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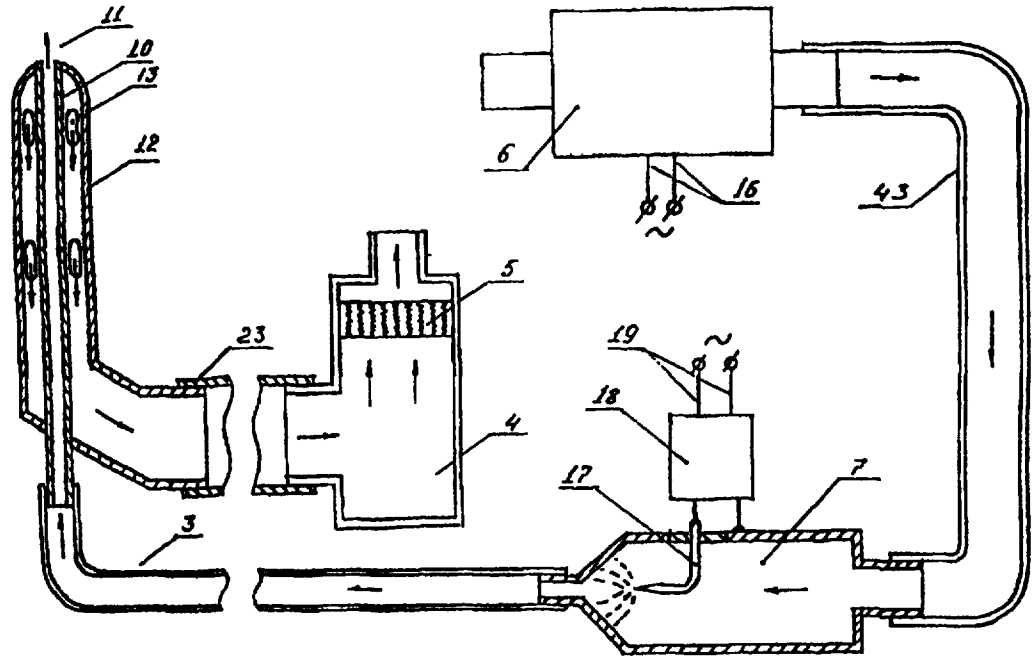

(57) **Abstract**

The invention relates to use of ozone in the manufacture of a gaseous medicament, for treating a disease of a body cavity tissue in mammals by introducing the medicament into the cavity, and to an apparatus incorporating an ozone generator and means for supplying ozonized gas therefrom at a pressure sufficient to drive a flow of such gas through delivery means and into the body cavity. Diseases which may be treated in this manner are e.g. mastitis in cows and cystitis.

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USE OF OZONE FOR TREATING DISEASES OF BODY CAVITY TISSUES AND APPARATUS THEREFOR

FIELD AND BACKGROUND OF THE INVENTION

The invention relates to a method and apparatus for the treatment of various diseases in the cavity tissues of the human or animal body by a flow of ozone. It relates particularly but not exclusively to an apparatus for the treatment of mastitis in farm animals and especially dairy animals such as cattle, sheep, goats and camelids.

Mastitis, both clinical and sub-clinical, is the most important disease of dairy cattle, which causes billions of dollars of economic losses annually. Sub-clinical mastitis, which is the most common, is not self-evident externally, but nevertheless affects milk production, leads to the production of low quality milk, and damages the mammary gland. Sub-clinical mastitis may be due to *Streptococcus agalactiae, Staphylococcus aureus*, other non-agalactiae streptococci, coagulase-negative staphylococci and other pathogens. In clinical mastitis the animal is clinically sick, e.g. it is feverish, the mammary gland is inflamed, red, tender and painful, the milk is affected, being watery and/or bloody. Clinical mastitis may be due to environmental organisms such as *E. coli*, *Klebsiella spp., Proteus spp., Serratia spp.,* and other enterobacteria such as *Pseudomonas spp.*, and various streptococci, as well as yeasts or other fungi. Both clinical and sub-clinical mastitis affect non-lactating animals, as well as lactating animals. The economic losses arise from the slowdown in milk production, production of milk which is unfit for human consumption, and damage to the animals which may ultimately require their slaughter. Treatment with antibiotics may occasionally cure the disease, but there exists the danger of the presence in the gland of destructive organisms resistant to the antibiotics, which neutralize their action. It will be evident that there is still a great need for an effective treatment of this disease, and it is believed that the present invention will provide a means for meeting this need.

However, as will be apparent from the description herein, the invention is not restricted to treating mastitis, but is relevant for treating other diseases in cavity tissues of mammals, both animal and human.

REVIEW OF THE PRIOR ART

The introduction of therapeutic agents into the bloodstream via the oral, parenteral and rectal routes is known, and ozone has also been used for therapeutic purposes by administration by these routes.

US 5,133,975 (Harley et al.) discloses a method for inactivating infective agents in a patients' blood in vivo, by autochemotherapy or rectal insufflation, using as active agent a mixture of oxygen containing e.g. 30-45 μg/ml ozone.

In US 4,743,199 (Weber et al), a mixture of ozone and air is used for removal of dental plaque by introducing into the oral cavity simultaneously with solid dentifrice particles through hollow toothbrush bristles.

In US 5,334,383 (Morrow), an electrolyzed saline solution which may contain ozone is injected intravenously for treatment of antigen related infections.

