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NASAL ELECTROPHORESIS

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- USSR -

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NASAL ELECTROPHORESIS

[Following is the translation of an article by Prof. G. N. Kassil' entitled "Nazal'nyy Elektroforez" (English version above) in Sovetskaya Meditsina (Soviet Medicine), Vol 24, No 7, Jul 60, Moscow, pages 95-103.]

From the Laboratory of Neuro-humoral Regulation of the Institute of Higher Nervous Activity of the Academy of Sciences USSR at the base of the clinic of nervous diseases (Head -- Corresponding member of the Academy of Sciences USSR, Prof. N. I. Grashchenkov) of the First Moscow Order of Lenin Medical Institute imeni I. M. Sechenov.

Report at the Session of the State Institute of Physiotherapy
21 March 1958.

The question of the significance of the site of administration of

one or another chemical substance into the organism is not new. It is well known that the rate of onset of the effect, the intensity, and sometimes also the character of action of medicinal and poisonous substances depends on the route of their entry into the organism. In the modern clinic, besides the oral taking of medications, their administration under the skin, in the muscle, in the vein, artery, the cerebrospinal fluid, via the lungs, etc. are widely used.

One of the most sensitive zones of the organism is the mucous membrane of the nose. In addition to the endings of the olfactory nerve, it includes a dense network of branchings of the trigeminal nerve, connected with elements of the vegetative nervous system. The endings of the olfactory nerve are connected via the olfactory bulbs with the nuclei of the brain trunk and the diencephalon. The wide anatomical and physiological bonds which exist between the mucous membrane of the brain and the subarachnoid spaces, the hypophysis, the diencephalic region, and also the different neural formations of the cerebral hemispheres of the brain (the optic thalami, the reticular formations, the cortex) have been studied in detail.

Reflexes from the olfactory nerve are transmitted via the cortex of the brain and the optic thalamus to the internal organs (N. I. Grashchenkov). Physical and chemical agents which act on the receptors of the mucous membrane of the nose, can evoke a reflex

reaction on the part of the facial, vagus, glossopharyngeal, sublingual, and other cranial nerves. Observations of various authors have shown that stimulation of the mucous membrane of the nose evokes a reflex influence on the activity of the stomach, the intestines, the organs of the small pelvis, the cardio-vascular system, etc.

A definite historical interest is presented by attempts to change the course of a pathological process by cauterization of strictly localized points of the mucosa of the nose, by stimulating them with an electrical current, by diverse chemical substances, etc.

One can find indications in the literature that the stimulation of certain points of the mucosa of the nose, for example by pricking with a needle, induces a patterned therapeutic effect.

However, until very recently any kind of systematized investigations devoted to the providing a basis for the therapeutic influence on the organism via the mucous membrane of the nose have been absent.

In 1948-1950 jointly with G. S. Vors we worked out and introduced into clinical practice a method of nasal electrophoresis with various chemical substances in the treatment of ulcers of the stomach and the duodenum, hypertension and bronchial asthma. Subsequent investigations have been conducted jointly with N. I. Grashchenkov.

As the clinical and experimental data showed, this method, based on the combined action of various salts, alkaloids, medicinal substances and a galvanic current on the mucosa of the nose, is very effective and can be used with success in the treatment of various diseases.

The greatest difficulties arise in the attempt to give a theoretical basis for the physiological effect which is observed in the presence of nasal electrophoresis. It is necessary to assume that several physiological mechanisms participate in this, each of which plays a definite role in the realization of the final effect.

1. Certain chemical substances (salts of calcium, magnesium, potassium, thiamine, carbocholine, atropine, and others), introduced into the mucous membrane of the nose by the electrophoresis method, stimulate the endings of the centripetal nerves and evoke a reflex response on the part of the central and peripheral divisions of the nervous system which, ^{generalizing itself,} leads to a general therapeutic effect. This is effectuated via stimulation of a limited number of receptors, and not by the penetration of one or another chemical substance into the general blood stream and by its action on individual nerve endings or receptor zones in other organs and tissues.

It ensues from this that only weak stimulants can be effective,

since in the presence of strong influences there takes place a simultaneous influence on the most diverse receptor zones, which can lead to the arising of mutually exclusive effects.

