computed tomography scan)

A CT scan uses x-rays taken from different angles, which are combined by a computer to make detailed pictures of the organs. Sometimes, this test can help tell if your bones have been damaged by myeloma. It can also be used to guide a biopsy needle into an area of concern.

Magnetic resonance imaging (MRI) scans

Like CT scans, MRI scans show detailed images of soft tissues in the body. But MRI scans use radio waves and strong magnets instead of x-rays. A contrast material called gadolinium may be injected into a vein before the scan to see details better.

MRI scans are very helpful in looking at bones, the brain, and the spinal cord. Because MRI can find plasmacytomas that can't be seen on regular x-rays, they can be helpful if the patient has pain in a bone but nothing abnormal is seen on the x-ray. MRI can also be used to look at the bone marrow in patients with multiple myeloma.

Positron emission tomography (PET) scans

For this test, a form of radioactive sugar is put into a vein and travels throughout the body. Cancer cells absorb high amounts of this sugar. A special camera then takes pictures that show the areas where the sugar collected throughout the body. A PET scan is often combined with a CT scan (known as a **PET/CT scan**).

When a patient appears to have a solitary plasmacytoma, a PET scan may be used to look for other plasmacytomas. Like MRI scans, PET scans can find plasmacytomas that can't be seen on regular x-rays, so they are helpful if the patient has pain in a bone but the x-ray result is negative.

Echocardiogram (ECHO)

Amyloidosis often affects the heart, so if your doctor diagnoses or suspects you have this disorder, an echocardiogram (ECHO) may be ordered. This test is basically an ultrasound of the heart. It uses sound waves to look at the heart muscle and how well it's working. The echocardiogram can see if the heart size is normal and if it is pumping normally. It also is especially helpful if amyloid is suspected because amyloid in the heart muscle looks different from normal heart muscle.

Diagnosing Multiple Myeloma

Multiple myeloma is often diagnosed based on tests, the patient's symptoms and the doctor's physical exam of the patient. A diagnosis of multiple myeloma requires either:

1. A plasma cell tumor (proven by biopsy) OR at least 10% plasma cells in the bone marrow AND

2. At least one of the following:

- High blood calcium level
- Poor kidney function
- Low red blood cell counts (anemia)
- Holes in the bones from tumor found on imaging studies (CT, MRI, PET scan)
- Increase in one type of light chain in the blood so that one type is 100 times more common than the other
- 60% or more plasma cells in the bone marrow

Smoldering myeloma

This term is used to mean early myeloma that is not causing any symptoms. People with smoldering myeloma have some signs of multiple myeloma, such as any of the following:

- Plasma cells in the bone marrow between 10% and 60%
- High level of monoclonal immunoglobulin (M protein) in the blood
- High level of light chains in the urine (also called Bence Jones protein)

But they have normal blood counts, normal calcium levels, normal kidney function, no bone or organ damage, and no signs of amyloidosis.

Light chain amyloidosis

A diagnosis of light chain amyloidosis is made when the patient has ALL of the following:

- Signs and symptoms of amyloidosis
- A biopsy that shows amyloid in any tissue (fat, bone marrow, or organ such as the heart)
- A positive test showing the amyloid protein is a light chain and not a heavy chain
- Abnormal plasma cells in the bone marrow, high levels of M protein in the blood, or high levels of M protein in the urine.

Amyloid can build up in any tissue, and a biopsy may be able to diagnose this disease. Sometimes it can be seen on a bone marrow biopsy. The biopsy done most often to look for amyloid uses a needle to remove some fat from the wall of the abdomen (belly). This is after the skin over the biopsy site is numbed with medicine. A doctor uses a special stain on the removed fat to look for amyloid.

Because amyloid often affects the heart and kidneys, they may also be biopsied to look for amyloid. This is rarely needed to find out if a patient has light chain amyloidosis, but it is sometimes done in someone with amyloid if it isn't clear that their heart or kidney problems are caused by the amyloid or some other problem.