In DE 3940389 (Pakdaman et al) a liquid which increases the oxygen in the blood and may contain ozone, is used (when administered by the oral, intravenous or rectal routes) as an immunostimulator in the treatment of cancer, and possibly also to clean wounds, for tumor infiltration and for improving oxygen transport.

DE 3237078 (Frenkel) describes inhalation of a controlled amount of ozone in air, for cosmetic purposes.

The entire content of the foregoing patents is incorporated herein by reference.

It has been reported by Carpendale, M.T., et al. (J. Clin. Gastroenterol., 1993, 17(2): 142-5), that the administration of oxygen/ozone mixture via the rectum may alleviate diarrhea in AIDS or AIDS-related complex patients. To the best of the present inventor's knowledge, this article is unique in that, otherwise, none of the known prior art describes the treatment of diseases in body cavity tissues by use of ozone in the gas phase.

OBJECTS OF THE INVENTION

It is a main object of the invention to provide a medical apparatus of simple design which is readily transportable and which is adapted to supply an

ozonized gas for treatment of diseases in body cavity tissues. Another object of the invention is to provide apparatus adapted for the stated purpose, and which is controllable in regard to the flow of gas and to the ozone contents thereof. Yet another object of the invention is to provide an apparatus that will supply gas at sufficient pressure to cleanse the udder of milk residues.

Still another object of the invention is to provide the apparatus adapted for the stated purpose with means serving to prevent gas or air containing a dangerous concentration of microorganisms or other contamination from escaping into the atmosphere.

It is an additional object of the invention to provide an apparatus for the above purposes which is easy to handle, foolproof in operation and economical to manufacture.

Yet a further object of the invention is to provide a method for the treatment of diseases of body cavity tissues.

Other objects of the invention will be apparent from the description which follows.

SUMMARY OF THE INVENTION

These and other objects of the invention are achieved by the present invention, which provides in one aspect a method for treating a disease of a body cavity tissue in mammals, wherein a gas containing an effective amount of ozone for treating such disease is introduced inside said body cavity, provided that where the mammals are AIDS patients, then the ozone is not introduced via the rectum. The term "AIDS patients" in this context is hereby defined to include also patients suffering from AIDS-related complex.

The invention also provides a medical apparatus for treatment of a disease of body cavity tissue by a flow of ozonized gas, which comprises means adapted for delivery of said flow of ozonized gas to body cavity tissue; means for generating said flow of ozonized gas and conduit means for transferring said ozonized gas to said delivery means; and means for providing unozonized gas and conduit means for transferring said unozonized gas to said generating means, said providing means being adapted, for example by use of an

electrically driven compressor or pump, to supply gas at a pressure sufficient to drive said flow of gas after ozonization through said delivery means and into said body cavity.

This apparatus in one embodiment is characterized additionally by at least one of the following features: (a) a filtering means and means for withdrawing used ozonized gas from said body cavity and for passing said withdrawn ozonized gas through said filtering means; (b) a tubular housing having a tapering and conductive front end with the apex thereof forming an orifice and said housing having an open rear end, a coronizing electrode concentrically mounted in said housing upstream of said tapering front end and with its pointed front end extending towards said orifice, and a high voltage source having a potential of at least 2200 volts having a first terminal connected to said electrode and a second terminal connected to said conductive front end of said housing; (c) said apparatus is adapted to deliver into said cavity gas containing about 1 to about 50 p.p.m. ozone; (d) said apparatus is adapted for simultaneous treatment of a plurality of mammals by connecting a plurality of said delivery means to said ozone generator. The delivery means may be e.g. selected from: a catheter which comprises an inner open-ended inlet tube for introducing said gas and an outer perforated outlet tube for removing said gas integral and coaxial therewith, the outlet tube being perforated by a plurality of openings; or a hollow needle; or a double lumen Foley catheter.

In a particular embodiment of the apparatus of the invention (which includes the hand-held portable apparatus described below), where the body cavity tissues are accessible via a large opening such as the mouth, the apparatus comprises a tubular housing of a solid material having a tapering front end of a conductive and anti-corrosive material with its apex open in the form of orifice which is sufficiently small so that said orifice constitutes said delivery means; a coronizing electrode concentrically positioned in said tube close behind the tapered front with its pointed front end extending towards said orifice, thus allowing flow of ozonized gas to be driven through said orifice thereby to contact the affected cavity tissue, and an electric high-voltage generating means attached to said apparatus characterized by a potential of at

least 2200 volts, said high-voltage generating means having its high-voltage terminal connected to said electrode and its zero terminal to said tapered front end.

This embodiment of the apparatus may be characterized additionally by at least one of the following features: (I) a filtering means and means for withdrawing used ozonized gas from said body cavity and for passing said withdrawn ozonized gas through said filtering means; (ii) the rear end of said tubular housing is of smaller or larger or of substantially equal diameter to that of said orifice, said rear end being optionally partly or completely open, in order to allow ingress of air as said unozonized gas; (iii) said apparatus is adapted to deliver into said cavity gas containing about 1 to about 50 p.p.m. ozone; (iv) the entire tubular housing is made of a conductive and anti-corrosive material; (v) said coronizing electrode is mounted inside said tubular housing by means of a cylindrical perforated support of a non-conductive material, permitting air to flow therethrough. (vi) an motor-driven fan mounted inside said tubular housing and so disposed that it directs a flow of unozonized air in the direction of said electrode, (vii) an at least partly hollow handle integral with said tubular housing and disposed generally transversely thereto.

