# Infection and Sepsis

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## 1 General Concepts

Infection is the main cause of death 5 days after injury, and the cause of death only second to shock. Although considerable progress has been made in debridement, tissue repair, and antibiotics, infection is still a common complication of trauma patients. If not handled properly, it can cause multiple organ dysfunction syndrome and death. According to statistical data, the infection rate of soft tissue trauma, colon injury and multiple injuries with open femoral fractures are about 12%, 8% and 90%, respectively. Infection depends not only on the wound, but also on the type of wound. For example, the infection rate of colon firearm injury can reach 58%.

No matter what type of wound infection, its prevention and treatment measures mainly rely on proper surgical treatment at each stage, and antibiotics only play an auxiliary role. Therefore, the prevention and treatment of trauma infection must not rely too much on antibiotics and neglect the correct surgical treatment.

For the convenience of description, the following basic concepts should be clarified first.

### 1.1 Infection

It refers to the inflammatory reaction caused by microorganisms invading the body.

### 1.2 Surgical Infection

It refers to the infection requiring surgical treatment, including trauma, burn, operation, and other concurrent infections.

### 1.3 Bacteremia

The presence of living bacteria in the circulating blood is called bacteremia. Also, there are several similar concepts such as viremia, fungemia and so on.

### 1.4 Toxemia

A large number of toxins rather than pathogens enter the blood circulation, causing severe systemic responses, such as endotoxemia.

### 1.5 Septicemia

In the past, the definition of septicemia refers to the systemic reaction caused by the presence of bacteria in the circulating blood or various toxins produced by them, but its concept is easy to be confused. Therefore, the American College of Chest Physicians (ACCP) and the Society for Critical Care Medicine (SCCM) suggest abandoning this name.

### 1.6 Systemic Inflammatory Response Syndrome (SIRS)

A series of systemic inflammatory reactions caused by various infectious and non-infectious pathogenic factors are called SIRS. SIRS can be found in many clinical situations, such as infection, pancreatitis, ischemia, multiple trauma, organ damage caused by immune response, the effects of TNF, IL-1, and other mediators. If developed further, it can lead to acute lung injury, renal dysfunction, shock, and multiple organ dysfunction syndrome (MODS).

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### 1.7 Sequential Organ Failure Assessment (SOFA)

SOFA is a scoring system developed by the working group on infection related issues of the European Society of Intensive Care Medicine (ESICM), mainly on the severity of respiratory system, nervous system, cardiovascular system, coagulation system, liver and kidney and organ failure. With clear evaluation indicators and simple and easy process, the score system can sequentially evaluate the organ dysfunction, properly evaluate conditions and prognosis of critically ill patients, reflect the changes of condition and therapeutic effects during dynamic monitoring, which is also convenient for retrospective analysis. In the third international consensus on the definition of sepsis and septic shock, SOFA has become the clinical standard for determining sepsis. At present, the expert group recommends that on the basis that the basic SOFA value is assumed to be 0, SOFA $\geq$2 points represent organ disorders.

### 1.8 Sepsis

In the past, sepsis was defined as SIRS in hosts caused by infection. In addition to the presence of infection in the entity, symptoms and signs of SIRS also appear clinically. However, the definition of SIRS often ignores the body's inflammatory response and adaptive response to inflammation. At the same time, its traditional definition is too broad with low specificity. Sepsis 3.0 redefines sepsis as a dysfunctional host response to infection, resulting in life-threatening organ dysfunction. Organ dysfunction refers to a new SOFA $\geq$2 after infection.

### 1.9 Systemic Infection

Some scholars advocate using the term "systemic infection" instead of "sepsis." Because the expression of "sepsis"is not accurate, it is easy to be understood as the toxin produced by abscess formation and pyogenic bacteria. In fact, systemic infection cannot be accompanied by abscess formation, and "toxin" mainly does not come directly from pyogenic bacteria, but refers to cytokines and inflammatory mediators produced by the body's defense system stimulated by bacteria and their toxins. However, the expression of "systemic infection" is far from perfect, which is easy to be misunderstood as infection in all systems of the whole body. In fact, over the years, "surgical sepsis"has been conventionally defined, that is, the clinical manifestations of severe surgical infection with systemic inflammatory response (such as burn sepsis) are not necessarily related to "purulence and toxins." Since the term "sepsis"is still widely used in the literature at home and abroad, it is impossible to abolish it in the short run. At present, we only need to know that these two expressions refer to the same clinical syndrome, which are commonly used. Let its advantages and disadvantages judged by time.

### 1.10 Multiple Organ Dysfunction Syndrome (MODS)

Since the traditional definition of multiple system organ failure (MSOF) is relatively vague, ACCP and SCCM put forward a new concept of MODS, that is, the clinical syndrome of two or more organ dysfunction caused by acute diseases (where trauma and infection are often the initiating factors), and organ dysfunction can occur simultaneously or sequentially. According to different pathogenic factors, MODS can be divided into primary and secondary MODS. Primary MODS is the direct result of etiology, while secondary MODS is mainly caused by abnormal host inflammatory response. Although some organ diseases related to the end-stage and pathogenesis of chronic diseases also involve multiple organs, they do not belong to the category of MODS.

## 2 Main Pathogens of Trauma Infection

### 2.1 Evolution of Major Pathogens

For decades, the main pathogens of trauma infection have undergone significant changes. *Streptococcus* was the main pathogen of trauma infection in the 1930s; in the 1940s, it was mainly penicillin-sensitive *Staphylococcus*; in the 1950s, a large number of penicillin-resistant staphylococci appeared; since the 1960s and 1970s, gram-negative bacilli represented by *Escherichia coli* and *Pseudomonas aeruginosa* have gradually replaced gram-positive cocci represented by *Streptococcus* and *Staphylococcus aureus* as the main pathogens of trauma infection. According to statistics abroad, from 1945 to 1956, two-thirds of the pathogenic bacteria of wound infection were gram-positive cocci. From 1957 to 1974, the wound infection rate caused by gram-negative bacilli increased 14 times. From the 1970s to 1980s, spore free anaerobes increased significantly in trauma infection, and some new opportunistic pathogens and "non-pathogenic bacteria" in the past continued to appear, such as various fungi, *Serratia marcescens*, *Klebsiella*, *Aerobacter*, cloacae bacilli, and *Acinetobacter*. It had been noted that the number of mixed infections involving anaerobic bacteria and fungal infections (such as *Candida albicans*, *Aspergillus*, *Mucor*, etc.) was increasing. Since the 1990s, gram-positive cocci represented by *Staphylococcus aureus* have made a comeback. The proportion of its infection has exceeded 50% of clinical infection cases, gradually replacing gram-negative

bacilli and becoming the main pathogen of trauma infection. For example, methicillin-resistant *Staphylococcus aureus* (MRSA) infection has posed a clinical threat and attracted much attention. In recent years, infections caused by multidrug-resistant bacteria such as *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Klebsiella pneumococci* have increased significantly. The evolution of pathogens of trauma infection is related to at least the following factors:

1. **The wide application of antibiotics** is an important reason for the evolution of pathogens. With the continuous development and application of new antibiotics, although they can effectively kill bacteria sensitive to antibiotics, they also cause the reproduction of drug-resistant strains. In addition, the abuse of antibiotics can cause the imbalance of human normal physiological flora, which is easy to lead to endogenous infection.
2. **The progress of microbiological detection technology** enables some new pathogens that clinicians are not familiar with to be found. For example, *Serratia marcescens* was recognized as a harmless bacterium in the 1960s, but it was later proved that it not only causes disease, but also death. With the improvement and application of anaerobic culture technology, it has been found that the proportion of anaerobic bacteria in trauma infection is increasing. At the same time, it also shows that in the past, traumatic anaerobic infection may be missed only because of the limitations of culture and detection methods.
3. **The improvement of surgical treatment** also leads to the evolution of pathogens. For example, in the early stage of World War I, Clostridium infection was quite common, but with the improvement of debridement technology, this kind of infection has decreased significantly.
4. **The application of new medical equipment and technologies**, such as respiratory devices, elastic dressings, transplantation of various arteriovenous catheters, sensors, and artificial materials, can often cause iatrogenic infection, such as fungal infection.

Thus, the main pathogens of trauma infection will change constantly. In different regions, the evolution process may be inconsistent, for which we should have a clear understanding.

## 2.2 Origin and Invasive Route of Trauma Infection Pathogens

During trauma, the main invasive route of pathogenic bacteria is brought in by injury causing instruments and projectiles, and then brought in by clothes, soil, and other dirt. This kind of infection is called exogenous infection. Another source is the resident bacteria of the human body itself, mainly distributed in the sweat glands, hair follicles, oropharynx, respiratory tract, gastrointestinal tract, and urogenital tract. Under physiological conditions, these normal flora do not cause disease, but form a symbiotic and mutually beneficial ecological balance with the human body. When the skin and these cavities are injured and damaged, bacteria can invade; If the structure is not damaged while its defense barrier function is reduced, bacteria can also pass through the skin and mucous membrane and enter the deep tissue to cause infection. This kind of infection is called autoinfection or endogenous infection. After the invasion of bacteria or other microorganisms from exogenous or endogenous sources, they mostly invade lymphatic vessels and blood vessels, or cause specific site and even systemic infection along natural pores. Minor injury and less serious simple trauma or burn mostly occur exogenous infection. While in the case of severe trauma and burn, both exogenous infection and endogenous infection, especially intestinal infection, can occur.

## 2.3 Clinical Significance of Bacterial Count

A major advance in the study of wound infection is the recognition that the growth level of bacteria in wound or the surface of a wound is more important than the existence of bacteria. Generally speaking, the more bacteria contaminate the wound or the surface of a wound, the greater the chance of infection. At present, it is recognized that the critical number of bacterial infection is $10^5$–$10^6$ bacteria per gram of tissue or per milliliter of liquid. This "threshold" is suitable for any bacterium. Some non-pathogenic bacteria, such as *Salmonella*, *Staphylococcus epidermidis*, and *Bacillus subtilis*, can also cause infection if the number in tissues or body fluids exceeds the above critical limit. It is worth mentioning that this "critical value" is not absolute. On the one hand, when the microbial virulence is particularly strong, such as group A beta-hemolytic streptococci can also cause infection when it is less than $10^5$ tissues/g. On the other hand, when the overall resistance of the wounded decreases and the local conditions are conducive to bacterial breeding rather than killing bacteria, even bacteria less than this "critical value," such as $10^2$ bacteria/g tissue, will cause infection. On the contrary, in some special cases, this "critical value" may also increase. For example, as the author reports, the critical number of bacterial infection in plateau area is $10^8$/g of tissue.

The quantitative examination of bacteria in wound tissue can not only be used as one of the basis to judge wound pollution and infection and guide the rational application of antibiotics, but also an objective index to guide debridement and suturing and predict the success or failure of wound treatment. Where the bacteria is less than $10^5$/g, the wound can be sutured immediately after debridement, without future wound infection and with a high healing rate. However,

if the bacterial count exceeds $10^5$/g tissue, even after thorough debridement, the wound infection rate after early suture is still very high, sometimes more than half.

## 3 Main Types of Trauma Infection

### 3.1 Post-traumatic Suppurative Infection

Common pyogenic bacteria include *Staphylococcus aureus*, *Staphylococcus epidermidis*, pyogenic *Streptococcus*, *Enterococcus*, *Pseudomonas aeruginosa*, *Escherichia coli*, etc. Pyogenic infection can be divided into local wound purulent infection, visceral and body cavity purulent infection and systemic purulent infection due to different location and scope.

#### 3.1.1 Clinical Manifestations

1. Local symptoms include wound pain, swelling of surrounding tissues, redness, fever, and local tenderness of the skin near the wound. The wound is covered with purulent exudates or necrotic tissues of different numbers and colors, and affected by organ dysfunction.
2. When local infection is formed, the whole body also has different reactions. If no bacteria invade the blood, the whole body symptoms are only caused by toxemia caused by bacterial toxin. If bacteria invade the blood, grow and reproduce in the blood and produce toxins, they can develop into systemic infection and sepsis. Some have multiple organ dysfunction and septic shock.

#### 3.1.2 Diagnosis

1. It can be diagnosed according to clinical symptoms and signs: the diagnosis of acute infection (wound suppuration, cellulitis around the wound, etc.) is made based on clinical manifestations, and generally there will be no difficulty. If there is no obvious purulent exudate in the wound or wound, bacterial culture can be counted. The critical number of bacterial infection is $10^5$–$10^6$ bacteria per gram of tissue or per milliliter of liquid. Bacteremia can be diagnosed if viable bacteria are cultured from the blood.
2. When the disease is comparatively serious (such as combined anaerobic infection, biochemical purulent lesions in internal organs and bones) and when the infection spreads to the whole body, in addition to routine smear microscopic examination, wound secretion and blood culture, the diagnosis must also rely on some modern equipment, such as ultrasound, CT, magnetic resonance, or laboratory methods, such as gas chromatography.

#### 3.1.3 Treatment Plan and Principles

1. The most important is undoubtedly to carry out radical surgery in time. Medical staff must extensively inspect the affected area, remove all lifeless tissues, cut open abscesses and swollen areas and drain them fully. Drainage can be carried out by suction flushing, running water flushing or wound gauze loose packing, plus hypertonic ointment with water-soluble matrix. After the infection was controlled, the wound should be closed as soon as possible by secondary suture, skin grafting or adjacent flap transfer.
2. When there are many secretions from infected wounds, wet compress can be used. Common wet compress solutions include bleach boric acid solution, hydrogen peroxide solution, hypertonic or isotonic saline, antibiotic solution, etc. Wet dressing with hypertonic saline could be applied for edematous granulation tissue. The affected limb should be raised without motion. Hypertonic ointment of water-soluble matrix, carbon fiber, and other absorbent, helium containing dressing, proteolytic enzyme fixed on different matrix, etc. can also be used.
3. Broad-spectrum anti-infective drugs may be used; and then select effective anti-infective drugs according to the results of bacterial culture and drug sensitivity test of secretions.
4. Active in vitro detoxification methods can be initiated to reduce the circulating concentration of toxic components in blood, lymph, and interstitial fluid. The most commonly used in vitro detoxification methods include intestinal absorption, blood absorption and lymph absorption, hemodialysis, plasma exchange, ultraviolet irradiation, and indirect electrochemical oxidation of blood and plasma.
5. Systemic support therapy can be used to enhance the resistance of the wounded, keep the balance of liquid, electrolytes and acid-base, correct metabolic disorders, supplement nutrition, etc., and when conditions permit, immunomodulatory therapy shall be implemented as appropriate.