Nasal therapy can scarcely be included among ^{the}vegetative-segmental physiotherapeutic influences, so brilliantly worked out and studied by A. Ye. Shcherbak. As A. R. Kirichinskiy indicates, the vasomotor, the secretory, and other trophic reactions in response to a physiotherapeutic influence arise predominantly in the organs and tissues of that segment to which the area of skin being stimulated belongs (segmental reflexotherapy). In the presence of nasal electrophoresis the reflex usually assumes a generalized character and embraces a whole series of organs and physiological systems. The segmental reaction is transformed into a systemic reaction and involves the entire whole organism in the orbit of its action.

3: The application of an anode or a cathode to the mucous membrane of the nose, in the direct vicinity of the base of the brain, and the repeated influence of a galvanic current on the nerve centers can in its turn play the role of a powerful therapeutic factor. As is well known, a galvanic current under certain conditions possesses deparalytizing and disinhibiting properties.

L. I. Vasil'yev (1950) considers, that an ascending current

intensifies, and a descending current weakens the manifestation of the exaltation phase. Anodization of the brain increases the deparabiotizing influence of the higher divisions of the central nervous system on the lower divisions.

The significance of a galvanic current in the complex of active factors in electrophoresis has been studied in detail by M. M. Anikin (1926), A. N. Obrosov, I. A. Abrikosov, E. D. Tykochinskaya (1955) and others. As the experimental investigations of the indicated authors have shown, the action of a constant current on the organism, in particular on its nervous system, determines the basic peculiarities of the method of electrophoresis. That is why in the choice of a method of adequate influence on definite physiological and pathological processes in the organism through the mucosa of the nose we considered it expedient in place of the ^{maximally diverse} cauterizations, injections, blockade, pricks (Chzhen'-Tazyu therapy), which were/widely used by ^{still} many authors at the beginning of the current century, to use the method of electrophoresis, i.e., to administer medicinal substances with the aid of a galvanic current.

Further laboratory and clinical experiments should show to what extent and at what stages the indicated mechanisms act. Stimulation of the receptors of the mucous membrane of the nose by ions of one or another chemical substance and the application of an anode or

of a cathode in the direct vicinity of the brain evoke a complex chain of nerve reactions, in which the cortical and the subcortical formations of the brain are involved. This leads to a prolonged stimulation of the higher divisions of the nervous system, which substantially changes the state of the "tonus" of the central innervation apparatuses. The stream of impulses which arises by virtue of the reflex reaction can induce a reorientation of the functional state of the peripheral effectors. The task of the physician is on the basis of the data of a careful clinical and clinico-physiological examination of the patient to direct these reactions in the direction most favorable for the organism.

3. In taking account of the data obtained by us jointly with B. I. Kamenetskaya and M. B. Dunayevskaya, we can consider, that there exists yet another mechanism of the physiological action of nasal electrophoresis. As early as 1948-1949 we advanced the hypothesis, that in the presence of nasal electrophoresis certain substances penetrate through the loose mucous membrane of the nose, and, advancing along the perineural fissures of the olfactory and trigeminal nerves, get into the cerebrospinal fluid and the nerve centers. Thus, they as it were go around the blood-brain barrier, which usually prevents the penetration of various chemical substances from the blood into the direct nutrient medium of the brain. The existence of

direct anatomical bonds between the mucous membrane of the nose and the subarachnoid space of the brain can be considered to be demonstrated.

To verify this hypothesis we used radioactive phosphorus (P^{32}), which was administered in a quantity of 80 μ c according to a method worked out by us via the mucous membrane of the nose. In the space of 15-30 minutes after a single-time procedure a lumbar puncture was performed, a sample of cerebrospinal fluid was taken, and a sample of blood, and the radioactivity in them was determined by the usual method.

Two control series of investigations were conducted simultaneously. In one series radioactive phosphorus was administered orally and its distribution between the blood and the cerebrospinal fluid was investigated. In a second series gauze tampons, moistened with a solution of P^{32} , were introduced into the nasal cavity, but no current was passed. The fluid was taken after 30 minutes upon completion of the procedure. Patients with various injuries of the central and peripheral nervous system in whom a lumbar puncture had been performed on account of medical indications, were under observation.

The radioactivity of the blood was taken as 100 in all cases. It was established that the average content of P^{32} in the cerebrospinal

fluid amounts to 3.7% in the presence of oral administration. Of 22 patients examined, it was equal to 0-3% in 10 and exceeded 7% in six. According to the data of A. M. Veyn, obtained in our laboratory on extensive clinical material, the average content of P³² in the presence of light cranio-cerebral trauma, i.e., in practically healthy individuals, does not exceed 2-2.5%.