Other tests are often done as well, to help confirm that the patient has light chain amyloidosis and not some other kind. These include a bone marrow biopsy, serum free light chains, and electrophoresis of the urine (these were discussed earlier in this

section).

Hyperlinks

1. www.cancer.org/treatment/understanding-your-diagnosis/tests/understanding-your-lab-test-results.html
2. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/low-blood-counts/anemia.html
3. www.cancer.org/treatment/understanding-your-diagnosis/tests/imaging-radiology-tests-for-cancer.html

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Multiple Myeloma Stages

After someone is diagnosed with cancer, doctors will try to figure out if it has spread, and if so, how far. This process is called **staging**. The stage of a cancer describes how much cancer is in the body. It helps determine how serious the cancer is and how best to treat[1] it. Doctors also use a cancer's stage when talking about survival statistics.

The Revised International Staging System

Multiple myeloma is staged using the Revised International Staging System (RISS) based on 4 factors:

- The amount of albumin in the blood
- The amount of beta-2-microglobulin in the blood
- The amount of LDH in the blood
- The specific gene abnormalities (cytogenetics) of the cancer.

RISS Stage Group	Factors
I	Serum beta-2 microglobulin is less than 3.5 (mg/L) **AND** Albumin level is 3.5 (g/dL) or greater **AND** Cytogenetics are considered “not high risk” * **AND** LDH levels are normal
II	Not stage I or III
III	Serum beta-2 microglobulin is 5.5 (mg/L) or greater **AND** Cytogenetics are considered “high-risk”*

	AND/OR LDH levels are high

*The bone marrow may be sent for tests to look at the chromosomes in the cancer cells. This test may also be called **cytogenetics**. Certain chromosome changes can mean a poorer outlook. For example, loss of a piece of chromosome 17 is linked to a poorer outcome. Another genetic abnormality that predicts a poor outcome is an exchange of material from chromosomes 4 and 14. This is called a **translocation**. A translocation involving chromosomes 14 and 16 is also linked to a poorer outcome. These 3 specific chromosome changes are considered**high risk**. Other chromosome abnormalities are considered **standard risk** or not high risk.

Cancer staging can be complex, so ask your doctor to explain it to you in a way you understand.

Factors other than stage that affect survival

Kidney function

The blood creatinine level shows how healthy the kidneys are. Kidneys eliminate this chemical from the body. When they are damaged by the monoclonal immunoglobulin, blood creatinine levels rise, predicting a worse outlook.

Age

Age is also important. In the studies of the international staging system, older people with myeloma do not live as long.

Overall Health

Overall health can affect the outlook of someone with myeloma. Poorly controlled health conditions, such as diabetes or heart disease, for example, can predict a worse prognosis.

Hyperlinks

1. www.cancer.org/cancer/multiple-myeloma/treating.html

References

American Joint Committee on Cancer. Plasma Cell Myeloma and Plasma Cell Disorders. In: *AJCC Cancer Staging Manual*. 8th ed. New York, NY: Springer; 2017:973.

Greipp PR, San Miguel J, Durie BG, et al. International staging system for multiple myeloma. *J Clin Oncol.* 2005;23(15):3412-3420.

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Survival Rates for Multiple Myeloma

Survival rates tell you what percentage of people with the same type and stage of cancer are still alive a certain amount of time (usually 5 years) after they were diagnosed. They can't tell you how long you will live, but they may help give you a better understanding about how likely it is that your treatment will be successful.

Keep in mind that survival rates are estimates and are often based on previous outcomes of large numbers of people who had a specific cancer, but they can't predict what will happen in any particular person's case. These statistics can be confusing and may lead you to have more questions. Ask your doctor, whois familiar with your situation, how these numbers may apply to you.

What is a 5-year relative survival rate?

A **relative survival rate** compares people with the same type and stage of cancer to people in the overall population. For example, if the **5-year relative survival rate** for a specific stage of multiple myeloma is 60%, it means that people who have that cancer are, on average, about 60% as likely as people who don't have that cancer to live for at least 5 years after being diagnosed.

Where do these numbers come from?