### 3.2 Post-traumatic Tetanus

Tetanus has been considered to be associated with previous wars since ancient times. Tetanus occurs six to seven times in every 10,000 trauma. According to the statistics of the World Health Organization (WHO), more than 160,000 people die from tetanus every year. The mortality among young people is 25–50%, while that of the elderly is as high as 70–80%. Due to the development of urbanized society, coupled with a large number of casualties caused by natural disasters and man-made accidents, the number of trauma cases is increasing in peacetime. Therefore, tetanus is not simply a war problem.

Tetanus is a special type of wound infection. Tetanus bacilli may invade the open wound of human body, proliferate, and secrete toxin, resulting in a series of clinical symp-

toms and signs. It has few local symptoms, but the central nervous system is seriously affected, manifested in worsening tonic spasm, hypoxia, and cardiopulmonary dysfunction.

### 3.2.1 Etiology and Pathogenesis

Tetanus bacillus is a gram-positive anaerobic clostridium, which is an absolutely anaerobic, gram positive, and 3–5 μm long, with two forms of propagules and spores. Propagules which have flagella around them, can move, but cannot form capsules so that they are easy to be killed; spores are round and located at one end of the thallus, so tetanus bacillus with spores has a drumstick-shaped appearance. Spore is the survival form of bacteria in adverse environment. It has strong resistance to the outside world. Its spore is extremely stubborn. It can survive for 1 h in boiling and 150 °C dry heat. Under normal conditions, it can survive for decades.

Tetanus bacilli are widely distributed in nature. It can be found in the intestines of herbivores such as cattle, horses, and sheep and 2–30% of adults. Tetanus bacilli can also be found in the surface layer of soil and dust polluted by feces. Therefore, feces and soil are important infectious sources of the bacillus. The rate of wound infection is very high, which can reach 20–80%, but the incidence rate of tetanus is only 1–2% of the polluters. This is because after entering the traumatic tissue, tetanus bacilli can grow and reproduce in a certain hypoxic environment. That is to say, spores can be transformed into propagules and produce exotoxins to cause disease. The trauma injuries of tetanus usually come from deep stab wound, bullet wound, animal bite, open fracture, crush injury, large-area burn, serious wound pollution or mixed infection. Its common characteristics are deep wound, many necrotic tissues and heavy pollution. A few of the wounded were slightly injured and did not attract the attention of the wounded, so they need to be carefully inquired and examined. Umbilical cord infection caused by local baby delivery can cause neonatal tetanus. Unclean delivery or induced abortion can also cause maternal tetanus infection. Some of the wounded may get tetanus after surgical removal of metal foreign bodies (bullets and shrapnel) that have remained in the body for many years. In addition, cases of tetanus caused by insect bite, tooth extraction, unclean injection or surgery, skin ulcer, furuncle, otitis media, paronychia, and bedsore have also been reported. Cryptogenic tetanus is defined as the wounded without obvious wound or exact trauma history, which occurs among 10–20% of the wounded.

The symptoms and signs of tetanus are caused by the strong exotoxin produced by tetanus bacilli. There are two kinds of exotoxins, namely tetanospasmin and hemotoxin. The former can damage the nervous system, while the latter can damage red blood cells. Tetanospasmin has special affinity for the central nervous system and is the direct cause of muscle tension and spasm. The main pathogenic mechanism is that the toxin binds to gangliosides of gray matter synaptic body membrane to prevent synapses from releasing inhibitory media, resulting in the loss of control of α and γ motor nervous system, resulting in characteristic spasm and rigidity of systemic striated muscle and uncoordinated movement. In addition, tetanospasmin may also block neuromuscular junctions in the periphery and can directly act on muscles to produce muscle contraction.

### 3.2.2 Clinical Manifestations and Diagnosis

Tetanus can be divided into systemic and local ones. The latter is rare, accompanied by long-term tetanus on the injured limb side, which is not life-threatening. This is because the tetanus will subside by itself with the treatment of the wound, but it should be remembered that some kinds of local tetanus, such as Rose tetanus facialis and Brunner cephalotetanus, can lead to death due to laryngeal spasm. The clinical stages of systemic tetanus are as follows.

1. **The incubation phase** varies in length, most of which are 5–14 days. Some of the wounded are less than 1 day or as long as several months or even years, or they only get sick when removing the foreign bodies left for many years. The shorter the incubation period, the more acute and severe the course of disease, and the worse the prognosis. If symptoms appear within 2–3 days after injury, the mortality is very high. The incubation period of neonatal tetanus is generally 5–7 days.
2. **The prodromal phase** is mostly between 12 and 24 h, and its symptoms include general fatigue, dizziness, headache, irritability, weak chewing, local muscle tension, pulling pain, jaw stiffness, inconvenient opening of mouth, dysphagia, tension or soreness of masticatory and cervical muscles, etc.
3. **The attack phase** usually occurs 24–72 h after the initial symptoms, and the affected muscles show clonic spasm. Masticatory muscles were first involved, and the teeth closed tightly; subsequently, facial expression muscles, neck, back, abdomen, and limb muscles were involved; finally, diaphragmatic and costal muscles; due to the continuous contraction of facial muscles, a characteristic "wry smile" can be formed, and the wounded frown and quarrel shrink down; the neck is stiff, the head is tilted back, and the back and abdominal muscles contract at the same time. Because the neck back muscle is stronger than the ventral side, the trunk is twisted into an arch, combined with the spasm of the neck and limbs, forming "angular arch tension" or "lateral arch tension"; there is a "typical tetanus triad," i.e. closed teeth, dysphagia, and neck muscle rigidity. Myospasm often leads to muscle rupture. When the diaphragm is affected, it can cause respiratory disorder, aggravate cough, and may inhale vomitus by

mistake. When the diaphragm spasm is serious, it can cause respiratory arrest. Spasm can also lead to cardiovascular dysfunction, manifested as unstable pulse, blood pressure, and heart rhythm. Any slight stimulation such as light, sound, vibration, drinking water, injection, etc. can induce strong spasms. The duration of each attack varies from a few seconds to a few minutes. Muscle tension persisted during both episodes. However, whether in attack or remission, the consciousness of the wounded is always clear.

4. **The convalescent phase** lasts generally 3–4 weeks, and more than 6 weeks in severe cases. After the second week, the symptoms gradually decreased with the extension of the course of disease. For a long time after tetanus is cured, some muscle groups can still have tension and hyperreflexia.
5. **Complications**. Atelectasis and pneumonia are common complications. Pneumonia is the cause of death in 50–70% of the wounded. It is also possible to have asphyxiating crisis, a fatal respiratory arrest, in a spasm attack. The direct causes of spastic asphyxia are laryngeal spasm and spastic contraction of diaphragm. Sudden and strong muscle spasm can cause muscle tear, bleeding, fracture dislocation, and tongue bite.

Tetanus symptoms are typical, which are not difficult to make a diagnosis. If there is a history of trauma and post-traumatic muscle tension, closed teeth, stiff neck, paroxysmal generalized muscle spasm, the possibility of this disease should be considered. When there are only some prodromal symptoms in the early stage, the diagnosis is difficult, and we should pay close attention to the changes of the disease.

Clinical manifestations of some diseases are often similar to tetanus, which should be differentiated. Temporomandibular arthritis, tonsil or posterior pharyngeal wall abscess, tooth, and gingival lesions can cause mouth opening difficulty due to local swelling and pain. Diseases of spine and muscles can cause local muscle rigidity. Encephalitis often has neck rigidity and general convulsions, but the consciousness of the wounded is not clear, and the examination of cerebrospinal fluid is abnormal, which is different from tetanus. The symptoms of strychnism are similar to those of tetanus, which is called pseudotetanus. However, the characteristics of muscle relaxation during spasm interval, history of medication and disappearance of symptoms 24–48 h after drug withdrawal can be helpful for differential diagnosis. Sometimes the clinical manifestation of hysteria is very similar to that of mild tetanus. Careful dynamic observation can find the inconsistency between hysteria and tetanus. In addition, children with low calcium tetany and rabies have their own characteristics, which is not difficult to identify clinically.

### 3.2.3 Prevention

1. **Wound treatment**. The wound with serious trauma and pollution must go through radical debridement. It can be washed repeatedly with 3% hydrogen peroxide solution and metronidazole solution to remove all necrotic and inactive tissues, remove foreign bodies, and open up the wound. Small and deep wounds should be fully expanded and drained.
2. **Active immunization** is an effective method to prevent tetanus. Tetanus vaccine is a toxoid produced by tetanus bacilli after several generations of special culture. It produces antibodies after injection into human body, which can produce more stable immunity. Specific methods: a total of 3 times before and after injection, each time 0.5 mL. The first subcutaneous injection interval is 4–8 weeks, and then the second injection can obtain "basic immunity." The third injection after half a year to 1 year can obtain more stable immunity. This immunity can be maintained for more than 10 years, and sufficient immunity can be maintained if an additional injection (0.5 mL) is given in the next 5 years. For those who have obtained "basic immunity," 0.5 mL tetanus toxoid should be injected after injury to prolong the time limit of active immunity.
3. **Passive immunization**. For those who did not receive active immunization before injury, joint immunization measures should be taken as soon as possible after injury. In addition to tetanus toxoid, 1500–3000 U of tetanus antitoxin (TAT) should be injected subcutaneously as soon as possible. After injection, the antibody titer in blood can increase rapidly, but it can only last for about 10 days. Due to the long incubation period of tetanus, the patients with deep trauma and serious pollution can be injected again after 1 week. Tetanus antitoxin is a horse serum preparation, which is prone to allergic reaction. Intradermal sensitivity test must be performed routinely before injection. If positive, desensitization method shall be used for injection.

### 3.2.4 Treatment

The treatment principle of tetanus is to control spasm; keep respiratory tract unobstructed to prevent asphyxia; neutralize free toxins as soon as possible; prevention of complications.

1. **Controlling and relieving muscle spasm** is the central link of treatment. The wounded shall be isolated in a quiet dark room to reduce the stimulation of sound and light. According to the condition, the following sedative and antispasmodic drugs can be used to reduce and control the occurrence of spasm:
   (a) **Diazepam** is suitable for those with mild symptoms. It has the advantages of rapid action, no interference with respiration and circulation, no obvious toxic and

side effects, large dosage range and safety. It is recognized as the first choice of sedative and antispasmodic drugs at present. Usually 10 mg intramuscular injection or intravenous drip, four to six times a day.

(b) **Chlorpromazine** has a good sedative and hypnotic effect. The common dose for adults is 50 mg intramuscular injection or intravenous drip, once every 6–8 h.

(c) **Chloral hydrate**: chloral hydrate 10 mL or 30 mL retention enema can be used. It is suitable for the combined application of sedative and antispasmodic agents in patients with mild or serious symptoms.

(d) **Hibernation therapy**: it is suitable for the wounded with severe spasm, especially those with high fever. It is usually injected with half amount of hibernation I (chlorpromazine 25 mg, promethazine 25 mg, and pethidine 50 mg) intramuscularly every 6–8 h, which can effectively reduce muscle rigidity and muscle spasm.

(e) **Thiopental sodium**: it is suitable for the wounded with severe spasm and convulsion. Intravenous therapy of thiopental sodium 0.1 g can quickly relieve spasm. The disadvantage is that it makes the wounded unconscious and has respiratory inhibition.

(f) **Muscle relaxants**: they have a good relaxation effect on the bones of the whole body and paralyze the respiratory muscles. Therefore, it can only be used under the condition that there is a ventilator to control breathing. It is only used for the wounded with severe symptoms and frequent respiratory spasm. Commonly used drugs include l-tubocurarine, succinylcholine chloride, imbretil, galaiodonium, hanjisong, etc.

2. **Keep the respiratory tract unobstructed and prevent asphyxia**. The wounded with severe tetanus should be given tracheotomy as soon as possible. On the one hand, tracheotomy can prevent asphyxia caused by laryngeal spasm, on the other hand, it can also prepare for the application of muscle relaxants and ventilator in case of respiratory spasm, so as not to be overwhelmed in case of asphyxia. The commonly used drug is thiopental sodium 0.5 g dissolved in 20 mL glucose solution, intravenous therapy of 2–4 mL, which can immediately relieve respiratory spasm, supplemented by short-term artificial respiration, and the wounded can resume spontaneous breathing. If respiratory spasm occurs frequently, dissolve the required sodium thiopental in advance, but the storage time shall not exceed 24 h. Muscle relaxants and respirators can be used to control breathing if conditions permit. At the same time, pay attention to suck out secretions, clean the catheter, inhale atomized gas, and drip antibiotic solution regularly.

3. **Neutralize free toxins**. In principle, TAT should be a small dose, with a total amount of 50,000–100,000 IU. After debridement and high-dose penicillin injection, 100,000 IU, 70,000 IU and 50,000 IU were injected, respectively, according to the severe, medium, and light wounded. The blood concentration gradually increased 6 h after TAT intramuscular injection, so intravenous administration is better. However, intravenous medication cannot effectively penetrate the blood–brain barrier, often combined with subarachnoid injection (intrathecal injection). Intrathecal injection has the advantages of fast control of convulsion, short course of treatment, and less medication. Generally, 5000–10,000 IU of TAT is used. In order to avoid nerve damage and inflammatory reaction caused by a small amount of toluene and phenol in TAT preparation, cerebrospinal fluid can be diluted and adrenal cortical hormone can be added during injection. Human tetanus immunoglobulin (TIG) can be used if conditions permit. It has been popularized in overseas countries, but it is rarely used in China due to drug source. Its curative effect is much better than that of TAT, and there is no risk of allergic reaction. It is not suitable for intravenous therapy, because it can cause elevated blood pressure. By deep intramuscular injection of 3000–6000 IU, the effective antibody titer can be maintained for 8–12 weeks, so it only needs to be used once.

