

# Clinical Clinical a BOOK 2 part (clinical cases are approved in the practice). For Clinical Pharmacists (own researches and the analysis of references)

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## Abstract

At timely introduction Anti-diphtheria serum intoxication symptoms quickly disappear, and touches are torn away by 6-8 day. After tearing away of touches still some time remain superficial necrosis. Simultaneously decreases and the hypostasis cervical cellulose's disappears. In the absence of timely specific treatment illness usually progresses and only in cases of the localised diphtheria probably recover, however, thus there can be complications in a kind myocarditis or peripheral paralyses.

Diphtheritic croup. At process localisation in respiratory ways there is a diphtheritic croup - the clinical syndrome accompanied by a hoarse or hoarse voice, rough barking cough and complicated (stenotic) breath.

**Key words:** chemical processing of pharmaceutical drugs; dosage form design; drug delivery

## Aetiropic Diphtheria Treatment

At timely introduction Anti-diphtheria serum intoxication symptoms quickly disappear, and touches are torn away by 6-8 day. After tearing away of touches still some time remain superficial necrosis. Simultaneously decreases and the hypostasis cervical cellulose's disappears. In the absence of timely specific treatment illness usually progresses and only in cases of the localised diphtheria probably recover, however, thus there can be complications in a kind myocarditis or peripheral paralyses.

Diphtheritic croup. At process localisation in respiratory ways there is a diphtheritic croup - the clinical syndrome accompanied by a hoarse or hoarse voice, rough barking cough and complicated (stenotic) breath.

With diphtheria of a nose children from chest age till 3 years, sometimes in more advanced age and even at adults is more often are ill. Last years it meets less often (from 10, 9 % in 1957-1958 has decreased to 2, 9 % in 1965 - 1971).

The skin diphtheria, according to various authors, makes 0, 5-20 % from other localisations. The diphtheria of a skin at children of early age, especially with the broken food, meets much more often, than is diagnosed (takes the second place after a nose diphtheria). The last is caused by anatomy-physiological features of an organism of children of this age - insufficient development of a horn layer of a skin, greater it's susceptibility to an infection in comparison with other covers.

Diphtheria of a mucous membrane of an oral cavity - the unusual occurrence is extreme.

The diphtheritic otitis can be both primary, and secondary as a result of distribution of process of a nose, a pharynx and a throat. Disease happens localised (defeat only an average ear) and extended.

Frequency of otitis is according to weight of a current of a diphtheria and age of the child.

This disease is more often observed at children of younger age and characterised by an easy current, absence of spontaneous punching of an eardrum. Character of a current of these aseptic otitis allows to consider as their result of local display of an infectious allergy because the mucous membrane covering a cavity of an average ear, has the general embrional an origin with a mucous membrane drink.

The diphtheria of external genitals meets seldom (within 0, 1-1,1 % of cases), basically at girls of 5-8 years as secondary localisation at a pharynx or nose diphtheria.

The diphtheria of a gastroenteric path meets very seldom, is usually combined with the widespread or toxic form of a diphtheria of other localisations.

Diphtheria of lungs - extremely rare localisation of an infection. Usually it is combined with defeat by a diphtheria of the top respiratory ways (a throat, a trachea, bronchial tubes).

Diphtheria-mikst. In some cases the diphtheria can be combined with any sharp infectious disease (a measles, a scarlet fever, a whooping cough, a flu, a chicken pox, etc.) or owing to joining of a diphtheria to other infections, or their stratification on a diphtheria. The diphtheria which has joined a scarlet fever, is characterised by more expressed local inflammatory reaction with slow disappearance of filmy touches and sharper and long reaction from the party regional lymph nodes. Subtoxic and toxic forms of a diphtheria of a pharynx proceed with long hypostases and an intoxication. The general reaction is characterised hyperergia's (proof leucocytosis, a heat).

In the diagnostic relation cases of joining of a diphtheria to a scarlet fever in an initial stage, when still strongly pronounced initial scarlet fever a tonsillitis are especially inconvenient.