In the presence of a single time (for 30 minutes) laying of a turunda in the nose, the content of P³² in the cerebrospinal fluid amounts to 17.7%. In the presence of ionogalvanization of the mucosa of the nose it reaches 32.7%. Of 15 patients investigated, in five the content of P³² in the cerebrospinal fluid fluctuated in limits of 12.3-20.5%, in four -- in limits of 20.5-40%, and in five in limits of 40-60%. In one patient the level of radioactive phosphorus reached 171% in the presence of administration by the method of nasal electrophoresis.

Thus, it is necessary to assume, that the physiological effect which is observed in these cases when the medicinal substances are administered through the mucosa of the nose by the method of electrophoresis, was occasioned not only by a reflex mechanism, but also by their getting into the cerebrospinal fluid, i.e., by direct chemical influence on the nerve centers. This point has substantial significance in the choice of medicinal substances for electrophoresis.

It has been established by the works of L. S. Shtern with co-workers, in particular by our investigations, and also by the later works of W. Feldberg that many chemical substances act in an opposite manner when they are introduced into the blood and into the cerebrospinal fluid. Thus, for example, nasal electrophoresis (or more correctly, iontophoresis) with a solution of calcium chloride evokes, according to our data, a pronounced parasympathetic effect, i.e., the same as is observed in the presence of the administration of calcium salt into the ventricle of the brain, although, as is well known, calcium salts, introduced into the blood, possess a sympatheticomimetic action. On the other hand, thiamine bromide and thiamine chloride when administered by nasal electrophoresis stimulate the sympathetic centers of the brain; at the same time when introduced into the blood these preparations act as inhibitors of cholinesterase, facilitate the accumulation in the blood and tissues of acetylcholine and the rise in the tonus of the parasympathetic nerve elements.

Technique of nasal electrophoresis. Two wadding or gauze turundas each 15 to 20 cm in length are moistened with the corresponding medicinal solution, warmed to body temperature. With the aid of a pincers the turundas are introduced into the nasal cavity

until they are in contact with the mucous membrane. The external ends of the turundas are placed on the upper lip and the nasal septum above the oil cloths, whence a small wadding tampon, moistened with that same medicinal substance, is supplementarily applied. A lead electrode (2 X 3 cm) with a soldered conductor is fixed on the wadding tampon by two to three turns of a bandage around the head.

A second padding of flannelette (3 X 12 cm) with a lead electrode applied to it (8 X 10 cm) was placed on the occiput, correspondingly to the foramen occipitale. This padding is fixed by the weight of the head. The procedure is conducted with the patient in a lying position.

The described distribution of electrodes facilitates the best influence of the electric force lines on the cortical and subcortical divisions of the brain, which appears to be one of the mechanisms of nasal electrophoresis.

First Scheme

1st session, current force				0.5 mA, duration 10 minutes			
2nd	"	"	"	0.8	"	10	"
3rd	"	"	"	1	"	12	"
4th	"	"	"	1	"	15	"
5th	"	"	"	1	"	15	"
6th	"	"	"	2	"	15	"
7th	"	"	"	2	"	20	"
8th	"	"	"	2	"	20	"
9th	"	"	"	2	"	25	"
10th	"	"	"	3	"	25	"
11th	"	"	"	3	"	25	"
12th	"	"	"	3	"	25	"
13th	"	"	"	3	"	30	"

and to the end of the course

After the electrodes had been fixed, the current was switched on. At the time of the procedure it was necessary to verify the force of the current and to regulate its oscillations. As a rule, the patient does not experience any unpleasant sensations.

Nasal electrophoresis is conducted according to two different

schemes.

Second scheme

1st session, current force	0.3 mA, duration 10 minutes		
2nd " " "	0.3	"	10 "
3rd " " "	0.3	"	10 "
4th " " "	0.5	"	12 "
5th " " "	0.5	"	15 "
6th " " "	0.5	"	20 "
7th " " "	0.5	"	20 "
8th " " "	0.5	"	20 "
9th " " "	0.5	"	25 "
10th " " "	0.5	"	25 "
11th " " "	0.7	"	30 "

and further

The sessions are conducted daily. At the time of the procedure it is necessary to verify the current force again.

We prefer wadding electrodes (turundas), well moistened with the medicinal substance, although gauze electrodes are also used.