4. **Prevention of complications**

(a) Pulmonary infection. Due to respiratory spasm, difficulty in expectoration, application of sedatives and long-term bed rest, tetanus wounded are often complicated with pulmonary infection and even respiratory failure. The key points of controlling pulmonary infection are effective application of antibiotics, strengthening nursing after tracheotomy, oxygen administration through tracheotomy, sputum suction, atomization inhalation or drug dropping.

(b) Heart damage. Long-term sympathetic hyperfunction and myocardial damage caused by hemolytic toxin can lead to cardiac failure. Therefore, the wounded with tachycardia and high blood pressure can be given propranolol orally or intravenously. Occasionally, it can be seen that the wounded in the recovery period suddenly have heart failure or even sudden death after getting out of bed. Therefore, the monitoring of the cardiac function of the wounded should not be ignored even in the recovery period.

(c) Malnutrition and disorder of water electrolyte balance. The wounded consume a lot due to frequent muscle convulsions, massive sweating, and infection, and can't eat normally for a long time. Therefore, nutrition maintenance is very important for the wounded with tetanus. Diet should be high-calorie, high-protein, and high-vitamin. Patients with mild

illness can be fed by mouth or tube, and those with frequent convulsions can be given total parenteral nutrition support.

## 3.3 Post-traumatic Gas Gangrene

Gas gangrene occupies a special position in trauma infection, because it is characterized by particularly serious infection, high mortality, and high disability rate among rehabilitated patients. During the Second World War, gas gangrene accounted for about 1.5% of all the wounded, and the mortality was as high as 60%. Among the recovered patients, 50% were disabled due to amputation. Gas gangrene, also known as Clostridium myositis or muscle necrosis, is an acute specific soft tissue infection caused by Clostridium. It is often seen in severe open contusion of muscle tissue after trauma.

### 3.3.1 Etiology and Pathogenesis

The pathogenic bacteria of gas gangrene are a group of gram-positive *Clostridium*, mainly including *Clostridium perfringens*, *Clostridium septicum*, Clostridium malignant edema, *Clostridium perfringens*, and *Clostridium histolyticum*, but *Clostridium perfringens* is the most common and important, with biological characteristics of easy-proliferation in hypoxia and inactivated tissues. This kind of bacteria grows and reproduces all year round in the human gastrointestinal tract, bile duct, and vagina. Its outstanding feature is that it has the ability to form spores, and spores are very tolerant to environmental conditions. Therefore, they widely exist in soil and human and animal feces, which is very easy to pollute wounds. Under appropriate conditions, they can grow and reproduce locally and produce a variety of exotoxins and enzymes to damage human body. All kinds of Clostridium can secrete exotoxins, which can cause hemolysis, vascular thrombosis, kidney damage, and muscle damage. The main characteristic of Clostridium toxin is to destroy connective tissue and muscle and make it necrotic. Its biochemical structure is very complex and consists of many components, such as α toxin (lecithinase C) β toxin (hemolysin) κ toxin (collagenase), n toxin (hyaluronidase), μ toxin, plasmin, and neuraminidase, among others. Each component has a certain pathogenic effect.

### 3.3.2 Clinical Manifestations and Diagnosis

Trauma complicated with gas gangrene generally occurs 1–4 days after injury, but it could also be as short as 6 h.

1. **Local manifestations**. Local severe pain of the wound is the earliest symptom. In the early stage, the wounded limb is heavy. Later, due to the rapid infiltration of gas and liquid into the tissue to the increase of pressure, there is swelling and cracking like severe pain, which is ineffective with painkillers. What can be noted include edema around the wound, pale, tense and shiny skin, and marble like markings on the skin surface, as well as a lot of foul smelling serous or bloody exudates and bubbles in the wound. Crepitus can be palpable in the limbs (also known as snow holding feeling). The wound muscle is massively necrotic, brick red, and inelastic, which does not shrink or bleed during cutting, and finally turns to black carrion.
2. **Systemic manifestations** mainly include severe toxemia caused by toxins. Soon after the local symptoms appear, the wounded can appear pale lips and skin, rapid and weak pulse, indifferent expression, trance, irritability, shortness of breath, irregular heart rhythm, where body temperature and pulse are not directly proportional, and the body temperature is not high, but with rapid pulse. Later, due to the aggravation of toxemia, the body temperature can reach more than 40 °C, and then coma, severe anemia, and multiple organ failure may appear.
3. **Laboratory examination** shows a large number of gram-positive short but thick bacilli and few leukocytes in the smear of the wound exudate. The blood routine test shows that the wounded is obviously anemic, the red blood cell count decreases to $(1.0–2.0) \times 10^{12}$/L, the hemoglobin decreases by 30–40%, and the white blood cell count increases, but generally does not exceed $(12–15) \times 10^{9}$/L. The urine analysis shows hemoglobinuria. Diagnosis can be confirmed by the anaerobic culture, but it takes a long time (2–3 days), which is not helpful for early diagnosis.
4. **Diagnosis**. Early diagnosis is very important. As the disease progresses very rapidly, delaying diagnosis for 24 h is fatal. The three main bases for early diagnosis include crepitus around the wound, gram-positive bacilli noted in the smear of wound exudate, and gas accumulation shadow in muscles in the X-ray scan. Indirect immunofluorescence can also be used for early diagnosis. In diagnosis, it should be noted that clinically, interstitial pneumoconiosis is not limited to Clostridium infection and should be distinguished. Anaerobic streptococcus and fragile bacteroides can also produce gas in infected tissues. Subcutaneous emphysema, twisting, and even fascia necrosis can also occur in physical examination, but the disease develops slowly, the symptoms of pain and systemic poisoning are mild, and the prognosis is also good. *Streptococcus* and gram-negative bacilli can be found in wound exudate smear examination.

### 3.3.3 Treatment

1. **Surgery therapy**. Once the diagnosis is established, emergency surgery shall be performed immediately. Even if the wounded is on the verge of death, surgery should be performed immediately while rescuing shock. The key to

treatment is complete debridement and drainage, maximum resection of necrotic tissue, and incision of fascia decompression. Preoperative intravenous administration of a large number of antibiotics (penicillin + metronidazole), blood transfusion, and infusion to correct the acid-base balance. The preoperative preparation time shall be shortened as far as possible, generally no more than 30–45 min. General anesthesia (such as intravenous ketamine) is used for the operation, and tourniquet is strictly prohibited for the injured limb. The surgical method is to conduct extensive and multiple longitudinal incisions in the lesion area, and quickly removes all necrotic and bloodless tissues until the normal tissues with normal color and good bleeding. Because the scope of infection often exceeds the scope of macroscopic lesions, the whole muscle should be removed, including its starting and ending points. If the infection is limited to a certain fascia space, the affected muscles and muscle groups can be removed from the starting point to the ending point. If the muscles of the whole limb have been involved, high amputation shall be performed at the healthy part, and the stump shall be open without suture. The wound cavity was repeatedly rinsed with a large amount of 3% hydrogen peroxide solution or potassium permanganate solution (concentration of 1: 4000) to improve the anaerobic state. The wound remained open after operation, and was loosely covered with gauze soaked in hydrogen peroxide and potassium permanganate solution. It was replaced several times a day until the wound infection was controlled.

2. **Antibiotics therapy**. The high-dose penicillin and metronidazole should be used continuously after the surgery. Antibiotics have a special therapeutic effect on this kind of infection, because such infection belongs to acute diffuse infection. The cultivation of anaerobic bacteria, especially the drug sensitivity test, requires special equipment and technology, which is difficult to achieve generally, and the time is not allowed. According to the materials of most laboratories, penicillin, metronidazole or other broad-spectrum antibiotics can be selected among the existing antibiotics. The dose of penicillin should be large, more than 10 million U/day. Aminoglycoside antibiotics (such as kanamycin, gentamicin, etc.) have proved ineffective against such bacteria.
3. **Hyperbaric oxygen therapy** should be used at the earliest stage after operation, which aims to increase the oxygen content between tissues to create an environment not suitable for bacterial growth and proliferation. It can be used as an adjuvant therapy for surgery. By the hyperbaric chamber of the Third Military Medical University, 11 cases of gas gangrene (aged 21–50 years old) confirmed by bacteriology were treated with hyperbaric oxygen (while local thorough debridement and systemic use of high-dose penicillin). Methods: to inhale oxygen for 20 min at an interval of 8 h under pure oxygen at 3 atm, for three times in the first 24 h and once per 12 h for 3 days. Results: six cases showed markedly effective; four cases were significantly improved; one case showed ineffective (this case was 50 years old, admitted late and in coma). Therefore, those with proper conditions should undergo hyperbaric oxygen treatment.
4. **Other therapies**. Hydrogen peroxide solution (hydrogen peroxide) is continuously injected into the wound to increase the oxygen content between tissues. The method is to place a catheter in the depth of the wound, fix it on the edge of the wound with a wire, and connect it to the infusion bottle containing 1% hydrogen peroxide isotonic saline, drip it continuously at the rate of 8–10 drops per minute, and wet compress the wound with hydrogen peroxide gauze, so as to maintain the local aerobic environment and facilitate flow diversion. It generally lasts 3–5 days until the wound infection is controlled. In addition, systemic support therapy includes multiple small blood transfusions; maintain water, electrolyte, and acid-base balance; give three high (high calorie, high protein, and high vitamin) diet; protect the functions of heart, lung, liver, and kidney to keep the daily urine volume above 1500 mL to facilitate the excretion of toxins. Gas gangrene antiserum has poor control effect and allergic reaction, so it is not used now.
5. **Anaerobic cellulitis**. The prognosis is good with timely incision, decompression, sufficient drainage, removal of certain necrotic tissue, and antibiotic treatment. The gas dispersion range can be quite wide, but it is not necessary to cut too much according to the gas dispersion range, let alone amputate rashly.
6. **Pollution disposal**. The pollution and polluted dressing contacted by the wounded shall be collected separately or disinfected or discarded (fire burning). Those disinfected with spore bacteria should be boiled for more than 1 h.

### 3.3.4 Prevention

Attention should be paid to the trauma prone to such infection, such as open fracture with extensive muscle injury or crush injury of thigh and hip; patients with important vascular injury or secondary vascular embolism; patients with a history of suture with tourniquet for too long, plaster too tight or incomplete early debridement. The key to prevention is complete debridement as soon as possible; including removing the inactivated and ischemic tissues, completely removing foreign bodies, especially non-metallic foreign bodies, and fully opening the drainage for deep and irregular wounds to avoid the existence of dead cavity; for those with increased tension under fascia, fasciotomy, and tension reduction should be carried out early; for open fractures with extensive soft tissue injury, early suture should not be carried

out after debridement. In addition, it is difficult to determine the vitality of contused and crushed soft tissue in the early stage. During this period, we should closely observe it. For penetrating abdominal injury, especially colon, rectum, and perineum trauma, we should be alert to the occurrence of such infection, because these bacteria are resident bacteria in human intestinal tract. Early use of large doses of penicillin or metronidazole has its indications for the above wounded. According to the US military report, the incidence of gas gangrene was 1.5% in World War I; during World War II it dropped to 0.7%; in the Korean War it was further reduced to 0.08%; in the Vietnam War it has declined again. The main experience is early full debridement and blood circulation reconstruction, which shows that the disease focuses on prevention and can be prevented.

## 3.4 Invasive Streptococcal Infection

If the wound of war wound is treated improperly or delayed, it can cause invasive streptococcal infection. The initial manifestation is local cellulitis around the wound, and then it can quickly develop into systemic poisoning symptoms. The characteristics of the disease are: any part of the skin can be infected, and the lesions are not easy to be limited, spread rapidly, there is no obvious boundary between the pathological tissue and the normal tissue, and the symptoms of systemic poisoning are obvious. However, local tissues generally do not have obvious necrosis and dissolution, so there are no traces after recovery.

### 3.4.1 Etiology

According to whether the streptococcus is hemolytic after growing and multiplying on the blood medium and its hemolytic nature, the streptococcus can be divided into three categories: (1) α-hemolytic streptococcus: there is 1–2 mm wide grass green hemolytic rings around the colony (aka α hemolysis). This kind of streptococcus is mostly opportunistic pathogen. (2) β-hemolytic streptococci: a 2–4 mm wide, well-defined, completely transparent colorless hemolytic ring forms around the colony (aka β hemolysis). This type of bacteria is also called as hemolytic streptococcus, strong in pathogenicity, often causing a variety of diseases in humans and animals. (3) γ-streptococcus: it does not produce hemolysin, and there is no hemolytic ring around the colony, which is also known as γ or non-hemolytic streptococcus. The bacteria are not pathogenic, often present in milk and feces, and occasionally cause infections.

Invasive streptococcal infection of war wound is usually caused by beta-hemolytic streptococcus, which is widely distributed in nature. It exists in water, air, dust, feces, and the oral cavity, nasal cavity, and throat of healthy people and animals. It can be transmitted through direct contact, air droplets or wound infection through skin and mucous membrane. Aerobic or partly anaerobic bacteria, spherical or oval, 0.6–1.0 m in diameter, arranged in chains, varying in length, composed of 4–8 to 20–30 bacterial cells. It does not form spores, and it is flagellum-free, easily colored by common alkaline dyes, Gram-positive, or Gram-negative after aging cell culture or phagocytosis by neutrophils. The resistance of the bacterium is generally not strong where it can be killed at 60 °C for 30 min. It is sensitive to common disinfectants, but it can survive for several months in dry dust. It is sensitive to penicillin, erythromycin, chloramphenicol, tetracycline, and sulfonamide.