This embodiment of the apparatus may be still further characterized by at least one of the following wherein features (α) feature (vii) is present and said high-voltage generating means is positioned inside a hollow portion of said handle. (β) features (I) and (vi) are present, the filtering means being disposed upstream of said fan. (γ) feature (vi) is present, and both said electrode and said fan are mounted firmly inside tubular means of smaller diameter than and concentric with said tubular housing which has a closed rear end, thus providing an annular space between the tubular housing and the smaller diameter tubular means, whereby depending on the relative positions of said electrode and said fan, either (A) air is drawn from said orifice into the annular space and directed out via the inside of said tubular means and through said orifice, or (B) air is drawn from said orifice into the inside of said tubular means and directed out via the annular space and through said orifice, and when feature (i) is also present, then in case (A) said filtering means is disposed in said annular space and in

case (B) said filtering means is disposed inside said tubular means upstream of said fan; (δ) soft frusto-conical sleeve Is removably mounted on the front end of said housing in order that it may be removed after each treatment.

In still a further aspect, the invention provides use of ozone in the manufacture of a gaseous medicament, for treating a disease of a body cavity tissue in mammals by introducing the medicament into the cavity, excluding introducing the medicament via the rectum where the mammals are AIDS patients. As before, the term "AIDS patients" in this context is hereby defined to include also patients suffering from AIDS-related complex. The invention yet further provides use of ozone in the manufacture of a gaseous medicament, for preventing a disease of a body cavity tissue in mammals

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 illustrates an apparatus containing a double catheter and a conduit circuit including pumping means, an ozone generator and a filtering device.

Figure 2 illustrates an apparatus including a supply of gas from a pressurized cylinder.

Figure 3A is a longitudinal section of a first embodiment of the portable apparatus of the invention;

Figure 3B is a longitudinal section of a second embodiment of the portable apparatus of the invention, characterized by ozone flow issuing from the central tube towards the diseased cavity;

Figure 3C is a longitudinal section of the second embodiment showing a reversed air and ozone flow, issuing from the annular channel towards the diseased cavity;

Figure 4 is a plan view of the soft removable sleeve to be attached to the apparatus illustrated in Figures 3B and 3C;

Figure 5 is a section along line A-A of Figure 4.

DETAILED DESCRIPTION OF THE INVENTION

As indicated above, the invention provides a method for treating a

disease of a body cavity tissue, where a gas containing ozone may be introduced, for example, via the teat canal (e.g. to treat mastitis), the rectum, the vagina, the uterus, the mouth or the larynx. Other relevant body cavities include e.g. the gastrointestinal tract, the peritoneal cavity, the bladder, the urethra or the urinary tract, e.g. for treating cystitis. In a particular embodiment, when the mammals are humans, the disease treated may be sinusitis; in another embodiment, in the case of non-human mammals, the disease treated may be mastitis.

It is known that ozone may damage body tissues, or have other toxic effects, e.g. when introduced into the lungs at certain concentrations and/or for certain periods of time. The present invention will of course be practiced under the direction of a skilled veterinarian (in the case of non-human mammals), or under the direction of a skilled medical practitioner (in the case of humans), who will be aware of the necessity to avoid toxic effects, by limiting the concentration and/or time of administration of ozone, in accordance with the invention. Moreover, in general it would be prudent to ascertain prior to any treatment with ozonized gas that it does not contain any noxious components (such as nitrogen oxides, in the case of ozonized air). However in scientific trials (see particularly Examples 5 and 6 herein) no such noxious components were produced using the apparatus of the invention. It may also be noted that in general, the gas containing ozone after use, i.e. after having contacted the relevant body tissue, is either released into the atmosphere, or more preferably it is filtered to remove contaminants.

The gas is most conveniently introduced by means of a catheter inserted into said body cavity, which preferably comprises an open-ended inlet tube for introducing said gas and a perforated outlet tube for removing said gas integral therewith. The catheter more preferably comprises two coaxial tubes, namely an inner tube defining said inlet tube and an outer tube defining said outlet tube, the latter being perforated by a plurality of openings. A catheter as just defined, also constitutes a part of the invention.

As also indicated above, the invention further relates to use of ozone in the manufacture of a gaseous medicament, for treating a disease of a body cavity

tissue by introducing said medicament into the cavity. By way of example, where the disease is mastitis, ozone is introduced via the teat canal, and where the disease of the urinary tract is e.g. cystitis or pyelonephritis, ozone is introduced to the bladder via the urethra. Where the disease is mastitis in a cow, the introduction of ozone through the teat canal serves also to remove milk residues from the udder of the cow. It is to be understood that the importany body cavities in mastitis are the teat canal, teat cistern, udder cistern, molk ducts and udder aveolar cavities in increasing order of importance, and such terms as "introducing the medicament via the teat canal should be construed accordingly" herein, and similar terms, should be construed accordingly Preferably, the inventive apparatus includes an ozone generator, an air or gas pump, and a double catheter in the form of an inner inlet tube surrounded by a perforated exhaust tube, the three components being connected in series, the exhaust tube being preferably connected by flexible conduit to a filtering device. Air or other suitable gas may be drawn into the apparatus by a small compressor or pump, such as an electrically driven compressor or pump (e.g. a piston pump), containing an upstream filter to remove undesired particulate matter, and which supplies the gas to the ozone generator at sufficient pressure to expand the afflicted cavity, viz., the udder, a pressure up to 0.15 bar (gauge) often being adequate. However, the pressure required may vary with the constitution of the animal to be treated. It should be particularly noted that the compressor utilized in connection with the present invention is most desirably one which gives oil-free air, e.g. that marketed under the name "Burkle" (Germany). The ozone generator is connected to the supply tube of the catheter by another flexible conduit. Both the ozone generator and the compressor or pump are adjustable for the purpose of regulating ozone content and the flow of the gas. All parts of the apparatus can be disassembled for thorough cleaning and sterilization. Where it is desired that the exhaust gas does not exit into the atmosphere, and is to be filtered for recirculation, the filtering device or the filter itself has to be changed from time to time.