Special attention should be paid to the careful observation of the

rules of nasal electrophoresis (the washing of the nose before the procedure, the heating of the solution, sufficiently profound introduction of the wadding turundas into the nasal cavity, the location of the indifferent electrode in the region of the occipital foramen, etc.). On the basis of our more than once published experimental data devoted to the significance of the physiological (initial) background, we ordinarily prescribe for the patient an hour before the procedure a small dose of some sort of preparation of barbituric acid (medinal, nembutal, luminal) or of sodium bromide (a single table spoon of the 3% solution). After the procedure rest is necessary, sleep is desirable. The course of treatment consists of up to 30 procedures 10 to 30 minutes in length.

As medicinal substances in the nasal therapy we use: 1) 2% solution of calcium chloride, 2) 2% solution of thiamine bromide or thiamine chloride, 3) 0.25-0.5% solution of dimedrol, 4) 0.25-4% solution of novocaine, 5) 0.02-0.05% solution of ergotamine, 6) 0.02% solution of phenamine.

In certain cases the combination of the indicated substances is recommended. It goes without saying that their action should not be mutually antagonistic. Thus, one should not combine calcium with vitamin B₁ or novocaine, etc.

We ordinarily use the following compositions of the chemical substances: 1) calcium chloride 2 g, dimedrol - 0.25 - 0.5 g, distilled water -- 100 ml; per procedure -- 5 ml of the mixture; 2) novocaine -- 4 g, dimedrol 0.25 - 0.5 g, distilled water -- 100 ml; per procedure -- 5 ml of the mixture; 3) thiamine 0.1 g, distilled water -- 5 ml per procedure; 4) phenamine -- 0.02 - 0.04, distilled water -- 100 ml; per procedure -- 5 ml of solution; 5) vitamin B₁ - two one ml ampoules of the 5% solution, to add 3 ml of distilled water (per procedure). All the indicated substances are administered from the anode.

The peculiar influence of calcium salts on the nerve centers has been studied by L. S. Shtern, G. N. Kassil', Ya. A. Rosin, Demole, and others. It has been established, that in the presence of the administration into the ventricle of the brain of calcium, the excitability of the cerebral cortex is lowered and a characteristic sleep-like state is evoked. By introducing calcium salts with the aid of nasal electrophoresis, we, as the experimental data have shown, raise the tonus of the vagus nerve which acts on the centers of the parasympathetic nervous system. A certain inhibition of the cortical and subcortical elements of the brain is induced simultaneously. On the basis of our own data, we have a basis for asserting that under these conditions both by a reflex, and

also by a humoral route the activity of the reticular formation of the brain is somewhat lowered. There is also undoubtedly an anesthetic and membrane-thickening action of calcium.

Nasal therapy with a 2% solution of calcium chloride is also prescribed in the presence of pathological states, associated with a high tonus of the sympathetic nervous system, accompanied by an accumulation of sympathins, adrenalin, and noradrenalin, with a low level of acetylcholine in the blood, and also in the presence of phenomena of excitation of the cortical and subcortical divisions of the brain.

We use calcium chloride in the presence of headaches of vascular origin (spasms of the brain vessels), in the presence of hydrocephaly, of a raised tonus of the sympathetic centers, and also in the presence of the sequelae of closed cranio-cerebral trauma.

The large amount of material obtained in various clinical and polyclinical institutions, shows that in a number of cases a lowering of the arterial and intracranial pressure occurs, and also an excitability of the central nervous system, an improvement of the general feeling of well being of the patients, a lengthening of the vestibular chronaxie, which argues in favor of a rise in the tonus of the parasympathetic centers.

Nasal therapy with thiamine chloride and thiamine bromide

is prescribed by us in the presence of pathological states associated with a high tonus of the parasympathetic nervous system, accompanied by a low level of sympathins, adrenalin, and noredrenalin, or by a high content of acetylcholine in the blood, and also in the presence of phenomena of a lowered tonus of the cortical and subcortical elements of the brain.

Nasal therapy with a 2% solution of thiamine chloride or with thiamine bromide (vitamin B₁) is widely used in the presence of the treatment of ulcers of the stomach and duodenum. A large amount of material, numbering several thousand observations in various therapeutic institutions, shows that this method of treatment facilitates the rapid removal of pain, the improvement of the general state of the patients, the cicatrization of the ulcer (according to various statistical data, of up to 90-95% of the cases). Our observations indicate that nasal therapy with vitamin B₁ is indicated in all cases of ulcer disease. It is recommended that a sparing diet be prescribed simultaneously with nasal therapy with gradual broadening of the diet, with ascorbic acid in a dose of 1-1.5 g per day and riboflavin (0.02 g per day).