### 3.4.2 Pathogenesis

The pathogenicity of β-hemolytic streptococci is related to the toxins produced and their invasive enzymes, mainly including: (1) Streptolysin: there are two kinds of hemolysins, O and S. O is a protein containing –SH, which is antigenic, and S is a small molecular polypeptide with a small molecular weight, which is thus not antigenic. (2) Fever-causing exotoxin: once known as erythrotoxin or scarlet fever toxin. It is the main toxic substance of human scarlet fever, which can lead to local or generalized red rash, fever, pain, nausea, vomiting, and general malaise. (3) Hyaluronidase, aka spreading factor or invasin. It can break down the hyaluronic acid in the intercellular matrix so as to increase the invasive power of bacteria and make the germs easy to spread in tissues. (4) Streptokinase, aka streptococcal fibrinolysin. It can turn plasminogen into fibrin ferment (plasmase), and facilitate the diffusion of bacteria in tissues. The enzyme is heat resistant, and can still maintain activity at 100 °C for 50 min. (5) Streptodornase, aka streptodornase or streptococcal DNA enzyme, which can rarify the pus, and expedite the spread of bacteria. (6) Leukocidin: it can make leukocytes unable to move, become spherical, and finally swell and rupture.

Because the pathogen produces toxin and invasive enzyme, and the texture of the invaded tissue is loose, its acute suppurative inflammatory lesions expand rapidly. The lymph nodes on the lesion side are often infected and often have obvious toxemia or bacteremia. Histopathological examination showed extensive acute suppurative inflammatory changes in dermis and subcutaneous tissues, and the infiltrating cells were mainly lymphocytes and neutrophils. Skin appendages were destroyed, blood vessels and lymphatic vessels dilated or embolized, and granuloma formation was seen in the later stage. It is often accompanied by lymphadenitis, lymphangitis, gangrene, metastatic abscess, and even sepsis.

### 3.4.3 Clinical Manifestations

1. **Local symptoms**. Cellulitis can occur in any part of the skin, more commonly in limbs and face.
   (a) General subcutaneous cellulitis. The wounded with skin injury often have cold, fever, and systemic dis-

comfort. The affected part is swollen and painful, and the epidermis is red. It can fade slightly after finger pressure. The boundary of redness and swelling is unclear. The color of the central part is dark and the surrounding color is light. Those with shallow infection site and loose tissue have obvious swelling and diffuse pain; When the infection site is deep or the tissue is dense, the swelling is not obvious, but the pain is severe. The lymph nodes on the lesion side are often swollen and painful, for example, swollen and painful axillary lymph nodes in case of cellulitis in the forearm, and swollen and painful cervical lymph nodes in case of cellulitis in the face. When the lesion worsens and expands, the skin can blister, part of it turns brown, or bursts into pus.

(b) Acute submandibular cellulitis: between various tissues of the maxillofacial region, such as subcutaneous tissues, muscles, salivary glands, and jawbones, there are varying amounts of loose connective tissues or fats with blood vessels, nerves, lymphatic tissues, and salivary gland ducts. Physiologically, this structure has the function of buffering the tension and pressure generated by movement; anatomically, it is a potential gap, connected by adjacent gaps. When the infection invades these potential spaces, it can cause the dissolution and liquefaction of loose connective tissue, and the obvious space appears when the inflammatory products are filled. Infection can originate from contaminated wounds in the mouth or face. Local manifestations include redness, swelling, heat, and pain, which often spread downward with comparatively severe systemic responses. After the infection affects the connective tissues in the platysma muscle, laryngeal edema and compression of the trachea can occur, resulting in dyspnea and even asphyxia. Sometimes inflammation can also spread to the mediastinum, causing mediastinitis and mediastinal abscess.

2. **Systemic symptoms**. Patients with acute infection may suffer high fever, chills, headache, fatigue, and systemic discomfort. Some may be accompanied by lymphadenitis, lymphangitis, gangrene, metastatic abscess or severe sepsis.
3. **Signs**. The lesion is locally red and swollen with obvious tenderness. The local redness and swelling in the patients with deep lesions are not obvious, often only local edema and deep tenderness.
4. **Complications**. They mainly include septic shock and sepsis.

### 3.4.4 Diagnosis

1. Clinical manifestations and signs. Diagnosis can be made according to typical local and systemic clinical manifestations and signs.
2. **Laboratory examination**
   (a) Peripheral blood routine test
   - White blood cell count: In general infection, the white blood cell count is beyond $10 \times 10^9$/L. If the white blood cell count is above (20–30) $\times 10^9$/L, or less than $4 \times 10^9$/L, or immature leukocytes exceeds 0.1%, or toxic particles are noted, septic shock and sepsis should be closely watched.
   - White blood cell classification and count. The increase of white blood cell count is often accompanied by the increase of neutrophil ratio.

   (b) Bacteriology
   - Bacterial culture. For patients with multiple and repeated infections, the pus can be directly extracted from the abscess for bacterial culture.
   - Drug sensitivity test. The drug sensitivity test should be carried out with the bacteria culture of pus. The results can provide a scientific basis for clinical drug treatment.
3. **Radiology examination**. It is helpful to judge the type of disease in the early stage and understand the severity of local tissue damage.
   (a) B-scan ultrasonography. The local tissue structure of the focus is disordered, with uneven medium and low echo shadow in the center, edema in surrounding tissues, and unclear boundary.
   (b) X-ray. Widened mediastinum with high density can be seen when the cellulitis in the floor of mouth, jaw, and neck causes mediastinal abscess.
   (c) CT. Edema in the peripheral tissues and liquefaction in the center. The mediastinum is widened with high density, indicating mediastinal abscess.
4. **Differential diagnosis**
   (a) Erysipelas. It refers to infection caused by hemolytic streptococcus invading skin and reticular lymphatic vessels. Local manifestations include crimson patches, fade after finger pressure, mild skin edema, slightly raised edges, and clear boundaries. Infection spreads rapidly, but does not suppurate. There is little tissue necrosis and is easy to occur repeatedly. If it is found repeatedly in the lower limbs, there may be subcutaneous lymphatic obstruction.
   (b) Necrotizing fasciitis. It is often a mixed infection of aerobic and anaerobic bacteria. Necrotizing fasciitis occurs rapidly with severe systemic symptoms, and not obvious local symptoms. The infection may spread rapidly along the fascia and a large number of necrosis of fascia and subcutaneous tissue. Patients often have anemia and toxic shock. Ulcers and thin pus can be seen on the skin, and a variety of bacteria can grow in pus culture.
   (c) Aerogenic cellulitis: it occurs after skin injury, and the germs are anaerobic, such as Enterococcus, facul-

tative *E. coli*, bacteroid, facultative bacillus proteus, or *Clostridium perfringens*. The inflammation is mainly in the subcutaneous connective tissue, and does not affect the muscular layer. The initial performance is similar to general cellulitis. It is characterized by rapid expansion and can touch the subcutaneous twist. There can be odor after collapse, and the whole body condition deteriorates rapidly. CT scan shows different degrees of subcutaneous pneumatosis and deep soft tissue emphysema.

(d) Gas gangrene. It is common in severe trauma deep to muscles, accompanied by injured limbs or physical dysfunction. In the early stage, the local skin is bright, tense, and twisted, and the lesion can involve the deep part of the muscle. The secretions have some kind of fishy odor, and Gram-positive bulky bacilli can be detected on smear. The muscle is stained and necrotic, myoglobinuria may be present, and free gas between the muscles can be seen on the X-ray film.

### 3.4.5 Treatment

1. **Local therapy**

(a) Incision and drainage. In the early stage of general cellulitis, incision and drainage should be carried out in time to alleviate the expansion of subcutaneous inflammation and reduce skin necrosis. If the finger is cellulitis, it should be cut and decompressed early to prevent phalanx necrosis. For cellulitis at the bottom of the mouth and under the jaw, if the short-term active anti infection treatment is ineffective, it should be cut and decompressed as soon as possible to prevent laryngeal edema from compressing the trachea and causing asphyxia. Once the inflammation is limited to form an abscess, it should also be cut and drained in time. Multiple smaller incisions can be made and the wet gauze strip can be used for drainage.

The indications of incision and drainage include local swelling, jumping pain and obvious tenderness, local depression edema with wave motion, or pus extracted by puncture, septic necrotic infection, the abscess which has been punctured, but the drainage is not smooth. The purpose of incision and drainage is: to make the pus and necrotic infections drain quickly and reduce the absorption of toxins; ease local swelling, pain and tension, relieve the pressure on the airway and pharyngeal cavity, and avoid asphyxia; prevent the spread of infection to the adjacent interstitial space, as well as the skull, mediastinum and blood, and avoid serious complications; prevent the occurrence of marginal osteomyelitis.

(b) Local wet dressing therapy. Fifty percent magnesium sulfate or normal saline can be used, and then wrap the wound with 10% fish fat ointment.

(c) Physical therapy. The early application of ultraviolet and infrared rays can limit abscesses and promote inflammation to subside; after the discharge of pus, diathermy can be selected, such as ultrashort wave and microwave, which can promote local blood circulation, granulation tissue growth, and accelerate wound healing.

2. **Systemic therapy**

(a) Early administration of sufficient and efficient antibiotics. The first choice is 4.8–8 million U/day penicillin, intravenous drip; if the patients is allergic to penicillin, erythromycin 1–1.5 g/day intravenous drip can be used. Or ciprofloxacin, 0.2 g each time, twice a day, intravenous drip. Oral ofloxacin, 0.2 g each time, twice a day. Xianfeng V 6G/day intravenous drip or cephalosporins with wide antibacterial spectrum can also be used. The general course of treatment is 10–14 days, which should be maintained for a period of time after the skin lesions subside.

(b) Systemic support therapy. It is to ensure that patients have a full rest. Severe infection cases should be properly nourished with calories and proteins, appropriate amount of fresh blood or plasma input, and vitamin supplements like vitamin C and vitamin B complex.

(c) Symptomatic treatment. Drugs can be used like analgesic and antipyretic drugs, such as antipyretic analgesic tablets (APC) and somitol tablets.

(d) Anti-shock therapy. Patients with septic shock should be given active fluid replacement and volume expansion, improve microcirculation and corresponding symptomatic treatment, and pay close attention to the patient's urine volume, blood pressure, heart rate, and peripheral circulation. The effect of dopamine intravenous drip is good for patients with hypotension. During rehydration, the concentration of glucose solution should be limited to avoid covering up oliguria symptoms due to osmotic diuresis, resulting in the illusion of sufficient rehydration.

### 3.4.6 Prognosis

If there are no serious complications, the prognosis is comparatively good after active and standardized treatment. People with impaired immunity and diabetes have the possibility of recurrence.

## 3.5 Necrotizing Fasciitis

Necrotizing fasciitis, also known as "flesh-eating bacteria" infection, is an acute necrotizing soft tissue infection caused by bacterial invasion of subcutaneous tissue and fascia. This disease is rare clinically, but has an acute onset, rapid pro-

gression, high destructive power, and high mortality, and can cause severe disability. The clinical manifestation is the infection spread along the deep and superficial fascia, the formation of thrombosis in the involved blood vessels, and the necrosis of the corresponding subcutaneous tissue, skin, and fascia. It can occur in all parts of the body, mostly in the limbs, especially in the lower limbs; Followed by perineum, neck, face, abdominal wall, back and hip, etc. In severe cases, the internal tissue of the infected part is completely exposed outside the body, and the necrotic part forms a depression, just like being eaten, which is very terrible.

### 3.5.1 Etiology

Necrotizing fasciitis is often a mixed infection of a variety of bacteria, including Gram-positive hemolytic streptococcus, *Staphylococcus aureus*, Gram-negative bacteria and anaerobic bacteria. With the development of anaerobic culturing techniques, it has been confirmed that anaerobic bacteria are an important causative agent and necrotizing fasciitis is often the result of the synergistic action of aerobic and anaerobic bacteria.

Trauma patients with comorbidities such as diabetes, nephrosis, obesity, peripheral vascular disease, malnutrition, or long-term use of immunosuppressive agents such as corticosteroids are more likely to develop necrotizing fasciitis.

### 3.5.2 Pathogenesis

Necrotizing fasciitis is the result of the synergistic action of aerobic and anaerobic bacteria. After immune damage occurs in the whole body or local tissue, a variety of bacteria invade the subcutaneous tissue and fascia. Aerobic bacteria first consume the oxygen in the tissue, reduce the redox potential, and enhance the reducibility of the system. At the same time, enzymes secreted by bacteria break down the hydrogen peroxide in the tissue, creating a less aerobic environment suitable for the survival and reproduction of anaerobic bacteria. Bacterial infection spreads rapidly and widely along the fascia tissue, causing extensive inflammation, congestion and edema of the infected tissue, and then inflammatory embolism occurs in the skin and subcutaneous small vascular network. Tissue nutritional disorder leads to ischemic tunnel like necrosis and even circular necrosis of the skin. Microscopic examination showed that there were obvious inflammatory manifestations in the blood vessel wall, neutrophil infiltration in the deep dermis and fascia, fibrous embolism in the blood vessels in the affected fascia, and cellulose necrosis in the arteriovenous wall. Gram staining could find pathogens in the damaged fascia and dermis, but there was no damage to the muscle tissue. An important feature of necrotizing fasciitis is that the infection only affects the subcutaneous tissue and fascia and does not involve the muscular tissue at the site of infection.

### 3.5.3 Clinical Manifestations

1. **Local symptoms.** It occurs acutely, with early local signs often hidden so that the patients always ignore them, which can affect the whole limb within 24 h.
   (a) Patchy redness, swelling, and pain. In the early stage, skin can be red and swelling, which is purplish red, patchy, and painful with unclear boundary. In this case, the subcutaneous tissue is already necrotic, and lymphadenitis and lymphadenitis seldom occur because the lymphatic pathways have been rapidly destroyed. Infection can affect the whole limb within 24 h.