The catheter preferably includes an inner supply tube of about 1 mm diameter (through which the ozonized gas is normally introduced) and this is

surrounded by a perforated tube (normally used for return of the gas) of about 3 mm diameter. In the alternative, the gas-ozone mixture may be injected through the outer tube and returned via through the inner tube, although the former method is more efficient. On the other hand, the catheter may consist of two parallel tubes, a small diameter tube for injection and a tube of somewhat larger diameter for returning the gas either to the filter or into the atmosphere. The catheter has to be thoroughly disinfected after each treatment, or alternatively a new sterile catheter may be used in each case. In an alternative embodiment of the invention, the compressor or pump may be omitted completely, and in this case the gas may be supplied from a gas cylinder through a pressure regulator and pressure gauge.

In the embodiment of the apparatus illustrated in Fig. 1, a catheter composed of an inner tube 10 is connected to a flexible supply conduit 3, with an open end 11, through which the gas-ozone mixture enters the udder or other body cavity. Inner tube 10 is surrounded by a coaxial outer tube 12 of a diameter permitting ready insertion into the body cavity, tube 12 being perforated by a plurality of oblong openings 13. for the return flow of the gas mixture from the udder or other body cavity. Tube 12 is connected to a flexible return conduit 23, leading to a filtering device 4, which contains a special replaceable filter 5 designed to absorb any residual ozone (which is corrosive); the exhaust gas may be passed additionally through a conventional liquid trap (not shown) to remove any microorganisms which may be present, before exiting to the atmosphere. Air is drawn into the by compressor or pump 6, which may contain an upstream filter (not shown) to remove undesired particulate matter (such as dust and larger particles), and which is connected to an electrical supply via cable 16. A conduit 43 connects the compressor to an ozone generator 7, which generates ozone by means of coronizing electrode 17, connected to a transformer-rectifier unit 18, which is in turn connected to an electrical supply by means of cable 19. The ozone-enriched gas reaches the catheter through flexible conduit 3. The ozone generator includes a tubular housing having a tapering and conductive front end with the apex thereof forming an orifice and said housing having an open rear end, a coronizing electrode concentrically mounted in said housing upstream of

said tapering front end and with its pointed front end extending towards said orifice, and a high voltage source having a potential of at least 2200 volts having a first terminal connected to said electrode and a second terminal connected to said conductive front end of said housing. In this preferred method for producing ozonized air by corona discharge, it has been found experimentally that the product is not only sterile, but that it is uniquely free from noxious substances, in particular nitrogen oxides, which would have to be specially removed if generating ozone from air by other methods. However, in general terms, it will nevertheless be understood that, in the alternative, any other known method of and apparatus for the generation of ozone may be employed.

In the embodiment of the apparatus illustrated in Fig. 2, all components correspond with those illustrated in Fig. 1, with the exception that pump or compressor 6 is replaced by a compressed gas cylinder 60. Cylinder 60 is connected to the inlet port of ozone generator 7 by means of a flexible tube 62, and the gas or other air flow is regulated by means of a pressure gauge 61. The apparatus can be used in the treatment of a disease in a cavity tissue of a human or animal body, as can the apparatus of Fig. 1 and as has been described hereinabove.

The apparatus of the invention may alternatively be constituted by a hand-held and portable device adapted to generate and to direct air containing ozone towards the opening of a large external body cavity, in particular the mouth, thereby to facilitate treatment of diseases, where the site of the disease is accessible via this body cavity. This device will be referred to in subsequent description herein as the "portable apparatus (of the invention)".

A first embodiment of the portable apparatus of the invention includes a tube of a solid material having a tapering front end of a conductive and anti-corrosive material with its apex open in the form of a small-diameter orifice, and having a rear end partly or completely open, but of larger cross section than that of the orifice. An electrode is concentrically positioned close behind the tapered front with its pointed front end extending towards the orifice. An electric high-voltage generator, e.g. a transformer is attached to the apparatus and is characterized by a potential of at least 2,200 volts; it has its high-voltage

terminal connected to the electrode and its earth terminal to the tapered front end which thus forms the second electrode. The generator is supplied energy from the domestic supply by means of a flexible cable.

As is well known, the motion of the ions creates a certain pressure causing the air and the ozone molecules to emerge out of the orifice which may have a diameter of between 2 to 10 mm. For treatment of a disease the tube is held with the orifice suitably directed to the body cavity (e.g. the mouth) of the patient for a predesignated period of time, the air and the ozone particles emerge out of the orifice and impinge on the diseased locus so as to effect, improve and accelerate the curative process.