On supervision S.C. Niconova's, O.D.Ten (1960), the diphtheria and measles combination is characterised by fall of the general reactivity of an organism. Inflammatory changes in a pharynx, an intoxication insignificant, proof leucopenia with relative limfocytosis are a little expressed. According to V.M.Molchanov (1960) measles create the raised predisposition to disease by a diphtheria that is a syndrome of strengthening of an infection (the modern term - the note of the author). More often diphtheritic process is localised in a throat and to a nose. At the croup which has developed during the late period of measles, it is necessary to suspect a diphtheria.

Diphtheritic croup proceeds at measles with some features - the mixed type of the short wind proof aphonia's, slow resorption filmy touches, recurrent character of a stenosis and almost always the forecast very serious becomes complicated a pneumonia, therefore. The chicken pox which has joined a diphtheria, promotes heavier current of disease. Thus toxic forms of a diphtheria of a pharynx are more often observed, the aggravation latently a proceeding diphtheria of a nose is provoked for a long time, clinical displays of complications of a diphtheria worsen (miocarditis, polyneuritis), time discharge at convalescent is extended.

Certain interest represents streptodiphtheria, as result combined to a diphtheria-streptococcal infection. Joining of a streptococcal infection to a diphtheria promotes more frequent development of heavy forms and complications.

The clinical picture happens is so brightly expressed, that streptodiphtheria is easily diagnosed. It is characterised by the expressed temperature and inflammatory reaction from a pharynx. Develops bright hyperemia the pharynx mucous membrane, delimited from the firm sky a line of demarcation, with the expressed painful syndrome along with typical filmy touches and painful regional limphadenitis.

#### **Clinic of a diphtheria at imparted children.**

Occurrence of disease at imparted probably owing to low level of antitoxic immunity. Decrease in intensity of immunity after the transferred infectious diseases is possible. Imparted children have toxic forms of illness and complication (these are data of official medicine) much less often.

Current of a diphtheria at imparted usually smooth. Intoxication symptoms disappear for 3-5th day of illness, the pharynx is cleared for 5-7th day. At the localised form recover without whey introduction is possible.

However these features are traced only at those children at whom disease arises against residual anti-diphtheria immunity. In cases, when immunity completely is absent (refractory children), can arise heavy toxic forms with complications and a lethal outcome. The clinic of a diphtheria at such patients practically does not differ from that at not imparted.

#### **Complications**

The most typical complications of a diphtheria arise from cardiovascular system (miocarditis), peripheral nervous system (neuritis and polyneuritis) and kidneys (nephrotic a syndrome).

Quickly appear and frustration of a warm rhythm progress. The Nephrotic syndrome is marked in the sharp period of illness, at intoxication height.

Typical complication of a diphtheria are peripheral paralyses.

Distinguish early and late diphtheritic paralyses.

Late paralyses arise on 4-5th week of illness, proceed on type polyradiculoneuritis. Are characterised by all signs of languid peripheral paralyses: decrease tendinous reflexes (usually on the bottom finitenesses), muscular weakness, coordination frustration, uncertain gait up to full immobility in finitenesses. In heavy cases probably defeat of muscles of a neck, a trunk; the patient cannot sit, hold a head.

There can be a throat paralysis (the voice and cough become silent), defeat drinks (cannot swallow food and even a saliva), a diaphragm paralysis (paradoxical movements of a belly wall - indrawing a stomach at a breath), defeat of mechanisms innervation hearts is possible.

Current diphtheritic polyradiculoneuritis (in the absence of defeat of respiratory muscles and a diaphragm) usually favorable. Paralyses disappear in 1-3 months with full restoration of structure and function of skeletal muscles.

#### **The diagnosis**

Clinical diagnostics has crucial importance as to hesitate with introduction anti-diphtheria serum and to wait results of laboratory research are not represented possible.

From methods of laboratory diagnostics the greatest value has bacteriological research. But express analyses are necessary!!!

#### **The differential diagnosis:**

The localised diphtheria of a pharynx should be differentiated from lacunary, follicular, is false-filmy and others anginas more often.

Toxic forms of a diphtheria of a pharynx differentiate from infectious mononucleosis, paratonsillar an abscess, parotitis infections.

The differential diagnosis of a diphtheritic croup.

Now diphtheritic croup meets seldom, incomparably it is necessary to deal with a croup syndrome at acute respiratory viral infection (ARVI) is more often.