   Individual cases can start slowly and be latent in the early stage. The affected skin is red or white, edematous, and painful by palpation, and the lesions are poorly defined and present as diffuse cellulitis.
   (b) Pain relief and numbness of the affected area: early infection is localized with severe pain due to the stimulation by inflammatory substances and the invasion of germs. When the sensory nerve at the site of lesion is destroyed, the intense pain may be replaced by numbness or anesthesia, which is one of the characteristics of the disease.
   (c) Bloody blister. Due to the destruction of nutrient vessels and vascular embolism, the color of the skin gradually turns purple and black, and blisters or bullae containing bloody liquid appear.
   (d) Strange smelly bloody exudate. Edema can be noted in the subcutaneous fat and fascia, as well as sticky, turbid, and blackened exudate which finally becomes liquefied and necrotic. The exudate is bloody and serous with strange odor. Necrosis spreads widely and is undermined, sometimes producing subcutaneous gas. Crepitus can be heard by examination.
2. **Systemic toxic symptoms**. Early in the disease, when the local infection symptoms are still mild, the patient has severe systemic toxic symptoms such as fear of cold, hyperpyrexia, anorexia, dehydration, impaired consciousness, hypotension, anemia, and jaundice. If not treated in time, diffuse intravascular coagulation, toxic shock, and multi-organ failure may occur.

### 3.5.4 Diagnosis

The disproportion between the severity of local signs and systemic symptoms is the main feature of necrotizing fasciitis.

1. **Diagnostic criteria**. Fisher proposed six diagnostic criteria, which have certain reference value.
   (a) Extensive necrosis of subcutaneous superficial fascia with extensive concealed tunnels diffused into the surrounding tissues.
   (b) Moderate to severe systemic poisoning symptoms with mental changes.

(c) No muscle involved.
(d) No Clostridium found in wound and blood culture.
(e) No significant vascular obstruction.
(f) Debridement and histopathological examination: extensive leukocyte infiltration, focal necrosis of the fascia and adjacent tissues, and microvascular embolization are detected.

2. **Laboratory examination**
   (a) Complete blood count (CBC)
      • Determination of red blood cell counts and hemoglobin: 60–90% of the patients experience a minor to moderate decrease in red blood cell counts and hemoglobin due to inhibition of bone marrow hematopoiesis by bacterial hemotoxin and other toxins.
      • Leukocyte count: a leukemia-like reaction with elevated white blood cells mostly between (20 and 30) $\times 10^9$/L, shifting to left in nuclear index, with toxic granules.
   (b) Serum electrolytes: hypocalcemia may be present.
   (c) Urine examination
      • Urine volume and urine specific gravity: oliguria or anuria when fluid supply is adequate, constant urine specific gravity, etc. are helpful to determine early damage to kidney function.
      • Urine protein characterization: positive urine protein indicates the presence of damage to the glomerulus and tubules.
   (d) Bacteriologic examination
      • Slide review: take the secretion and vesicular fluid from the edge of the lesion.
      • Bacterial culture. Take secretion and blister fluid for aerobic and anaerobic culture, respectively, and no Clostridium is found, which is helpful to judge the disease.
   (e) Serum antibody: the presence of streptococcal-induced antibodies in the blood (hyaluronidase and deoxyribonuclease B released by streptococci can induce the production of antibodies with high titers) is helpful for diagnosis.
   (f) Radiology
      • X-ray radiography: there is gas in the subcutaneous tissue.
      • CT: a small bubble shadow is found in the tissue.
   (g) Biopsy: Frozen section of fascia tissue is also helpful for the diagnosis of necrotizing fasciitis.
   (h) Differential diagnosis
      • Erysipelas: patchy erythema, no edema, clear boundary, and often lymph node and lymphangitis. The patient can suffer fever, but relatively mild systemic symptoms without characteristic manifestations of necrotizing fasciitis.
      • Streptococcal necrosis: Streptococcal necrosis is caused by beta-hemolytic streptococcal infection. It is manifested by skin necrosis without involving fascia. In the early stage, the local skin is red and swollen, and then becomes dark red, with blisters, containing bloody serous and bacteria. Skin necrosis is followed by a dry, burn-like eschar.
      • Bacterial synergistic necrosis: Bacterial synergistic necrosis is mainly skin necrosis, rarely involving fascia. Pathogenic bacteria include non-hemolytic streptococci, *Staphylococcus aureus*, obligatory anaerobic bacteria, bacillus proteus, enterobacteria, etc. The patient's systemic poisoning symptoms are mild, but the wound pain is severe. The center of the inflammatory area is purplish red induration, the surrounding is flushed, the central area is necrotic and forms an ulcer, the skin edge sneaks, and there are scattered small ulcers around.
      • Gas gangrene: Gas gangrene is an infection of obligate anaerobic bacteria, which often occurs under the condition of wound pollution. In the early stage, the local skin is bright, tense, and twisted, and the lesion can involve the deep part of the muscle. A smear of the secretion can detect Gram-positive bulky bacilli. Myoglobinuria may be present in stained and necrotic muscles, and free gas between the muscles may be detected by actinographema.
      • Clostridium anaerobic cellulitis: it is a severe skin tissue necrosis resulting from clostridia with extensive gas formation, mostly in areas of stained or incompletely debrided wound, especially the perianal region, abdominal wall, buttocks, and lower extremities that are easily contaminated. Its clinical manifestations are similar to those of necrotizing fasciitis, represented by the sudden appearance of red, swollen, and painful skin, which soon develops into a plaque with a black center gradually becoming gangrenous, with fever and chills, but there is also a number of anoxic gangrenes whose secretions are black and foul-smelling, often containing lipid droplets, with obvious crepitant rales around the lesion. There is much gas seen in the soft tissue via X-ray examination, but none in the patients infected with mixed anaerobic flora.
      • Fournier gangrene: It is a severe gangrene that occurs in the male penis, scrotum, perineum, and abdominal wall. It may be caused by Enterobacter, gram-positive bacteria or anaerobic bacteria infection. It is commonly seen in patients with diabetes, local trauma, incarcerated phimosis, urethral

fistula or genital surgery. The clinical manifestations include sudden redness and swelling of local skin, and many develop into dark red patches and ulcers in the center. The edge of the ulcer is latent, with serous exudation on the surface, severe tenderness, and often fever.

### 3.5.5 Treatment

Necrotizing fasciitis is a critical surgical emergency, which develops rapidly. Once diagnosed, extensive incision and drainage should be carried out immediately. It has been reported that the time of incision and drainage is directly related to the mortality. Necrotizing fasciitis spreads along the fascia. Sometimes the fascia has necrosis, but the skin is normal. Therefore, the incision and debridement should not take the affected skin as the edge, but should be cut to the normal fascia. If the involved area is too large, it is necessary to make multiple incisions for decompression and repeatedly flush the incision with hydrogen peroxide solution to eliminate the anaerobic bacterial growing environment. Apply high-dose antibiotics systemically as early as possible by starting with high-dose penicillin injections or cephalosporin antibiotics. Simultaneously apply glucocorticoids for severe systemic symptoms. Reinforce supportive therapy and symptomatic (or expectant) treatment.

The treatment principle of necrotizing fasciitis include early diagnosis, debridement as soon as possible, application of a large number of effective antibiotics and systemic support treatment.

1. **Debridement and drainage**. Thorough debridement and adequate drainage are the key to successful treatment. The necrotic fascia and subcutaneous tissue should be completely removed until the tissue cannot be separated by fingers. Commonly used methods:
   (a) Remove the healthy skin from the infected area for backup: remove the necrotic tissue and clean the wound; perform free skin grafting to cover the wound surface. This method can prevent a large amount of serous exudations from the wound surface and help maintain the postoperative fluid and electrolyte balance.
   (b) Make multiple longitudinal incisions on healthy skin: remove the necrotic fascia and adipose tissue, flush the wound with 3% hydrogen peroxide solution, metronidazole solution, 0.5–1.5% potassium permanganate solution, etc. to create an environment unfavorable to the growth of anaerobic bacteria; then, apply a gauze soaked with antibiotic solution (i.e. metronidazole, gentamicin) as wet dressing, and change the dressing once every 4–6 h. When changing the dressing, probe for the separation of skin, subcutaneous tissue, and deep fascia to determine whether further expansion of drainage is needed.
   (c) Pick a date for skin grafting: when the skin defect is large in area and difficult to heal on its own, pick a date for dermepenthesis after the inflammation has subsided.

   Attention should be paid to the protection of healthy fascia during operation, which is easy to cause the spread of infection after injury. Metronidazole local wet compress can delay skin growth and should not be used for a long time.
2. **Antibiotics**. Necrotizing fasciitis is a mixed infection of a variety of bacteria (various aerobic and anaerobic bacteria). Systemic poisoning symptoms appear early and the condition is serious. Antibiotics should be used in combination. Metronidazole is highly effective against bacteroides fragilis, which can be controlled by application of clindamycin at the same time; aminoglycosides (e.g. gentamicin, tobramycin, amikacin), can control enterobacter spp.; ampicillin is sensitive to enterococci and anaerobic peptostreptococci; cephalosporins such as cefotaxime and ceftriaxone have a broad antimicrobial spectrum and are effective for both aerobic and anaerobic bacteria.
3. Supportive therapy. Actively correct water and electrolyte disorders. In terms of anemia and hypoproteinemia, transfuse fresh blood, albumin or plasma; ensure adequate caloric intake via nasal feeding or hyperalimentation.
4. Hyperbaric oxygen therapy. In recent years, there is a growing number of concomitant anaerobe infections among surgical infections, and hyperbaric oxygen is effective for obligatory anaerobic bacteria. It is important to note that hyperbaric oxygen therapy can never replace surgical debridement and antibiotic therapy, though it may reduce the mortality of necrotizing fasciitis and the need for additional debridement.
5. Observation of complications. Closely observe the blood pressure, pulse, and urine volume observed throughout the treatment of necrotizing fasciitis; perform examinations such as hematocrit, electrolytes, coagulation mechanism, and blood gas analysis; immediately treat cardiac and renal failure, and prevent disseminated intravascular coagulation and shock.

## 3.6 Post-traumatic Sepsis

Sepsis is one of the most serious surgical infections. There are more than 18 million new cases of sepsis in the world every year, and the number of patients increases at a rate of 1.5–8.0% every year. About 14,000 people die of sepsis every day. Foreign epidemiological surveys show that the mortality of sepsis is higher than that of acute myocardial infarction. More than 350,000 people die of sepsis in Europe and the USA every year, and the treatment cost is as high as

USD 25 billion. Among them, there are about 750,000 new cases and 215,000 deaths in the USA every year. Although China is short of detailed clinical epidemiological data, according to the previous research results and the current clinical information, it is estimated that there are three to four million new sepsis patients and more than one million deaths every year. In the field of field surgery, sepsis can be divided into trauma sepsis, burn sepsis, and ordinary sepsis (sepsis in daily life such as soft tissue, odontogenic, and otogenic ones). Among them, the chance of sepsis in severe trauma and burn patients are increased, and sepsis is closely related to the occurrence and development of multiple organ dysfunction syndrome (MODS). In recent years, significant progress has been made in the pathogenesis, prevention and treatment of sepsis, and it has become one of the important research directions in the field of trauma infection.

### 3.6.1 Pathogenesis

Pathogenic microorganisms and their toxins are the trigger factors of post-traumatic sepsis. There is evidence that bacterial cell wall components such as lipopolysaccharide, peptidoglycan and phosphoteichoic acid, gram-positive bacterial exotoxins such as streptolysin O, *Staphylococcus aureus* enterotoxin B and toxic shock syndrome toxin (TSST-1) can participate in the pathogenic process of sepsis. However, the occurrence and severity of sepsis depend on the reactivity of the body to a greater extent. The essence of sepsis is the individual response to inflammatory substances, which is very complex and widely involves neuroendocrine immune network, complement, coagulation, fibrinolysis, kinin system, and vascular endothelial cell system, in which the immune system and vascular endothelial cell system play a particularly important role.

The characteristic of post-traumatic sepsis is that it gradually develops from a progressive, continuous high dynamic and high metabolic state to a process of decline of visceral function, and pulmonary function is often damaged first. Visceral damage is often the result of two blows. When the body receives the first blow or primary injury (trauma, major surgery, infection, etc.), immune cells such as neutrophils, monocytes macrophages, lymphocytes, and endothelial cells are activated and in an "excited state." When there is a second blow (secondary infection, surgery, iatrogenic error or stimulation, etc.), even if the degree is not serious, it is easy to cause the immune cells and endothelial cells in the excited state to have a super reaction and release excessive humoral media, that is, the so-called amplification effect. However, these humoral mediators are only the primary products of body reaction. When the target cells are activated, they can also produce "secondary," "tertiary," and even more secondary products, namely waterfall effect. The mediators involved in inflammatory response can be broadly divided into two categories: (i) directly cytotoxic: lysosomal enzymes, elastase, myeloperoxidase, cationic proteins, and oxygen radicals, which can directly kill target cells. (ii) cytokines: tumor necrosis factor(ii) (TNFα), interleukin 1 (IL-1), interleukin 6 (IL-6), interleukin 8 (IL-8), interferon-α (IFN-γ), platelet activating factor (PAF), granulocyte-macrophage colony-stimulating factor (GM-CSF), arachidonic acid metabolites, etc. The above humoral media can have adverse effects on the body. The main manifestations are: high dynamic circulatory state of "high excretion and low resistance," myocardial inhibition, endothelial injury and increased vascular permeability, blood hypercoagulability and microthrombosis, mandatory and "autophagy" hypermetabolism. These changes will eventually lead to the impairment of multiple organ function. In addition to direct cell damage, it is mainly ischemic damage. Especially when the heart and lung function are damaged, it will accelerate and aggravate the damage process of various organs of the body.

### 3.6.2 Diagnosis

The third international consensus on the definition of sepsis and septic shock published in the Journal of the American Medical Association JAMA in February 2016 divides the types of sepsis into two categories: sepsis and septic shock. This is based on the further understanding of sepsis pathology and the results of clinical big data analysis, and forms a new diagnostic standard.

1. **Diagnosis of sepsis.** The latest definition of sepsis is the life-threatening organ dysfunction caused by the maladjusted host response to infection. It not only emphasizes the importance of unsteady host response caused by infection (which has exceeded the possible lethality of direct infection itself), but also emphasizes the necessity of timely diagnosis.