The portable apparatus is preferably provided with a hollow handle which carries the generator inside and which enables the operator to position the apparatus in a correct position for treating the ailment. Instead of having only the frontal tapered end made of a conductive material, it is proposed to make the entire tube, including the front end of a suitable conductive and anti-corrosive material, thus saving costs. The size of the orifice can be made of a suitable size, smaller or larger, depending on its particular application; it may be desirable to increase the voltage potential, where the orifice is relatively large.

In a second embodiment of the portable apparatus, the air flow is recirculated by a motor-driven fan positioned therein. In this embodiment, the tube containing the electrode has two open ends and is enclosed in a housing in the form of a larger tube having its rear end closed, whereby an annular channel is formed between the two tubes. An axial fan mounted inside the inner tube sucks in air from the front end of the channel and blows it across the corona discharge generated by the electrode in the direction of the affected body cavity. An annular filter positioned in the annular channel serves to filter the air returned from the body cavity and to permit clean air to reach the fan and the electrode.

Similarly as in the case of the first embodiment, in this embodiment the portable apparatus is provided with a handle and a high-voltage generator enclosed in the handle. The inner tube is either made completely of a conductive and non-corrosive material or is composed of two parts, a

conductive portion surrounding the corona and the remaining portion of any other material.

In still another embodiment of the portable apparatus, the air-flow is reversed, i.e. air is sucked in through the inner tube, filtered by a circular filter positioned in this tube before reaching the electrode, and is ejected through the annular channel to the front, and thence in the desired direction.

In all embodiments of the portable apparatus, a soft resilient sleeve may be mounted on the front of the apparatus which is disposed of after each session of treatment in order to prevent infectious transfer from one patient to another. High-voltage charge on the electrode is generated by a transformer provided with rectifier and attenuating means to effect one side, connected to the electrode, to produce high voltage connected to the electrode and the other, zero, side, connected to the inner tube and to earth.

Figure 3A shows the principle of the working of a portable ozone treating apparatus. It includes a tubular oblong housing 101 of a conductive material which is open at its rear end 102 defining an air inlet, and has a tapering front end 103 closing the housing, except for a small orifice defining the air-ozone outlet 104. It further includes a centrally positioned coronizing electrode 106 which is provided with a pointed front end pointing towards the orifice in concentric alignment therewith and being held in position by an annular perforated support 105 of an inert material. It is important that the housing is anti-corrosive, at least in the tapering portion which is exposed to the oxidizing action of the ozone.

A handle 110 is attached to the outside of the housing, facilitating operation of the apparatus and contains a high-voltage generator or transformer 107 in its hollow interior. The high-potential terminal of the transformer is connected to electrode 106 by conductor 109, and its low-potential terminal to the housing 101 at point 109.

The high voltage - at least 2200 volts - generates, in a known manner, a corona discharge 111 towards the tapering front end of the housing which splits and combines a small portion of the oxygen molecules in the surrounding air, whereby atoms O combine with O_2 to form ozone molecules O_3. The corona

exerts a very small pressure towards the orifice thereby driving the air and ozone out of the housing and directed towards or into the patient's body cavity.

It is possible to control the ozone output by changing the size of the orifice and /or the air inlet 102,. while respectively increasing or decreasing the voltage potential.

In order to prevent the spread of ozone-containing air into the surrounding space and in connection also with the treatment a body cavity with a broad air-ozone flow, the following embodiments have been developed which recirculate and filter the contaminated air after its contact with the patient's body cavity.

The apparatus illustrated in Figure 3B is composed of tubular housing 120 of a solid material which has an open front end and a rear end closed by a hemispherical cover 122 and of an inner concentrically positioned tube 121 of a conductive and anti-corrosive. material, having two open ends. Both tubes are in concentric alignment, forming an annular channel 123 therebetween which contains a highly absorbing annular filter 124 in its front. The filter and three to four arms 135 extending inwardly from the housing hold the inner tube in its position. A coronizing sharp-pointed electrode 125 is positioned in the center of the inner tube by means of a circular perforated support 126 with its sharp point extending towards the open front of the apparatus. It is connected to the high-potential terminal of a transformer or other high-voltage generator 127 which is mounted inside a handle 130, the low potential terminal being connected to the conductive tube 121.

An axial blower 128 is mounted inside the inner tube 121, configured to blow clean air towards the electrode and out through the open front; its electric motor is supplied domestic current through wiring 129 extending through the housing 120 and the handle 130.

A frusto-conical sleeve 131 of a soft and resilient material - as shown in Figures 4 and 5 - is removably attached to the front of the housing and is disposed of after each treatment.

The electrode being supplied with high voltage creates a corona discharge towards the inner, earthed tube generating a certain small amount of

ozone which is driven towards the patient's body cavity opening by the force of the axial fan. The used air is returned into the apparatus by suction action of the axial fan; it passes the filter 124 where all remaining ozone molecules are absorbed and is recirculated through annular channel 123 into the inner tube as shown by arrows, thereby preventing ozone from being dispersed into the surrounding space.

Figure 3C shows an apparatus similar to that shown in Figure 3B, and the same numerals are employed in both figures to denote identical components, even if they are in a different position in both cases. In Figure 3B, the housing 120, the handle 130 and the inner tube 121 are completely identical with those illustrated in Figure 3B, the difference lying in the reversed air flow. Air is sucked in by action of fan 128 and is conveyed through a cylindrical filter 144 - inside tube 121 - to electrode 125 which points towards the rear of the housing. The ozone-containing air now passes through the annular channel 123 and the soft sleeve 131 into the patient's body cavity. The air from the patient's body cavity is returned to the electrode after having passed the highly efficient filter 144 mounted in the front end of the inner tube, the filter preferably containing activated carbon for absorbing the remaining ozone molecules.