For diphtheritic croup it is characteristic weakly expressed the beginning and gradual development of the basic symptoms of disease: disphonia, reaching to aphonia's, the rough «barking» cough getting then silent character and gradually, but progressively accruing phenomena of a stenosis. The croup at acute respiratory viral infection (ARVI) (a flu, a paraflu, etc.) differs the sudden beginning, quite often disease develops at once from an attack of an asthma and rough barking cough. Thus the voice remains sonorous or slightly grainy, but sonorous notes always remain and appear usually during an attack and crying of the child. For acute respiratory viral infection (ARVI), accompanied by a croup syndrome, quite often heat and an intoxication are characteristic catharal the phenomena.

In more rare cases diphtheritic croup should be differentiated from a syndrome of the croup arising at a measles, a chicken pox, aphthous a stomatitis and other diseases.

Sometimes there is a necessity to differentiate a croup from retropharyngeal an abscess, papillomatosis throats, alien bodies in respiratory ways.

Important! Now disease of a diphtheria is at sporadic level.

Important! For example, in 2015 in Russia 2 cases of disease are officially registered by a diphtheria.

Important! Almost all cases infection pathogenic of a strains *C.ulcerans* were accompanied by development of symptoms similar to a classical diphtheria that speaks presence in a chromosome of the activator of genes moderated  $\beta$  a-prophage bearing operon of diphtheritic toxin! But changes in the gene device occur at influence of the infection and at vaccination, including (the note of the author).

### **Biorhythmology diseases of a diphtheria.**

Important! Epidemic liftings of a diphtheria in the world are registered on the average each 25 years. In Russia other periods occurrence of flashes of illness (the note of the author) have been noted also.

Important! The situation is aggravated with that antitoxic immunity does not protect from disease by a diphtheria but only provides neutralisation of diphtheritic toxin allocated with bacteria.

Important! Cases of repeated disease by a diphtheria, in that «toxic» forms with lethal outcomes at imparted children and adults (the note of the author) are described!!!

Important! Among diphtheria complications remained serumal illness and anaphylactic a shock which have no direct relation to the illness and represent accompanying (yatropatic) illness - reaction to alien fiber Anti - diphtheria serum.

Own research allows to agree with conclusions of other authors considering «cardiopatia's» as specific, sharp defeat of heart, mentioning all its anatomic departments.

### **The same it is possible to tell about nervous system.**

Diphtheritic «polyneuropatia» proceeds on demyelinating or aksonal-demielinizing to type and represents a specific picture of sharp defeat of nervous system (paresis craniocerebral nerves, bulbar a paralysis, a diaphragm paralysis, peripheral polyneuropatia).

Diphtheritic defeat of kidneys (infectious nephropatia «sharp defeat of kidneys» will well be co-ordinated with the modern international term.

Important! In Russia in last epidemic of a diphtheria course doses of whey fluctuated in the range from 100 thousand units to several millions (!!!).

M.H.Turjanova's researches with coauthors. (1991, 1994) have allowed to draw the conclusion - is the most effective way unitary intravenous introduction of supporting doses of the whey, providing fast inactivation toxin.

Unitary introduction of supporting doses of serum (SDS) intravenously at any form of a diphtheria already in the first days leads to presence at patients of a high caption of antitoxic antibodies whereas at intramuscular introduction the maximum concentration of antibodies are found out only for 2-3rd day, and in much lower caption. Complications from intravenous introduction of whey by authors it is not registered.

Diphtheria treatment - today.

### **Today sick the diphtheria offers only two kinds of treatment:**

Antibiotics. The schedule of decrease in disease and death rate shows, that introduction of antibiotics has no influence. Death rate continues remain at level of one case on 24 diseased.

Antitoxin. Usually, if it near at hand, it is appointed after the test for the sensitivity, spent on a skin and on one eye. It becomes because antitoxin is made on whey of horses, and in itself is the extremely dangerous preparation. It should be used with the greatest care, especially, if the patient suffers from such allergic diseases, as an asthma or exema. In urgent cases it can be appointed and intravenously but only after 30 minutes prior to intravenous

introduction the test with an intramuscular injection Anatoxin's has been carried out. Adrenaline and Antihysmanines (antiallergic) preparations should be near at hand from the very beginning and within two weeks, for treatment of following possible complications:

Anaphylaxia, shown by a hypotension, a bronchospasm, dispnoe (the complicated breath), a diarrhoeia, urticaria and a shock.