   Although the international consensus in 2001 proposed extended diagnostic criteria and could indicate the existence of inflammation or organ dysfunction through bedside and routine laboratory tests, there is still no clinical method to reflect the concept of dysregulated host response.

   Critical medicine research shows that the prognosis of critically ill patients is closely related to the number of failed organs and the degree of functional failure, and the evaluation of organ function of critically ill patients is helpful to evaluate their prognosis. Recent big data clinical studies show that, the effect of using SOFA system to predict the risk of death (the area under the working curve of the subject is 0.74, 95% CI: 0.73–0.76) is better than that of SIRS standard (the area under the working curve of the subject is 0.64, 95% CI: 0.62–0.66); the overall mortality risk of infected patients with SOFA score of more than 2 is 10%, which is higher than that of myocar-

dial infarction patients with ST elevation (8.1%); the death risk of infected patients with SOFA score above 2 is 2–25 times higher than that below 2. The above results suggest that the clinical criteria involved in SOFA score are more suitable for the judgment of sepsis in infected patients, that is, on the basis that the basic sofa value is assumed to be 0, SOFA ≥2 indicates organ disorder. This can become the diagnostic criteria for determining patients' sepsis and be included in the third international consensus on the definition of sepsis and septic shock.

Practice has proved that sofa and its derived quick SOFA (qSOFA) system are conducive to the screening of sepsis. A clinical model determined that two of the following three items met, which was similar to the complete SOFA score: Glasgow score less than 13; Systolic blood pressure is less than 100 mmHg (1 mmHg = 0.133 kpa); respiratory rate is more than 22 times/min. This model has been verified in out of hospital, emergency and ward (data outside the USA and non--U.S.). For patients suspected of infection in ICU, the SOFA score is better than this model, and can well reflect the correction effect of intervention measures (such as vasopressor, sedative, mechanical ventilation). Increasing blood lactate measurement does not improve the prediction effect, but it can help identify patients at moderate risk. This new measure, qSOFA, can provide a simple and rapid bedside standard for judging the possible poor prognosis of adult infected patients. Although qSOFA in ICU is not as effective as SOFA score, it does not need experimental examination and can be evaluated quickly and repeatedly. Therefore, qSOFA standard is used for clinicians to timely identify and further investigate possible organ dysfunction, start or upgrade treatment, consider intensive care treatment or increase the frequency of monitoring. In addition, patients who have not considered infection but meet the positive qSOFA criteria should pay attention to the possibility of infection.

2. **Diagnosis of septic shock**. The latest definition of septic shock is a form of sepsis, characterized by obvious abnormalities of circulation and cell metabolism, which significantly increases the mortality. This definition emphasizes the difference between septic shock and simple cardiovascular dysfunction and the importance of abnormal cell metabolism. Compared with simple sepsis, septic shock is more serious and has a higher risk of death.

   According to the Delphi consensus process and the test results of actual patients, the variables of septic shock were determined as: hypotension, elevated blood lactate, and continuous use of vasopressor. The combination of hypotension and high lactic acid can reflect cell damage and cardiovascular dysfunction, which has been accepted by most experts (72.2%). In other words, if sepsis patients still have continuous hypotension after full fluid resuscitation, and need to use vasopressors to maintain the average arterial pressure above 65 mmHg and blood lactate above 2 mmol/L, they meet the diagnostic criteria of sepsis shock, and their clinical mortality exceeds 40%. Therefore, sepsis and septic shock can be diagnosed hierarchically by using SOFA score and three variable indexes of septic shock.

### 3.6.3 Prevention and Treatment

According to the methods recommended in the current international guidelines for sepsis related treatment, the treatment measures for sepsis mainly include early infection control and organ support treatment, and put forward many precautions such as "no basis for goal orientation, no recommendation for early goal directed therapy (EGDT), targeted blood glucose control and many hazards of deep sedation," and suggested the direction of molecular targeted treatment.

1. **Early goal directed therapy**. Active early resuscitation treatment should be used for sepsis and septic shock, and even advance the resuscitation phase to when the wounded is in the emergency department. The goal of resuscitation is not only to make the common indicators such as central venous pressure, blood pressure, and urine volume basically full, but also to make the mixed venous oxygen saturation ≥70%. Therefore, infusion, vasoactive drugs, and blood transfusion can be used to achieve the goal.
2. **Low tidal volume ventilation**. The ventilation concept of ARDS and acute lung injury has changed from normalizing the blood gas indicators to normalizing the blood gas indicators plus protecting the lungs. Low tidal volume ventilation can avoid excessive expansion of damaged lungs, so as to reduce "secondary lung injury." The results show that the ventilation strategy of AVC mode, TV 6 mL/kg, and platform pressure ≤30 $cmH_2O$ has better prognosis than classical ventilation (TV 12 mL/kg; platform pressure <50 $cmH_2O$).
3. **Medium dose glucocorticoid**. The valuable literature report has completely denied the high-dose and short-term glucocorticoid strategy (hydrocortisone 30 mg/kg, 1–2 days), and advocated the use of medium-dose and long-term treatment scheme (50 mg/kg, once every 6 h for 7 days).
4. **Blood glucose control**. Hyperglycemia in sepsis is not a simple adaptive response or reduced receptor affinity. There is evidence of islets β. The function is damaged, so it is reasonable and necessary to give insulin. Hyperglycemia inhibits immune function and leads to increased susceptibility to infection. Therefore, it is of great clinical significance to control hyperglycemia.
5. **Proper antibiotics application**. Although only half of the blood cultures of sepsis are positive, infection is still

an important factor. Therefore, antibiotics should be used prophylactically.

6. **Anticoagulant therapy**. Low molecular weight heparin, urokinase, antithrombin III, etc., can be used.
7. **Plasma exchange**. It can remove both endotoxin and cytokines. If conditions permit, the hospital can use plasma exchange to treat the wounded with severe sepsis.
8. **Remove the infected foci**. Debridement and drainage must be carried out in time for the definite infection focus.
9. **Traditional Chinese medicine application**. The application of Xuebijing injection has been successfully developed in China, which can antagonize both endotoxin and the uncontrolled release of TNF alpha. The combination of antibiotics and Xuebijing can play the role of "simultaneous treatment of bacteria/endotoxin/inflammatory mediators."

### 3.6.4 Early Warning

The following indicators are mainly used to predict the development of post-traumatic sepsis: (1) epidemiological information of the injured: e.g. age, sex, race, injury severity, mechanism/site/number of injuries, and physiological score; (2) biochemical and immunological indicators: lactate clearance rate, procalcitonin (PCT), IL-6, IL-18, neopterin, Gc globulin, N-terminal pro C-type natriuretic peptide (NT-proCNP), kynurenine/tryptophan ratio, human leukocyte antigen DR of monocytes (HLA-DR), etc. Clinical studies show that only PCT among the above indicators can be used to identify sepsis and non-infectious SIRS patients, and guide the use of antibiotics (shorten the use time of empirical antibiotics), which has been included in the early warning and auxiliary diagnostic indicators of sepsis.

At present, the following indicators are mainly used to predict the adverse outcome of sepsis: (1) routine clinical indicators; (2) scoring system; (3) acute phase reactive protein; (4) cytokines and adhesion molecules; (5) immune function; (6) vasoactive and immunomodulatory neuropeptides; (7) coagulation system indicators; (8) myocardial damage markers, etc. It is very difficult to accurately predict the occurrence and outcome of sepsis due to the different causes and backgrounds of patients (such as age, basic disease or basic state). In terms of infection/sepsis caused by trauma, there are few predictive studies. Some scholars have found that the relative risk of postoperative sepsis in children with penetrating abdominal injury was >2, including age >10 years old, gunshot injury, number of abdominal organs >2, colon injury, injury severity score (ISS) >15, penetrating abdominal trauma index Other data showed that the SIRS score of trauma patients from 3 to 7 days was a predictor of nosocomial infection and length of hospital stay, and the continuous SIRS until the seventh day would significantly increase the risk of death (relative risk was 4.7). For patients with blunt trauma, early detection of serum C-reactive protein (CRP) and IL-6 levels is not helpful for the diagnosis of sepsis. Some literature have confirmed that the migration rate of polymorphonuclear leukocytes in peripheral blood of patients with multiple injuries decreased, and the positive predictive value, negative predictive value, sensitivity, specificity and likelihood ratio of predicting infection were 0.72, 0.93, 0.88, 0.82, and 5.0, respectively. It is suggested that peripheral blood polymorphonuclear leukocyte migration rate is a highly sensitive predictor of infection, and its early determination will guide active anti-infective treatment. Hyperglycemia is related to the high mortality of trauma patients. The incidence of infection complications such as pneumonia, urinary tract infection, wound infection, and bacteremia in hyperglycemia group is also significantly higher. Multiple logistic regression analysis showed that under the control of age, gender and ISS, hyperglycemia is an independent predictor of death, hospital stay, ICU stay and infection complications. Recent studies have confirmed that the increase of plasma procalcitonin (PCT) level in patients with severe trauma indicates an increased risk of sepsis. Although the level of PCT in trauma patients is better than IL-6 in predicting post-traumatic sepsis, if both levels increase in the early stage of trauma, it indicates that the risk of developing post-traumatic mods increases sharply.

Due to the limited biomarkers for early warning and diagnosis of sepsis, the use of genomics, proteomics, metabolomics, and bioinformatics to find biomarkers in the early stage of sepsis is gradually gaining attention. Some scholars have found that the changes of protein expression profiles in liver and heart of septic rats are related to energy metabolism. Some scholars have tried to detect the changes of serum proteomics and whole blood cell gene expression profile in patients with sepsis. Unfortunately, the research of this technique in the field of traumatic sepsis has not been reported.

By predicting the occurrence of post-traumatic sepsis, trauma patients can be divided into high-risk group and low-risk group, If early intervention treatment measures can be implemented for patients in the high-risk group of sepsis (this measure is undoubtedly more advanced than the treatment measures after being diagnosed with sepsis), it can effectively curb the development process of sepsis in the "embryonic" state, so as to reduce the incidence of sepsis. Patients with sepsis can also be divided into high-risk group and low-risk group by predicting their adverse outcomes (such as MODS and death). If strict monitoring and treatment measures can be implemented for patients in high-risk group, the prognosis of patients with sepsis can be effectively improved and the mortality of sepsis can be finally reduced. Pusajo et al. calculated the abdominal reoperation predictive index (ARPI) of the wounded accompanied with sepsis after the surgery, including the following eight parameters affecting the outcome of patients with sepsis, that is, the

first operation as an emergency operation (3 points), respiratory failure (2 points), renal failure(2 points), intestinal obstruction 72 h after operation (4 points), abdominal pain 48 h after operation (5 points), wound infection (8 points), consciousness change (2 points), and symptoms that occur 4 days after the surgery (6 points). The integral value of the index is accumulated after scoring each patient. Patients with an index of 1–10 should be observed conservatively. If the symptoms persist, further laboratory and imaging examinations should be performed. For the positive results of the examination, the second operation shall be performed (for the negative results, the observation shall be continued); if the index is 11–15, the laboratory and imaging examination shall be performed immediately, and for the positive results, the second operation shall be performed (for negative results, continue to observe. If the symptoms persist during the observation period, perform the second operation); if the index is 16 or above, perform the second operation immediately. The ARPI is based on the parameters affecting the outcome of sepsis patients after abdominal surgery. After clinical application, it not only reduces the interval between two operations and ICU stay time, but also reduces the mortality of reoperation patients from 67% to 45%.

The author recently proposed the sepsis predictive score post-trauma (SPSPT) for the first time by analyzing the data of nearly 3000 trauma cases in multiple centers in China. According to the injury severity score (ISS), the LD50 of ISS (the ISS value that causes half of the deaths in a certain age group), the wound surface/track initial contamination degree, and the systemic inflammatory response syndrome (SIRS) score, the clinical values are described below: (i) SPSPT $< 4.25$ indicates a low probability of sepsis, routine treatment is recommended; (ii) SPSPT $\geq 4.25$ indicates a high probability of sepsis, and early intervention is recommended; (iii) SPSPT $\geq 6.45$ indicates an extremely high probability of sepsis and a high mortality, suggesting early and aggressive definitive intervention. The SPSPT values (4.25 and 6.45, respectively) were accurate (84.6% and 82.1%, respectively) in predicting the occurrence of sepsis and the death from sepsis among trauma patients during hospitalization. The scoring system is simple and practical. It can be calculated according to the blood routine test results and relevant simple scores. There is no need for complex biochemical index detection. It is suitable for the early warning of trauma sepsis in grass-roots hospitals, but its accuracy still needs to be verified by prospective multi-center and large sample size.

## 4 Principles of Antibiotics

Wounds are contaminated. A wound bacteriology survey conducted by the Research Institute of Field Surgery of the Third Military Medical University showed that a few hours after injury, the early wound bacteria before debridement were complex, and 29 kinds of aerobic bacteria and 16 kinds of anaerobic bacteria could be detected. These bacteria were the same as those in the soil of the combat area. After debridement, the number of bacterial species decreased, but the positive rate was still as high as 66.7–75%. According to statistics, the infection rate of soft tissue trauma is about 12%, that of colon injury is about 8%, and that of multiple injuries with open femoral fractures is about 90%. Infection depends not only on the wound, but also on the type of wound. For example, the infection rate of colon firearm injury can reach 58%.

The basic principles of wound infection prevention and treatment are still active treatment of wounds, rational application of antibiotics, symptomatic and supportive treatment.