In the foregoing description the inner tube has been mentioned as being preferably of a conductive and anti-corrosive material. It should however be mentioned that only that portion of the tube which is in contact with the corona discharge may be made of this material, while the remaining portion may be of any suitable solid material, whether conductive or not.

It will be understood that the three embodiments of the portable apparatus described represent only examples of possible designs of the various components therein and of the apparatus as a whole, and that a person skilled in the art may modify or redesign the above embodiments, provided that the modifications are in the spirit of the invention arid the scope of the appended claims.

Referring now to treatment of mastitis, if only one teat is affected, it will be possible to treat only this teat, while obtaining milk from the other teats. A particular advantage of the invention lies in the fact that the milk obtained will be

suitable for consumption immediately after treatment has been concluded, whereas when using antibiotics, consumption must be delayed for several days.

Where several animals are infected, it may be possible to connect several catheters to the same gas-ozone supply, for simultaneous treatment.

Although the present is particularly directed to the treatment of mastitis, by introducing a gas containing ozone through the teat canal, it will be understood that it is likewise suitable for ozone treatment of various diseases in cavity tissues of the human or animal body, such as the rectum, the vagina (e.g. vaginitis), the uterus, the mouth or the larynx. Uterine diseases, e.g., metritis and endometritis, frequently occur especially in a veterinary context either spontaneously or in cases of retained placenta or postpartum complications; for treatment of such diseases ozone would be introduced through the cervical opening.

The present invention is also of relevance to treatment of diseases in other body cavities such as the gastrointestinal tract, the peritoneal cavity, the bladder, the urethra or the urinary tract, e.g. for treating cystitis.

The present invention also contemplates treatment of gastroenteritis, particularly in the veterinary field, e.g. in relation to neonatal animals. As is known, gastroenteritis may be associated with various microorganisms such as bacteria, fungi, viruses and protozoa. Conditions of the bladder/urethra/urinary tract which are contemplated as amenable to treatment in accordance with the invention include acute or chronic bladder inflammation due to various microorganisms, cystitis, pyelonephritis and ureteritis.

The invention will be illustrated by the following non-limitative examples, which preferably utilize the described apparatus.

EXAMPLE 1

For the treatment of mastitis in dairy animals, it has been found that a flow of gas of about 1 to 5 liters (e.g. 3-4) per minute, containing from 1 to 50 (e.g. 20-30) p.p.m. of ozone, for intermittent periods of 1 to 20 (e.g. about 10) minutes, using the catheter described herein, has given excellent results and can be effective in curing the disease within a few days, although one or two days may be sufficient. In most cases. The gas to be ozonized will usually be clean

(uncontaminated) air, but in the alternative it is also possible to use bottled gas such as oxygen, which has been ozonized. See also Examples 5 and 6m below.

EXAMPLE 2

For the treatment of gastroenteritis, use may be made of the catheter described herein, for introducing ozonized air into the rectum, via the anus, the parameters otherwise being as described in Example 1. Alternatively, the ozonized air may be introduced through a needle inserted through the linea alba into the peritoneal cavity. In either case, the pressure must be carefully controlled.

EXAMPLE 3

For the treatment of cystitis, use may be made of a double lumen Foley catheter, for introducing ozonized air into the bladder, via the urethra, the parameters otherwise being as described in Example 1.

EXAMPLE 4

For the treatment of metritis, endometritis or pyometra, use may be made of a double lumen Foley catheter, for introducing ozonized air into the uterus, via the cervical canal, the parameters otherwise being as described in Example 1.

EXAMPLE 5

In this Example, the efficacy of intramammarily administered ozone gas was evaluated in experimental *Escherichia coli* mastitis in dairy cows.

Experimental Cows

Twenty three clinically healthy, multiparous Israeli black and white cows were used in this study. All cows were in early lactation, range 50 to 191 d of lactation, with an average milk production of at least 25 L milk/d. Potentially suitable cows were purchased from commercial dairy herds, brought to the experimental dairy herd at the Volcani Research Center (Bet Dagan, Israel) and allowed a period of 7 days for acclimatization before the induction of experimental infection. Cows were kept under a loose housing system, milked three times a day and were fed total mixed ration. The milking equipment consisted of double sided, three stall auto-tandem milking parlour with automatic removal of milking units. The milking equipment was computer controlled with an electronic auto-identification, pedometer and milk conductivity

monitoring system (Afimilk®, computerized dairy management systems, S.A.E. Afikim, Kibbutz Afikim 15148, Israel). All cows were also identified by freeze brand marks. Mammary glands were eligible for experimental infection only if the foremilk SCC was less than 400,000/ml of milk and if major udder pathogens were not isolated from milk samples collected daily for three consecutive days prior to the day of infection. (Cow 852 was salvage slaughtered on day 12 after infection due to metatarsal fracture.)