The American Cancer Society relies on information from the Surveillance, Epidemiology, and End Results (SEER) database, maintained by the National Cancer Institute (NCI), to provide survival statistics for different types of cancer.

The SEER database tracks 5-year relative survival rates for myeloma in the United States, based on how far the cancer has spread. The SEER database, however, does not group cancers by the Revised International Staging System (stage 1, stage 2, or

stage 3). Instead, it groups cancers into localized, regional, and distant stages:

- **Localized:** Only one tumor (a solitary plasmacytoma[1]) is growing in the bone or outside the bone.
- **Regional:** This stage does not apply to myeloma, because this type of cancer does not spread to the lymph nodes.

- **Distant:** Many tumors are found inside or outside the bones, or multiple myeloma has been diagnosed.

5-year relative survival rates for myeloma

These numbers are based on people diagnosed with plasmacytomas or multiple myeloma between 2012 and 2018.

SEER Stage	5-year Relative Survival Rate
Localized (solitary plasmacytoma)	79%
Regional	Not applicable
Distant (multiple myeloma)	57%
All SEER stages combined	58%

Understanding the numbers

- **These numbers don't take everything into account.** Survival rates for myeloma are generally based on if a single plasmacytoma is found or if multiple myeloma is diagnosed. But other factors, such as the tumor's cytogenetics (chromosome changes), the levels of certain proteins and other substances in the blood, your kidney function, and your age and overall health, can also affect your outlook.
- **People now being diagnosed with myeloma may have a better outlook than these numbers show.** Treatments have improved over time, and these numbers are based on people who were diagnosed and treated at least 5 years earlier.

Hyperlinks

1. www.cancer.org/cancer/multiple-myeloma/about/what-is-multiple-myeloma.html

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Questions to Ask About Multiple Myeloma

It's important to have frank, open discussions with your cancer care team. They want to answer all of your questions, so that you can make informed treatment and life decisions. For instance, consider these questions:

When you're told you have multiple myeloma

- Where is the cancer located?
- Has the cancer spread beyond where it started?
- What is the cancer's stage(extent), and what does that mean?
- Will I need other tests[1] before we can decide on treatment?
- Do I need to see any other doctors or health professionals?
- 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

- What are my treatment[2] options?
- What do you recommend and why?
- How much experience do you have treating this type of cancer?

- Should I get a second opinion[3]? How do I do that? Can you recommend someone?
- What would the goal of the treatment be?
- How quickly do we need to decide on 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 risks or side effects are there to the treatments you suggest? Are there things I can do to reduce these side effects?
- How might treatment affect my daily activities? Can I still work full time?
- What are the chances the cancer will recur[4] (come back) with these treatment plans?
- What will we do if the treatment doesn't work or if the cancer recurs?
- What if I have transportation problems getting to and from treatment?

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 asking 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[5] should I tell you about right away?
- How can I reach you on nights, holidays, or weekends?
- Do I need to change what I eat during treatment?
- Are there any limits on what I can do?
- Can I exercise during treatment[6]? If so, what kind should I do, and how often?
- Can you suggest a mental health professional I can see if I start to feel overwhelmed, depressed, or distressed?
- What if I need social support during treatment because my family lives far away?

After treatment

- Do I need a special diet after treatment?
- Are there any limits on what I can do?
- What other symptoms should I watch for?
- What kind of exercise should I do now?
- What type of follow-up will I need after treatment?

- How often will I need to have follow-up exams and imaging tests?
- Will I need any blood tests?
- How will we know if the cancer has come back[7]? What should I watch for?
- What will my options be if the cancer comes back?

Along with these sample questions, be sure to write down some of your own. For instance, you might want more information about recovery times. Or you may want to ask about clinical trials[8].

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, can answer some of your questions. To find out more about speaking with your health care team, see The Doctor-Patient Relationship[9].

Hyperlinks

1. www.cancer.org/treatment/understanding-your-diagnosis/tests.html
2. www.cancer.org/cancer/multiple-myeloma/treating.html
3. www.cancer.org/treatment/treatments-and-side-effects/choosing-your-treatment-team/seeking-a-second-opinion.html
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