### 4.1 Basic Principles of Antibiotic Prophylactic Application

#### 4.1.1 Timing of Administration

A large number of studies have shown that 6 h after wound contamination is the key period. With the passage of time after injury, the number of bacteria increases exponentially. Therefore, the most effective measure to resist infection is early debridement 6–8 h after injury. Although the application of antibiotics cannot replace debridement, a considerable part of the wounded may delay the initial surgical treatment due to the poor environment and the limitations of transportation tools. Therefore, early anti infection treatment is very important. Early application of antibiotics can prevent bacterial growth and invasion to deep tissues. A retrospective analysis of penetrating abdominal injury found that the incidence of postoperative infection complications was 7% in those who used antibiotics before operation, while 33% and 30% in those who used antibiotics during and after operation. A meta-analysis showed that 669 of the 1241 patients with thoracic trauma who had placed thoracic duct were using prophylactic antibiotics, 572 patients were not used, and incidence rate of empyema was 2.1% and 6.8%, respectively. Meta-analysis showed that the risk of empyema after using these prophylactic antibiotics in these patients was about three times lower than that of non-users. The above experimental studies have proved the superiority of early use of antibiotics after trauma, that is, to reduce the risk of infection complications.

As for the specific time of prophylactic use of antibiotics, some scholars have confirmed through animal experiments that the application of antibiotics 1 h after injury can control the growth of bacteria within 12 h after injury, so as to win time for debridement. It was also reported that 90% of the wounds were not infected when penicillin was given to experimental animals contaminated with *Staphylococcus*

*aureus* 2 h after injury. Some scholars recommend that a single dose of oral, intravenous or intramuscular antibiotics should be given as soon as possible within 3 h after trauma. However, the preventive use of antibiotics for contaminated wounds has no obvious therapeutic value 3 h after injury. The reason is that the extravasated fibrin at the wound can wrap around the invading bacteria and form a barrier that antibiotics cannot cross. At present, most scholars believe that the "golden time" of preventive medication is within 3 h after injury, which is also the acute reaction period of the body. The local hyperemia reaction is conducive to the diffusion of drugs and play its bacteriostatic or bactericidal role. Delayed use, such as the use of antibiotics after 6 h after injury, will significantly increase the risk of infection.

### 4.1.2 Antibiotic Selection

The types of prophylactic use of antibiotics after trauma are not the more the better, but should be determined according to the situation. A study showed that there was no difference in the incidence of sepsis, organ failure, length of hospital stay and mortality between the use of single antibiotics (time <24 h) and multiple antibiotics (time >24 h).

After trauma, especially war injury, it is controversial whether to choose broad-spectrum antibiotics or narrow-spectrum antibiotics for preventive use of antibiotics. The U.S. military recommends the use of broad-spectrum antibiotics, especially when surgical treatment cannot be accepted in an emergency. In October 1993, the US military launched the largest urban ground attack after the Vietnam War in Mogadishu, the capital of Somalia. In December 1998, the United States Special Operations Command convened relevant experts and personnel to summarize the problems and lessons encountered in the treatment of the wounded in this urban war. In this battle, due to the delay of operation time, the incidence of infection is very high. Therefore, it is necessary to give antibiotics as soon as possible. Experts believe that cefoxitin has a wide antibacterial spectrum and good effect, so it should be the first choice; ceftriaxone is the second. Although its antibacterial spectrum is narrower and more expensive than cefoxitin, it is only needed once a day, which has great advantages in the case of extended evacuation time. The amount of antibiotics it penetrates into interstitial fluid can reach 92%, and the half disappearance time in vivo is 8 h. From 1981 to 1989, it was used in 140 units and 22,901 wounded patients. The failure rate was only 5.49%. The dosage was 2G once a day, which could prevent infection of contaminated wounds for 48 h. In addition, fluoroquinolones have a wide antibacterial spectrum and can be absorbed quickly after oral administration, so they are suitable for use under harsh conditions. In wartime, in addition to considering the antibacterial spectrum, the selection of antibiotics allocated to individual soldier kits and health worker kits should also be comprehensively considered in combination with factors such as their bactericidal ability, tissue penetration, safety, stability, convenience of use and whether they are limited by storage conditions. At present, the U.S. military distributes oral moxifloxacin to individual medicine boxes and medical kits. The antibiotic is 8-methoxyfluoroquinolones.

A British study shows that penicillin based therapy is sufficient for the prevention of limb injury infection. For the prevention of war wound infection, the British Army used relatively narrow-spectrum antibiotics, typically penicillin plus β-lactamase inhibitors. During the Falklands war, the British Army required all the wounded with open wounds to be injected with ampicillin intravenously, sulfamethazine for head penetrating injury, and gentamicin and metronidazole for abdominal injury.

The International Committee of the Red Cross recommends that penicillin be used as much as possible before hospitalization for the war wounded, because its biggest infection killer is beta-hemolytic streptococcus and Clostridium, and penicillin is still the best antibiotic for these pathogens.

Whether broad-spectrum or narrow-spectrum, antibiotics should be selected for most contaminated wound sites. The selected antibiotic antibacterial spectrum should cover bacteria that may pollute the wound (such as normal skin and intestinal flora, *Staphylococcus aureus*, *Escherichia coli*, and anaerobic bacteria in digestive tract). There are different kinds of pathogens in different parts of trauma. For example, after abdominal trauma, almost all pathogens come from the intestine, and a large part of the infection is a mixed infection caused by the cooperation of aerobic and anaerobic bacteria. Therefore, antibiotics or antibiotic compatibility that can cover both aerobic and anaerobic bacteria should be selected. Do not directly initiate preventive treatment against multidrug-resistant bacteria. After all, multidrug-resistant bacteria such as *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Klebsiella pneumococci* are not representative bacteria of the wound at the time of injury. Empirical use of vancomycin to prevent methicillin-resistant *Staphylococcus aureus* (MRSA) infection is not necessary. For some wounded, such as those with deep wounds, many necrotic tissues and heavy pollution, tetanus immunoglobulin, and tetanus toxoid should be given appropriately.

The use of "appropriate" antibiotics usually means narrowing the antibacterial spectrum or stopping antibiotics. The unrestricted use of broad-spectrum antibiotics makes the infection of multidrug-resistant bacteria and opportunistic bacteria more common. Considering the drug resistance associated with the application of broad-spectrum antibiotics, the application of narrow-spectrum antibiotics may bring

greater long-term benefits, but this needs to be confirmed by a lot of practice.

### 4.1.3 Dosage

It is found that insufficient or excessive use of antibiotics will lead to bacterial drug resistance, which will be complicated with various drug-resistant bacterial infections, such as ventilator-associated pneumonia, catheter-related infection, and fungal infection. Therefore, the maximum allowable dose should be used for the first time in the prophylactic use of antibiotics after trauma.

### 4.1.4 Treatment Course

The traditional view of prophylactic use of antibiotics after trauma is about 1 week, but the current view is that the duration of antibiotic use should be minimized, that is, the time of antibiotic administration should be reduced from 5 to 7 days to 3 days or 1 day, or even one prophylactic dose. Prospective studies have shown that prophylactic use of antibiotics for 1 day was equivalent to the traditional recommended use of antibiotics for 5 days. Long-term administration of antibiotics to prevent infection after injury does not bring benefits. Studies have shown that there is no difference in the incidence of complications between short-term ($\leq$24 h) and long-term (>24 h) prophylactic use of antibiotics in abdominal trauma. Severe trauma is not a reason to prolong the preventive use of antibiotics. The study found that the preventive use of more than one antibiotic in severe trauma for more than 24 h cannot prevent the occurrence of organ failure and sepsis, nor reduce its mortality. On the contrary, it increases the possibility of infection with drug-resistant bacteria. For war wounded, under the ideal conditions of emergency evacuation, early pre-hospital first aid and sufficient basic health conditions, antibiotics can be used in a single dose or no more than 24 h. However, under the conditions of limited medical resources, such as unsatisfactory health environment and delayed evacuation, antibiotics can be used for up to 5 days until the delayed initial suture. The course of prophylactic use of antibiotics was different in different parts of trauma, which was recommended in relevant literature.

### 4.1.5 Administration Route

Intravenous infusion should be the first choice for the administration of post-traumatic prophylactic antibiotics, especially in patients with hemodynamic instability, intravenous therapy of antibiotics is better than intramuscular injection. Of course, not all traumatic patients need systemic medication, and burn patients do not need systemic medication unless there is a clear systemic infection or combined with other trauma. Some scholars believe that local medication is better than systemic medication because it is less affected by metabolism in the body, and the probability of systemic allergic reaction and toxic and side effects is significantly reduced. It can also avoid the imbalance of flora caused by systemic use of antibiotics, especially is suitable for removing bacteria colonized on the skin. For example, applying antibiotic powder directly to the wound can achieve higher drug concentration level and longer duration. When dealing with the wounded in the Pearl Harbor attack, the U.S. military not only emphasized early debridement, but also stipulated the routine use of sulfonamides on the wound surface, which greatly reduced the infection rate. Since then, sulfa powder has been carried in American backpacks. In addition to vascular plug, the range of blood circulation disorder in patients with deep burn is very wide. After systemic medication, the effective dose cannot reach the local area. Switching to local medication can achieve a certain effect. Therefore, many burn wound drugs have been developed, such as silver sulfadiazine (zinc), silvadene–silver nitrate, 1% gentamicin, and so on. Some scholars recommend that patients with burns should be wet applied with silver sulfadiazine or mafenide acetate. During the Vietnam War, the USA gave antibiotics to some of the wounded who could not go through early debridement (including tetracycline or neomycin, bacitracin, polymyxin, etc.), and the wound infection rate was also significantly reduced (from 39% to 16.3%) compared with those without medication. Therefore, as long as the local medication is reasonable, it can work. For drug selection, first consider the drugs that are not prepared for systemic use, but pay attention that the concentration should not be too high and the wound should not be too large to avoid drug absorption and poisoning. In addition, abscess, intraperitoneal medication and airway atomization are also different forms of local medication. In recent years, antibiotics are made into biodegradable polymers by drug controlled release technology. Foreign countries have made some progress in the research of in the wound antibiotic sustained-release capsules or sustained-release beads. Its advantages are local high concentration, high efficiency and small side effects. The disadvantage is that local administration is difficult to reach the deep part of the wound. There is evidence that the application of antibiotic sustained-release beads is appropriate for those open fracture patients waiting to be evacuated from the theater, but it is not accurate for the patients who are evacuated to the definitive treatment institution 1–3 days after the injury. It is suggested that the combination of systemic and local medication will have a better effect.

Post-traumatic infection is caused by many factors, including the immune response of the injured body, the environment, mechanism and location of the injury. Prophylactic use of antibiotics is to reduce post-traumatic infection and its complications. Antibiotics should be selected based on practical guidelines. In case of infection, antibiotics should be selected empirically according to the local antibacterial spectrum before the results of bacterial culture and drug

sensitivity test, and unnecessary empirical broad-spectrum antibiotics should be avoided, because unreasonable preventive antibiotics will also lead to the occurrence of bacterial drug resistance. The study found that about 50% of patients had high resistance to ampicillin and sulbactam due to inappropriate empirical antibiotic treatment. In the process of diagnosis and treatment, the rational use of antibiotics needs specific analysis, corresponding treatment plans according to different environments and individual conditions, and pays attention to the drug type, course of treatment, dose, and timing of administration. In conclusion, reasonable selection and use of antibiotics can reduce the occurrence of drug side effects and bacterial resistance, shorten the length of hospital stay and save medical resources.

A recent systematic literature review by the U.S. Surgical Infection Society (SIS) on whether prophylactic antibiotic application affects the incidence of infection after open fractures has supported some important and practical conclusions: (1) early and short course of first-generation cephalosporins after injury, along with the implementation of prompt and modern treatment measures for fracture, will greatly reduce the risk of infections; (2) there is inadequate evidence to support that other usual means of treatment is effective, such as extended courses or repetitive short-course application of antibiotics, coverage of the antibiotic spectrum to Gram-negative bacilli or Clostridium spp., and topical application of antibiotics like sustained-release beads; (3) extensive randomized and blind trials are needed to prove or disprove the value of these traditional routes.

## 4.2 Basic Principles of Antibiotic Therapy

The confirmed bacterial infection should be comprehensively considered according to the type and severity of wound infection, the general condition of the wounded, the type of pathogenic bacteria, the sensitivity of bacteria to drugs, the permeability and effective concentration of drugs in tissues, maintenance time and side effects. Before obtaining the results of bacterial culture, clinicians need to make preliminary strain judgment and drug selection. The following information can be used as a reference for empirical medication:

### 4.2.1 Bacterial Strain Analysis According to the Wound Site

There are both exogenous and endogenous bacterial sources of trauma infection, and the latter has attracted more and more clinical attention in recent years. It is important for clinicians to be familiar with the resident bacteria in different parts, because the pathogenic bacteria of trauma infection are often consistent with the resident bacteria in the adjacent parts of trauma.

1. **The superficial wounds around the skin, subcutaneous tissue, mouth and nose** are often dominated by gram-positive cocci, such as *Streptococcus*, *Staphylococcus*, etc.
2. **Infection with extensive muscle damage**. In addition to gram-positive cocci, anaerobic infection should be focused on particularly.
3. **Infected fracture wounds**. In addition to *Staphylococcus*, *Proteus* infection is also quite prominent.
4. **Abdominal (especially gastrointestinal penetrating injury), perineum, perianal and thigh root injury**. The common pathogenic bacteria are intestinal flora. The intestinal flora is complex, mainly including three types: intestinal anaerobic bacteria, intestinal gram-negative bacilli and fecal streptococcus.
5. **Complex oral injury**. In addition to gram-positive cocci, anaerobic infection often occurs in.

As for the common pathogenic bacteria of intracranial and thoracic trauma infection, there is no certain law due to different reports.

### 4.2.2 Bacterial Strain Analysis Combined with Local Conditions

1. ***Streptococcus***. The inflammation is obvious and diffuse rapidly which is easy to form Peritraumatic cellulitis and lymphangitis. The pus is thin and sometimes bloody.
2. ***Staphylococcus***. The local suppurative reaction is severe with thick pus which is easy to form focal destruction.
3. ***E. coli* infection**. The pus can be comparatively thin. In the past, it was thought that there was fecal odor, which was actually the fault of intestinal anaerobic bacteria.
4. ***Pseudomonas aeruginosa***. The infected dressing is green, and when it coexists with necrotic tissue, it has musty smell or sewer odor.
5. ***Anaerobic* bacteria**. It varies with strains. In case of gas gangrene, due to protein decomposition and fermentation, it often has special odor such as hydrogen sulfide and ammonia, local gas production or subcutaneous emphysema and tissue corruption; Gram positive bacillus can be found by secretion smear staining. It should be noted that no matter what kind of anaerobic infection, it often grows aseptically in ordinary bacterial culture (other bacteria can grow in mixed infection).