Pathological serum reactions. Symptoms include a fever, mialgia's (pains in muscles) and skin rashes, usually in a kind urticaria, but can be as well on erythematous or macular to types. Arthritises begin with one or two joints and quickly progress, grasping many joints - usually joints wrist, anklebones, knees, and also small joints of a brush. Sharp glomerulonephritis at which in an urine deposit are found out erythrocytes and fiber; nephritic function can decrease. Can be miocarditis, neuritis, uveitis and peripheral neuropatias. Seldom meets meningoencephalitis.

Phenomenon Arthus's – subacute the reaction of hypersensitivity similar on pathological serum of reaction, but limited exclusively a skin.

Rash Arthus's – hemorrhage the reaction developing within 4-10 hours, and connected with expressed polymorphonuclear infiltration of venules with a hypostasis and hemorrhages.

### **Preventive maintenance**

Major importance in diphtheria preventive maintenance active immunization, but not vaccines, and Immunomodulators (has the note of the author). It Imunofan - candles for children, pricks for adults. This preparation can be applied without research Immunogrammas. Other preparations it is necessary to select with research Immunogrammas 2 levels of complexity from 3-year-old age (the note of the author).

Pharynx processing - solutions Lugol's, Sangviritrine's and others (the note of the author). Throat rinsing by disinfectant solutions: 0, 02 % Furacylline's,

0, 01 % of potassium permanganate, a solution of soda with salt (on a teaspoon of each component on a water glass).

Antitoxic Anti-diphtheria whey (serum) is a measure of first aid and a unique effective remedy of treatment of all forms of a diphtheria.

Way of introduction. Anti-diphtheria whey (serum) enter intramuscularly or hypodermically from 10 000 to 120 000 IU. At toxic forms intravenous introduction is supposed. The preparation dose depends on the form of illness and a condition of the patient.

The action mechanism Anti-diphtheria whey.

Antitoxin connects and neutralises the toxin circulating in blood. If diphtheritic toxin has already contacted cages and has caused their damage whey does not render neutralised action, therefore, the earlier whey is entered, the treatment is more effective. But express analyses on a diphtheria (the note of the author) are for this purpose necessary.

Whey in first three days of illness is most effective. Antitoxic treatment of a diphtheria necessarily supplement with reception of antibiotics.

Early introduction of whey provides a favorable outcome even at heavy toxic forms. For the prevention anaphilactical a shock preliminary enter under a skin of whey of 0,1 ml, through 30 mines of 0,2 ml and still through 1-1,5  $\mu$  intramuscularly other quantity.

For hypersensibility revealing preliminary skin test with the horse whey dissolved in 100 times is spent.

At the localised forms of a diphtheria whey enter usually unitary but if clarification of a pharynx from touches is late, through 24  $\mu$  enter whey repeatedly. At toxic form II-III of degree Anti-diphtheria whey is entered by 2 times a day throughout the first 2 or 3 days of treatment. Whey introduction stop after the obvious tendency to reduction of touches.

At an intoxication of I degree it can be cleaned traditional herbal medicine (the note of the author).

For reduction of symptoms of an intoxication and improvement of haemodynamics the patient with toxic diphtheria II-III of degree accepts intravenous introduction native plasmas (50-150 ml), Neocompensan's, Reopolyglucine's, the Haemomisinformation (50-150 ml) in a combination to drop introduction of 10 % of a solution of glucose from calculation of weight of a body of the child of 20-50 ml/kg a day.

It is forbidden to lift the patient and even to set him in bed. All procedures connected with treatment, feeding, a toilet, should be made in lying position. At toxic diphtheria I-II of degree a confinement to bed appoint on 3-5 weeks, at III degree - on 5-7 weeks.

The great value in complex therapy of a diphtheria has the nursing factor.

In this connection sick of a diphtheria it is expedient to hospitalise in boxing. At the slightest suspicion (the pneumonia, an otitis, etc.) appoint to bacterial complication antibiotics, it is possible and Sangviritrine (the note of the author).

#### **Treatment bacteriocarrier.**

Carriers not toxigenic diphtheritic sticks do not require isolation and do not demand special treatment. There is necessity to treat and so-called tranzitor no carriers toxigenic a diphtheritic stick (unitary detection of a diphtheritic stick). It is Enough to irrigate a pharynx with antibacterial preparations (solution for external application Sangviritrine). The means strengthening immunity (Imunofan, Immunol and others) are necessary.