We had the possibility of observing an indisputable therapeutic effect in the presence of nasal therapy of ulcer disease

under polyclinic conditions without discontinuing work. In a number of cases in the presence of ulcer disease it is expedient to conduct prophylactic courses of nasal therapy (10-12 procedures) in the autumn and summer months). Excellent results are observed in the presence of treatment of cases of gastritis, colitis, ulcerous colitis, etc.. As a rule, the pains are weakened and disappear in the patients, the secretory and motor activity of the stomach is normalized, the "niche" symptom disappears in an overwhelming number of cases. In the presence of ulcer disease, the treatment is conducted according to the first scheme from the anode.

In the presence of allergic states (bronchial asthma, headaches accompanied by accumulation of histamine in the blood and by a disturbance of its metabolism, Quincke's edema, urticaria, certain forms of pruritus) nasal therapy with an 0.5% solution of dimedrol or of some other antihistamine is being used with success. The administration of dimedrol by the method of nasal electrophoresis proves to be many times more effective than the ordinary oral taking of antihistamines. Upon the completion of the course of treatment, the level of histamine in the blood is considerably lowered and the capacity of the organism to bind free histamine (histaminopectic effect) is raised.

In the presence of bronchial asthma we prescribe a course of nasal therapy with a 4% solution of novocaine and an 0.5% solution of dimedrol according to the first scheme. It is recommended that ascorbic acid be given simultaneously in a dose of up to 1.5 g per day.

Nasal electrophoresis with antihistamines is also indicated in the presence of neuralgias of the trigeminal nerve. In these cases we use ionization with a solution of novocaine (4%) and dimedrol (0.5%) according to the second scheme.

In the presence of electrophoresis with dimedrol it is recommended that small doses of dimedrol, alfadryl, suprastin (0.02 - 0.025 g per day) be prescribed simultaneously internally to neutralize the activity of histamine in the blood. We had the possibility of observing in these cases a rapid improvement of the state of the patients, a diminution of the allergic phenomena, a cessation of the headaches.

In the presence of sympathico-adrenal crises accompanied ordinarily by severe headaches and by a raised arterial pressure, we prescribe for raising the tonus of the parasympathetic centers, iontophoresis with a 2% solution of calcium chloride, an 0.5% solution of dimedrol, and an 0.05% solution of ergotamine (before the procedure

it is necessary to add 5 drops of ergotamine solution or dihydroergotamine solution in ampoules). In all cases electrophoresis is conducted according to the second scheme from the anode.

It is expedient simultaneously to prescribe a course of intramuscular injections of vitamin B₁ (2 ampoules each of one ml of the 5% solution), which in these cases and in the presence of this method of administration, i.e., in the presence of administration into the blood, facilitates the rise of the tonus of the parasympathetic nervous system.

Using various concentrations of novocaine, we have sought in some cases, starting with the installation of A. D. Speranskiy, somewhat to stimulate the peripheral and central divisions of the nervous apparatus (0.25% solution of novocaine), and in other cases to evoke an interruption of the reflex arc (4% solution of novocaine) and thereby to terminate the pathological impulsion both in the afferent, and also in its efferent divisions.

Our data show, that the use of weak concentrations of novocaine by the method of nasal therapy stimulates the sympathetic nervous system, improves the general state of the patients, raises the protective forces of the organism; it was shown in the presence of disturbances of the vegetative regulation, and also of certain trophic disorders.

A four per cent solution of novocaine is used in the treatment of bronchial asthma, neuralgia of the trigeminal nerve and in the presence of certain allergic states. As has already been indicated, dimedrol is usually added to the novocaine solution.

Nasal therapy with an 0.02% solution of phenamine is prescribed according to the first scheme in the presence of lowering of the tonus of the cerebral cortex and of the reticular formation (ready inhibition of the cortical formations, an acutely lowered tonus of the central nervous system, somnolence, right up to narcolepsy).

In the presence of the appropriate indications, of a correct choice of the medicinal substance and of an irreproachable technique,

nasal therapy evokes a significant and prolonged improvement of the state of the patient. In the clinic of nervous diseases we prescribe nasal electrophoresis in the presence of various forms of diencephalic pathology, vegetativo-vascular dystonias, allergic states. There is no effect in the presence of gross organic disturbances of the activity of the central nervous system.