Intramammary Challenge

Two quarters of each cow were challenged intracisternally with *Escherichia coli* strain P-4, serotype O32:H37, serum resistant, which had originally been recovered from a case of clinical mastitis and had been used in experimental studies of coliform mastitis (see Shpigel, N.Y., et al., Efficacy of the fourth generation cephalosporin cefquinome for the treatment of experimentally induced Escherichia coli mastitis in cows. J. Dairy Science, 1996, 80:318-323; and Bramely, A.J. Variations in the susceptibility of lactating and non-lactating bovine udders to infection when infused with Escherichia coli. J. Dairy Sci., 1976, 43: 205-211, 1976). Challenge inoculum was prepared by inoculation of a lyophilized stock culture of *E. coli* onto brain-heart infusion broth for incubation at 37°C for 12 hours. The resulting broth culture was streaked onto trypticase soy (TS) blood agar (BA) plate to determine purity. After incubation, several colonies were transferred to 150 ml TS broth and incubated for further 24 hours at 37°C. The broth was swirled vigorously and plunged into ice water. Appropriate dilutions of culture were made in sterile PBS to achieve a geometric mean of 500 cfu/ml. The actual inoculum concentration was determined before and after udder inoculation by pour plating in eosin methylene blue (EMB) agar, the counts ranged 400 to 750 cfu/ml. Infections were made immediately after the morning milking. Teats were dipped in iodophor teat dip, scrubbed with 70% ethanol and allowed to dry. Using a sterile, disposable, 2.5 inch blunt cannula, 1.0 ml of the bacterial suspension was infused via the teat canal. Seventeen cows were infused into diagonal front and hind quarters, 3 into front quarters, 2 into left quarters and 1 into hind quarters (see Appendix 4 for individual cow quarter inoculation site).

Treatment

Cows were randomly allocated into 2 treatment groups, 12 cows per group (one cow developed clinical mastitis before experimental inoculation and was withdrawn). Eleven cows received a priming dose of 20 g of sulfadiazine Na and 4 g of trimethoprim (Diaziprim Forte®; Vitamed Ltd., Batyam, Israel) intramuscularly and additional intramuscular treatment of 10 g of sulfadiazine Na and 2 g of trimethoprim after 24 hours. Twelve cows were treated intramammarily, 6 times at 8 hours intervals, with a gaseous mixture (generated as described herein) containing air and ozone applied to the inoculated quarters only. Prior to treatment it was ascertained that the ozonized air did not contain any noxious components such as nitrogen oxides. The gaseous mixture contained 40 ppm ozone and was applied at a pressure of 1 atm. and a flow rate of 150 L per hour for 5 minutes. The concentration of ozone in gaseous mixture was measured using the U.V. Photometric Ozone Analytical Instrument model 1008-AH (Dasibi Environmental Corp., Glendale, CA, USA). The treatment started 12-h after inoculation when clear clinical signs of acute mastitis became evident. Veterinarians and animal technicians responsible for animal care, clinical examination and data collection were blind to animal group allocation and nature of treatment.

Clinical Observations

Systemic and local clinical signs were monitored throughout the study period. Rectal temperature, heart rate, respiratory rate and rate of primary rumen contractions were determined once daily for 3 days before infection, immediately before infection, 4, 8, 12, 16 and 24 h after infection and then twice daily (a.m. and p.m.) for 7 d and once daily for another week. Systemic signs and clinical status of inoculated and control quarters were graded clinically. Cows attitude and appetite, milk appearance and quarter size, quarter edema, quarter pain and quarter temperature were graded as previously described (clinical mastitis score (CMS); 7-35 scale used).

Milk and Blood Samples

Duplicate quarter milk samples were aseptically collected from all quarters of each cow for bacteriological culture and SCC at 6 hours after

infection, immediately pre-treatment time and 7 and 14 days post treatment (cow 852 was sampled on day 12 before salvage slaughter).

Bacteriological examination for udder pathogens was performed as previously described, using standard methods. Milk SCC were measured with Fossomatic instrument (Foss Electric, Hillerød, Denmark). Concurrently with the clinical examination, the California Mastitis Test (CMT) was performed and recorded using 0, 1, 2, 3, 4 scale.

Jugular blood samples were collected in plain and EDTA vacuum blood tubes once daily for two consecutive days before infection and 4, 12, 16 and 24 hours after udder inoculation and once daily for the following 7 days. Whole blood was analyzed for complete white blood cell counts (WBC), and hematocrit (Ht). Serum samples were analyzed for total calcium, total serum protein (TSP), aspartate serum transaminase (AST), urea, creatinine, inorganic phosphorus and sodium. The biochemical analysis was determined enzymatically by use of an automated analyzer (Kone Autoanalyzer).

Statistical Analyses

Quarter bacteriological infection rates and cure rates among treatment groups were compared by chi-square tests. A quarter was considered infected if either the milk sample at 6 h postinfection or the pretreatment milk sample, or both were positive for *E. coli*. Treatment differences among all other parameters were tested by analysis of variance; data were blocked by day from challenge. Differences among treatment means were determined using Tukey pairwise comparisons of means. For all comparisons, $P < 0.05$ was considered to be significant. Statistical analyses were performed using the program Statistix® (Analytical Software, Tallahassee, FL).

RESULTS

Clinical Findings

All cows developed acute clinical mastitis as assessed by the Clinical Mastitis Score (CMS) and California Mastitis Test (CMT). CMS peaked for both treatment groups between 12 and 36 hours after infection, thereafter gradually decreasing to levels above pre infection levels by two weeks. CMT peaked 3

days after infection, thereafter declining to around levels above 2 for both groups. The disease was associated with typical systemic, hematological and blood biochemical changes. Rectal temperature peaked 12 hours after infection and was associated with increased heart rate and respiratory rate, and decreased rumen motility. These changes were associated with decreased white cell counts, hypocalcemia, decreased serum phosphate, increased serum AST levels, and increased serum urea and creatinine levels. Milk production declined sharply up to 24 hours after infection and thereafter increasing to levels lower than pre infection levels for both treatments groups. All other parameters followed a similar pattern for both treatments groups and or failed to show significant deviations from pre infection levels.