At persistent carriage a diphtheritic stick appoint Erythromycin, Tetracycline (till 14 years it is impossible!) and other antibiotics (Sangviritrine from 3-year-old age strictly in 30 minutes after meal). It is necessary to define sensitivity of microflora to Antibiotics, except Sangviritrine (the note of the author).

#### **Primary Preventive Maintenance:**

- 1.any bactericidal and antivirus grasses (inside and pharynx and nasopharynx rinsings) or are lemons with a peel
- 2.solution Lugol's
- 3.solution Sangviritrine and other preparations

#### **Secondary Preventive Maintenance:**

- 1.Midocamycyn (Macrofoams) - macroleads. They can be applied and at a whooping cough (the note of the author) – Aetirotropical treatment - remarkable alternative of vaccines (the note of the author).
- 2.Polymixines P (inside) and M (externally). The preparation «works» in the alkaline environment. It is better to accept with mineral waters.
- 3.Octenisept - solution for external application with a spray - for diphtheria carriers. Not to use together with iodine-containing antiseptics!
- 4.Myrtle tincture - receiving drops.

Indications to pharmacotherapy - Aetirotropical therapy (an author's technique).

Vitamins - C - doses above averages therapeutic - intravenously!

Antioxidants – Mexidol or Mexiprim - intravenously (only the adult) in the rehabilitation period (the control saturation oxygen is necessary). To children - oxygen cocktails (during the period convalescent's).

Cytoprotector - Cytochrome C - intravenously and intramuscularly - doses on age) - a competitive preparation to cytochrome B that diphtheritic sticks (the note of the author) develop.

Sangviritrine - only externally as the preparation possesses antistrange action (the note of the author). From 3 summer age the preparation can be applied inside in tablets - doses under indications and it is strict after meal!

Recombinant Interferons (Viferon candles for children, etc.) - aim to lower frequency and weight of specific complications.

Traditional herbal medicine (an author's technique - here I do not describe).

From pharmacotherapy, except Nurofen's it is better than nothing to apply (Paracetamol, Tailenol and others)!!!

A food at diphtherias (diet)

At a diphtheria it is recommended to adhere to a diet №2. A food should be high-grade and high-calorie. At cooking it is necessary to consider, that it is heavy to patient to swallow. Dishes should be warm, a semi-fluid consistence, it is desirable wiped.

Important! It is possible not to eat 1-3 days, only to drink!!!

Remember! The success of treatment depends on that how much quickly to the sick will enter Anti-diphtheria whey. And it can be made only in the conditions of a hospital. Delay at some o'clock per times increases risk of development of complications.

Unfortunately, till now the serious estimation of different categories of carriers of the activator of a diphtheria (the note of the author) is not spent.

Danger more all proceeds from immune carriers (in pre-vaccination time – is result propylenediene the population, now - a consequence of inoculations) as immunity has basically antitoxic character.

At such carriers it is noticed long - to 3 months vegetation and activator allocation in an environment.

Susceptibility and immunity. A susceptibility not immune people to the activator of a diphtheria the general. However possibility of development not only heavy, but also easy forms of illness, and also carriage (asymptomatic forms of an infection) testify to a certain role of nonspecific factors of protection of an organism, virulent and degrees toxigenic the activator, but especially - infecting doses at infection.

Chest children to 6 months are not susceptible to a diphtheria because of presence at them the passive immunity transferred from mother placenary by. Children at the age from 1 year till 5-6 years are most susceptible to a diphtheria. By 18-20 years immunity also is more senior reaches 85 % that is caused by acquisition of active immunity.

Important! The maintenance in blood of specific antibodies of 0, 03 AE/ML provides their protection against disease. However it does not interfere with formation carriage pathogenic microbes (the note of the author).

Important! This fact is interesting to that inoculations are directed only on neutralisation of toxin and do not possess antimicrobial action.

#### **We understand with inoculations.**

The diphtheria is caused by bacterium *Corynebacterium diphtheriae*, which in itself is harmless enough. But, if this bacterium is infected by a specific virus then it starts to make and allocate strong toxin. This toxin also is responsible for heavy symptoms of a diphtheria. Diphtheritic toxin destroys fabrics in a drink, and forms in it a pseudo-membrane, a without toxin the bacterium can cause only a pharyngitis. If this toxin gets to blood system complications can lead miocarditis and to a time paralysis. Death rate makes 5-10 %.