However, an undoubted improvement is noted in the presence of the most diverse injuries of the diencephalic region.

Particularly excellent results are observed in the presence of occult forms of diencephalic disturbances, which are often encountered in polyclinical

practice. Patients of this group, who are usually admitted with the diagnosis of "neurosis", "vegetative neurosis", or "vegetative dystony", already mention a considerable improvement after the first sessions of the nasal therapy.

In many cases the objective indexes were normalized (the appearance of an alpha-rhythm on the electroencephalogram when it had been absent, the restoration of the normal biological activity of the blood, etc.). The lowering of the raised level of 17-ketosteroids in the urine to normal, i.e., the possibility of influence on the hypothalamo-hypophysis region and through it on the adrenals (suppression of the secretion of ACTH) is extraordinarily interesting.

Experience in the use of nasal electrophoresis shows that it can be recommended for clinical and polyclinical practice. Its advantages are: a) simplicity and accessibility, b) the absence of any unfavorable subjective sensations, c) the absence of contraindications, d) the possibility of use under rural hospital and polyclinic conditions, e) the rapid onset of the therapeutic effect, the considerable improvement in the general state and sense of well being of the patients.

A positive effect is chiefly absent in the presence of organic (in particular, inflammatory) changes in the central nervous system,

and also in cases with pronounced organic symptoms which have progressed far.

Sometimes the absence of an effect was occasioned by the incorrect choice of the medicinal substance. The substitution of one chemical preparation by another, for example, of vitamin B₁ by novocaine or dimedrol, the prescription of electrophoresis with ergotamine or phenamine, the combination of several pharmacological substances often induced pronounced shifts in the course of the disease.

In the last few years the method of nasal electrophoresis has received wide dissemination in therapeutic, neurological, dermatological, gynecological clinics. The hoped for results have been observed in the treatment of stenocardia (with atropine 1:1,000), hypertension (with calcium), toxicoses of pregnant women (with thiamine and novocaine), afflictions of the female sexual sphere (disturbance of the cycle, climax), etc..

D. I. Gimpel'son has obtained excellent results in the treatment of toxicoses of pregnant women by nasal electrophoresis with vitamin B₁ and an 0.5% solution of novocaine.

In various therapeutic institutions an irreproachable methodology is not used in all cases, the instructions are far from always carried out, the pharmacological preparations are incorrectly

prescribed, electrophoresis is conducted with distilled water without the addition of any medicinal substances, i.e., a pharmacological action is in fact excluded, etc..

Our experience shows, that nasal electrophoresis is effective only in those cases in which the methodology described above is strictly observed.

This is not a universal agent, suitable for the treatment of all pathological processes in the organism. At the same time, we take upon ourselves the boldness to assert, that nasal therapy can find the most wide use either as an independent form of treatment, or in a complex combination with other therapeutic measures in the presence of a number of diseases, as, for example, bronchial asthma, neuroses, dermatoses (particularly neurodermatoses), certain endocrine disturbances, in particular hyper- and hypofunction of the thyroid gland, etc.. The working out of a method of nasal electrophoresis with various antibiotics in the presence of inflammatory processes in the membranes of the brain, cases of encephalitis, etc., stands next. Under these conditions one should take into account the possibility of the penetration of antibiotics into the cerebrospinal fluid and the nerve centers, bypassing the blood-brain barrier. It is necessary to underline, that the negative results which have been observed by individual authors often depend on an

incorrect methodology and on an insufficient persistence on the part of the physician. One should not terminate the treatment in the absence of an effect after the first procedures. In our practice cases have been encountered in which an appreciable improvement did not ensue at once, but sometimes after the 10-15th procedure. An exacerbation of the disease after the first procedures or in the process of treatment also requires a careful analysis of the causes which induced it in each case. It is necessary to elucidate whether or not it is an index of an incorrect choice of the pharmacological preparation, of excessive duration of the procedure, strong current force, etc. Sometimes an exacerbation indicates definite shifts in the course of the disease. Thus, in the presence of a successful treatment of ulcer disease, an insignificant intensification of the pains often ensue usually after the third to the fifth and the 15-20th sessions.

We assume, that a further deepened study of the physiological and biochemical mechanisms which lie at the base of nasal electrophoresis, should be continued and broadened, and hope that the common efforts of theoreticians and clinicians will render this method still more effective and will facilitate the wider introduction of it into medical practice.

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