### 4.2.3 Bacterial Strain Analysis Combined with Conditions

For those with rapid onset, rapid deterioration, rapid occurrence of hypothermia, low leukocyte and hypotension, and dyspnea, gram-negative bacilli and anaerobic bacteria infection are common. For those with relatively slow development, mainly presented as high fever and metastatic abscess, gram-positive cocci are common. *Candida* infection should be considered in patients with prolonged course of disease,

persistent fever and poor response to general antibiotic treatment.

### 4.2.4 Antibiotics Selection for Pathogenic Bacteria

As the bacterial drug sensitivity may be different in different regions and units, drug sensitivity tests should be carried out if conditions permit. Here, only the general situation of bacteria sensitive to drugs is used as a reference for drug selection.

1. ***Hemolytic streptococcus***. Penicillin is the first choice. Although it has been used clinically for more than 50 years, penicillin resistant hemolytic streptococcus is still rare. The wounded who are allergic to penicillin can choose lincomycin, erythromycin, etc.
2. ***Staphylococcus aureus***. Penicillin has strong vitality and good tissue dispersion among antibiotics, which can still be used for non-drug resistant *Staphylococcus aureus* infection. For penicillin resistant *Staphylococcus aureus* infection, semi synthetic penicillin, cephalosporin, lincomycin, clindamycin, ampicillin, erythromycin, Tylenol, etc. can be selected. Vancomycin can be used for multi-drug resistant *Staphylococcus aureus*.
3. **Intestinal gram-negative bacilli**. The most common in aerobic bacteria are *Escherichia coli*, *Klebsiella*, aerogenic bacilli, proteus, etc. The sensitivity of these bacilli to drugs is similar, such as gentamicin, amikacin, polymyxin B, the third generation cephalosporin, and Tylenol.
4. **Anaerobic bacteria**. Anaerobic bacteria that are common to see include Bacteroides, Clostridium anaerobes, anaerobic streptococcus, Clostridium, etc. The cultivation of anaerobic bacteria is difficult, and the drug sensitivity test is more difficult. The latter still lacks standard methods. If the drug sensitivity test needs to be carried out on the wounded one by one, it not only requires high conditions, but also takes time. Therefore, at present, it is more necessary to borrow the materials of some special laboratories to assist in drug selection. Almost all aminoglycoside antibiotics (such as amikacin, gentamicin, neomycin) and polymyxin B are not sensitive to anaerobic bacteria. Penicillin is mostly sensitive to the above anaerobic bacteria, with the exception of fragile bacilli. The antibacterial spectrum of lincomycin is similar to that of penicillin. It can be used when the wounded are allergic to penicillin. Among the commonly used antibiotics, chloramphenicol, clindamycin, and metronidazole are available. In recent years, many pharmaceutical departments have paid attention to the development of broad-spectrum antibiotics that can take into account both aerobic and anaerobic bacteria, such as the second and third generation cephalosporins, Tienam (imipenem/cilastatin), soproxen (Cefoperazone/sulbactam), piperacillin/tazobactam, and so on.
5. ***Pseudomonas aeruginosa***. The drugs available include gentamicin, polymyxin B, amikacin, Tylenol and the third generation cephalosporins. It was also found that some strains were quite sensitive to chloramphenicol.
6. **Fungal infection**. Amphotericin B and fluconazole can be used for fungal infection.

### 4.2.5 Drugs Selection According to Its Tissue Distribution

The drug sensitivity tests adopted in clinic are based on the effective inhibitory concentration in serum, which does not reflect the effective concentration of drugs in different tissues. For example, due to the blood–brain barrier, the drug concentration in cerebrospinal fluid is often significantly lower than that in serum. Besides, there are obvious differences in the ability to penetrate the blood-brain barrier of different kinds of antibiotics. For example pathogenic bacteria of intracranial infection are highly sensitive to gentamicin, kanamycin and polymyxin B in vitro, which can hardly penetrate into cerebrospinal fluid, so that they should not be used. In contrast, chloramphenicol, tetracycline, sulfadiazine, and ampicillin are better; lincomycin and cephalosporin can also be considered. In addition, there are significant differences in drug concentrations in the prostate and bile. Ampicillin is often used in clinic in case of biliary tract infection, because it is involved in the enterohepatic circulation so that if the biliary tract is not blocked, the bile concentration can reach several times of the serum concentration. Cephalosporin has a good effect on bone and soft tissue infection, which is also related to its good diffusion effect on the above tissues. Therefore, in the selection of antibiotics, in addition to the sensitive ones, the distribution of the bacteria to relevant tissues should also be considered.

## 5 Principles of Medical Treatment in Echelons of Trauma Infection

### 5.1 Medical Treatment in Echelons of War Wounds

**Anti-infection strategy in the medical treatment in echelons of war injuries**. The treatment rules of war injuries issued by our army in 2006 defines the medical treatment in echelons of war injuries, including five basic treatment links according to the treatment technical system, that is, battlefield (on-site) first aid, emergency treatment, early treatment, definitive treatment, and rehabilitative treatment. Article 16 of Section II (basic requirements for treatment) of Chapter II (organization of war wound treatment) stipulates that the wounded shall take anti-infective drugs from the battlefield (on-site) first aid. When conditions permit, anti-shock treatment such as fluid infusion can be taken in the battlefield (on-site) first aid. From the rescue center of

regiment and brigade level units of arms, debridement, injection of tetanus toxoid or antitoxin serum and anti-shock treatment based on fluid infusion and blood transfusion shall be carried out. In the emergency treatment stage described in Chapter III (technical scope of war wound treatment), it is stipulated to debride muscle and superficial tissue; bandage the wound as soon as possible and take oral antibiotics. If possible, intravenous antibiotics shall be given to the wounded with serious wound pollution; in the early treatment stage, it is stipulated that relatively complete debridement operation shall be carried out as well as broad-spectrum antibiotics injected intramuscularly or intravenously; tetanus toxoid and tetanus antitoxin serum shall be supplemented for the wounded who have not received tetanus automatic immunization"; in the definitive treatment, it is stipulated to continue systemic anti-infection therapy. Chapter 8 (treatment of the wounded in special environment operations) also puts forward requirements for anti-infection measures for the wounded in special operation environment. For example, for war injuries combined with seawater immersion, it is proposed to use broad-spectrum anti-infective drugs locally in the early stage. For the treatment of war wounds in mountains and forests, it is proposed to thoroughly debridement and give anti infection treatment as soon as possible. For plateau war wound (open wound), timely debridement is emphasized, and primary suture is not suitable. For war wounds in Gobi desert, debridement and washing should be carried out as soon as possible and covered with sterile dressing. For war injuries in humid and hot environment, first aid should be given on site and broad-spectrum antibiotics should be taken orally.

## 5.2 Management Principles for Prevention and Treatment of War Wound Infection

1. **Early debridement**. The prevention and treatment of war wound infection mainly depends on good early surgery, while antibiotics only play an auxiliary role. Debridement should be performed as soon as possible after injury, which should generally be performed within 6 h after injury, and should not exceed 72 h at the latest. Normal saline and sterile water without additives can be used as the lavage solution for flushing the wound. If sterile water cannot be obtained, the wound can be flushed with drinking water. It is not recommended to use the liquid added with antibiotics for wound lavage. In addition to the eyes, brain and spinal cord, debridement in other parts can completely remove necrotic tissue and foreign bodies. For infected wounds, necrotic tissue and foreign bodies should be removed as much as possible and drainage should be established. The wounded who undergo debridement unconditionally shall be evacuated as soon as possible with the support of continuous anti shock and anti-infection measures.
2. **Delayed suture**. After debridement, initial suture or positioning suture shall be performed in special parts such as head, face, hand and vulva. For penetrating wounds of skull, chest, abdomen, and joint cavity, the thoracic peritoneum, dura mater, and joint capsule must be sutured. After debridement of wounds in other parts, only sterile dressing shall be used for dressing or covering, and initial suture is prohibited. For the wound with clean surface, fresh and neat granulation tissues, and no purulent secretion, or redness, swelling and tenderness in the wound edge, delayed suture should be performed 4–7 days after debridement, generally. If the wound is infected or the timing of delayed suture is missed, after the infection is controlled, the wound is cleaned and the granulation tissue is healthy, and the secondary suture is generally carried out 8–14 days after debridement. When induration formed at the bottom of the granulation of the wound affects the healing, the induration tissue should be removed before suture (late secondary suture). If the larger wound cannot be sutured at one time, suture the part that can be sutured at first, and cover the rest with skin transplantation. For the wound that cannot be sutured at a later time or secondary suture, skin grafting, flap transfer with vascular pedicle or flap transplantation with anastomotic vessels can be performed as appropriate.

   In the self-defense counterattack against Vietnam, many serious suppurative infections and gas gangrene of limbs were caused by primary suture in violation of the most basic principle of delayed suture. Among the 199 wounds immediately sutured after debridement, 198 wounds (99.3%) had serious infection, including four cases of gas gangrene. After the Wenchuan earthquake on May 12, 2008, when many wounds were cleaned and sutured in the disaster area and transported to major hospitals in Chengdu, Chongqing, and other places, almost all of them were infected and had to be cleaned again.
3. **Usage of antibiotics**
   (a) Timing: the sooner the better. Even if delayed, antibiotics should be used within 3 h after injury. The longer the delay, the higher the incidence of infection.
   (b) Administration route. Intravenous infusion is the first choice, followed by intramuscular injection and oral administration.
   (c) Medication course. The International Committee of the Red Cross recommends that under the conditions of rapid evacuation, early pre-hospital first aid and adequate health infrastructure, a single dose of antibiotics is usually selected or the preventive use of antibiotics is limited to 24 h. In the case of limited medical resources and delayed evacuation, anti-

biotics are usually given for 5 days until delayed suture.

(d) Antibiotics types. The U.S. war wound infection prevention guidelines recommend the use of broad-spectrum antibiotics (such as cephalosporins) at least for those who cannot receive rapid surgical treatment. Because the use of broad-spectrum antibiotics is easy to cause subsequent drug-resistant bacterial infection, the excessive use of broad-spectrum antibiotics should be avoided. The main infection threats faced by a large number of war wounded are gas gangrene, tetanus and invasive streptococcal infection, which can be treated with relatively narrow-spectrum antibiotics. Penicillin and metronidazole are the first choices recommended by the International Committee of the Red Cross. Gentamicin should be added if there are systemic symptoms of suppurative infection.

4. **Dynamic monitoring**. The treatment of batch wounded is a continuous process, which is not interrupted by the evacuation and transfer between steps. Similarly, the continuous implementation of wound infection prevention and control measures depends on the dynamic monitoring of contaminated wounds. A large amount of evidence shows that the bacteria of wound pollution and subsequent infection evolve over time. At the moment of injury, there is a risk of multiple microbial contamination, especially Clostridium and beta-hemolytic streptococcus, followed by contamination from its own skin and gastrointestinal flora, and finally the intervention of hospital-acquired infection bacteria.

   Do not perform routine preoperative or postoperative microbial culture unless there are clear signs of clinical infection. Because the wound bacterial culture results cannot fully indicate the subsequent infection or the pathogen of infection, the bacterial culture results may mislead the use of unnecessary antibiotics or abuse of broad-spectrum antibiotics. Dynamic observation of wound is a simple and feasible method. The transparent dressing developed by foreign scholars provides convenience for wound dynamic monitoring.

5. **Comprehensive intervention**. Comprehensive anti-infection strategies include lavage, debridement, drainage, antimicrobial therapy, dressing and stabilization for fractures. Secondary interventions include controlling bleeding, reducing hyperglycemia, providing adequate oxygen, reducing blood transfusion, and avoiding hypothermia. Other measures to prevent nosocomial infection are followings. Medical staff shall perform operations in a special operating room with strict sterilization, keep good hand hygiene habits, change the dressings in the ward regularly, isolate infected patients, and make proper cleaning, disinfection, and sterilization of hospital facilities.

## 5.3 Problems to Be Solved

1. **Specification for the use of antibiotics**. Due to the lack of randomized controlled trials on the application of antibiotics in batch wounded, many suggestions are based on a large number of expert opinions and publications. The two main issues debated are: whether to use the broadest spectrum of antibiotics after injury, and what is the duration of prophylactic antibiotic use. This needs to be proved by large-scale, randomized and double-blind clinical trials.
2. **Early warning and intervention measures of sepsis**. If wound infection is not handled properly, it can cause sepsis, septic shock, multiple organ dysfunction syndrome (MODS), and death. Sepsis refers to systemic inflammatory response syndrome (SIRS) caused by infection. The condition is dangerous, and the incidence and mortality have been high. Although modern medical methods such as vaccines, antibiotics, and intensive care have made progress, sepsis is still the main cause of death caused by infection, and its in-hospital mortality is as high as 30–60%. The key reason is that once the pathological process of sepsis starts in the body, the "SIRS → MODS" pathological process with sequential development is difficult to be effectively contained. If we can accurately predict (not diagnose) the occurrence of "SIRS → MODS" caused by post-traumatic sepsis and implement early intervention measures, it is expected to interrupt this pathological process at an early stage. However, at present, the treatment in echelons and time effective treatment strategies for the prevention of sepsis of batch wounded have not attracted great attention in the academic community.

The infection of batch wounded in wartime has been and will still be an important problem in the field of trauma surgery. The future development trend is: on the premise of following the traditional principle of "early debridement and delayed suture," we should follow the basic law of treatment in echelons of anti-infection, advocate the concept of dynamic monitoring and comprehensive prevention and treatment, and implement the strategy of "early warning in echelons and continuous intervention," so as to effectively reduce the incidence and mortality of war wound infection of batch wounded.

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