The majority of people, having caught a diphtheritic bacterium, do not fall ill, and simply are the tank of bacteria and a carrier. During epidemics the majority of children are carriers, but are not ill. The majority of cases of illness occur in the winter and in the spring (the note of the author).



The vaccine from a diphtheria separately is not made, it is always combined with a tetanus (DT, Td), and usually with a whooping cough (DTaP/DTP). Also as well as for a tetanus, the vaccine represents toxoid (toxin inactivated of formalin).

And last years in Irkutsk the whooping cough walks, to very many children began to impart not AKDS, and ADS-M. From Russian vaccines AKDS it is a lot of complications on nervous system - monotonous crying after introduction and further (in other publications - the note of the author).

For inhabitants of Crimea a problem actual at least because of the neighbourhood with Ukraine. On the country the measles have already dispersed - there is a risk of distribution and a diphtheria which can go over and to Crimea.

In 1926 Glenny and its group experimented a diphtheritic vaccine and tried to improve its efficiency. Casually they have found out, that aluminium addition in a vaccine gives stronger immune reaction. Since then aluminium is added in all not live vaccines.

Glenny safety of aluminium in a vaccine did not interest 90 years ago. It does not interest anybody and today, and in vain (the note of the author).

Features of a vaccine.

As the vaccine from a diphtheria is toxoid's, it cannot prevent infection, but can prevent complications from illness. Though, it is possible other medicines (read in the text - the note of the author). It was logical to expect, that with introduction of a vaccine death rate from a diphtheria will decrease. However it has not occurred. In spite of the fact that the quantity of cases of a diphtheria constantly decreased, death rate remained approximately at level of 10 % with 1920 on 1970, despite growing coverage of the population by inoculations.

As the diphtheritic vaccine is always combined with a tetanus/whooping cough.

The inoculation (without a whooping cough) leads to syndrome Gijena-Barre, anaphylactic to a shock and humeral neuritis, lowers level limfocytes, raises risk of allergies, and antiphospholipid to a syndrome.

In VAERS with 2000 for 2017 after an inoculation from a diphtheria without pertussis a component (DT/Td) it is registered 33 cases of death, and 188 cases of physical inability. From a diphtheria for this time were ill 6 and one has died. Considering, that in VAERS 1-10 % of all cases are registered only, the probability to die of an inoculation in hundreds times exceeds probability to be ill with a diphtheria!!!

The important note! Syndrome Gijena-Barre arises at a flu and vaccines from a flu (the note of the author).

As the vaccine from a diphtheria has appeared even in 1920, any clinical tests, especially tests of efficiency it did not pass.

### **The vaccine Contains Aluminium.**

Diphtherias are subject basically alcoholics and the homeless, and even they are ill exclusively seldom. To be ill today with a diphtheria it is practically unreal.

Important! The diphtheria is treated by Vitamin C as diphtheritic toxin exhausts Vitamin C stocks it should be entered!!!

The probability to die of an inoculation many times over exceeds probability to be ill with a diphtheria.

### **Opinion of the Grandmother.**

When the pediatricist convinced us to inoculate, he has stated such thought, that we should inoculate at least not to lower quantity of imparted children to a dangerous threshold when there is a danger of occurrence of flash of an infection.!!! On my question and how to be with our kid if suddenly it again has a reaction, moreover and it is more terrible, than after AKDS, he

has told, it is very improbable but what to do... Certainly, such answer has not convinced me absolutely. How much I understand, the doctor, especially the pediatricist, first of all should think about health of EACH concrete child, in this case - ours. And questions of preventive maintenance of infections is, sorry, should go after that! And if you to me tell, that in it I am not right, I and to you will cease to trust because to me my grandson more expensively. I do not wish to endow its health, and, can, and a life, for the good of all the others.

### **Conclusion**

The inoculation only neutralises toxins, it does not influence bacteria. However, as well as vaccine BCG. Whether there is a sense to do inoculations? For Aetiopropic treatments, neutralisations of toxins are other medicines (read in the text - the note of the author).

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