No adverse drug reactions or any adverse events were observed following treatment with ozone intramammarily.

Bacteriological Findings

The bacteriological infection success rate was assessed by duplicate culture samples taken 6 hours post inoculation and at pretreatment time. The bacteriological cure rate was assessed by duplicate culture samples taken at days 7 and 14 post treatment. All samples taken from successfully infected quarters at a specific time should have been negative for *E. coli* to achieve bacteriological cure. *E.coli* were cultured at 6 hours after inoculation and/or before treatment from 100% (24/24) and 95.5% (21/22) of inoculated quarters of ozone and STM treatment group cows respectively. The cure rate for the ozone treatment group was 50% (12/24) on day 7 post infection and 83.3.8% (20/24) on day 14 post infection. Twelve quarters (50%) of the successfully infected quarters were culture negative for *E. coli* on both post treatment samples. The cure rate for the STM treatment group was 42.9% (9/21) on day 7 and 85.7% (18/21) on day 14 post infection. Eight quarters (38.1%) of the successfully infected quarters were culture negative for *E. coli* on both post treatment samples. None of the differences in rates between the treatment groups were statistically significant. Results are shown in Table 1.

Table 1: Bacteriological infection rates and cure rates of infused quarters in the ozone and sulfatrimethoprim (STM) treatment groups.

Treatment group	Infection rate	Recovery rate (day 7 post infection)	Recovery rate (day 14 post infection)
Ozone	100 % (24/24)	50% (12/24)	83.3% (20/24)
STM	95.5% (21/22)	42.9% (9/21)	85.7% (18/21)

DISCUSSION

All cows of both treatment groups developed typical coliform mastitis with systemic signs and hematological and blood biochemical changes similar to those previously observed in both experimentally induced and field cases. Clinical recovery of the affected quarters and the return of systemic, hematological, biochemical and milk production to pre infection levels, was better for the STM treatment group. However, these differences were not statistically significant.

The bacteriological cure rates were higher for the ozone treatment group in comparison to the sulfadiazine trimethoprim treatment group, however, these differences were not statistically significant.

CONCLUSIONS

The therapeutic effect of 40 ppm gaseous ozone in air mixture by intramammary administration was studied in experimentally induced *E. coli* mastitis in dairy cows. The course of the disease before treatment was similar for STM and ozone treated groups. The clinical recovery and return to milk production was better for the STM treated group. Both treatments provided similar bacteriological cure rates of the infected quarters. No local or systemic adverse or toxic affects of ozone therapy were observed.

EXAMPLE 6

In this Example also, the efficacy of intramammarily administered ozone gas was evaluated in experimental *Escherichia coli* mastitis in dairy cows.

Experimental Cows

Eleven clinically healthy, multiparous Israeli black and white cows were used in this study. All cows were in early lactation, range 27 to 144 d of lactation, with an average milk production of at least 25 L milk/d. Potentially suitable cows were purchased from commercial dairy herds, brought to the experimental dairy herd at the Volcani Research Center and allowed a period of 7 days for acclimatization before the induction of experimental infection. Cows were kept under a loose housing system, milked three times a day and were fed total mixed ration. The milking equipment consisted of double sided, three stall auto-tandem milking parlour with automatic removal of milking units. The milking equipment was computer controlled with an electronic auto-identification, pedometer and milk conductivity monitoring system (Afimilk®, computerized dairy management systems, S.A.E. Afikim, Kibbutz Afikim 15148, Israel). All cows were also identified by freeze brand marks. Mammary glands were eligible for experimental infection only if the foremilk SCC was less than 400,000/ml of milk and if major udder pathogens were not isolated from milk samples collected daily for three consecutive days prior to the day of infection.

Intramammary Challenge

Two quarters of each cow were challenged intracisternally with Escherichia coli strain P-4, serotype O32:H37, serum resistant, which had originally been recovered from a case of clinical mastitis and had been used in experimental studies of coliform mastitis (Shpigel, 1996 and Bramely, 1976).. Challenge inoculum was prepared by inoculation of a lyophilized stock culture of E. coli onto brain-heart infusion broth for incubation at 37°C for 12 hours. The resulting broth culture was streaked onto trypticase soy (TS) blood agar (BA) plate to determine purity. After incubation, several colonies were transferred to 150 ml TS broth and incubated for further 24 hours at 37°C. The broth was swirled vigorously and plunged into ice water. Appropriate dilutions of culture were made in sterile PBS to achieve a geometric mean of 5000 cfu/ml. The actual inoculum concentration was determined before and after udder inoculation by pour plating in eosin methylene blue (EMB) agar, the counts ranged 4000 to 7500 cfu/ml. Infections were made immediately after the

morning milking. Teats were dipped in iodophor teat dip, scrubbed with 70% ethanol and allowed to dry. Using a sterile, disposable, 2.5 inch blunt cannula, 1.0 ml of the bacterial suspension was infused via the teat canal. Four cows were infused into diagonal front and hind quarters, 3 into front quarters, 2 into left quarters and 2 into right quarters.

Treatment

Cows were randomly allocated into 2 treatment groups, 6 cows per group (one cow developed clinical mastitis before experimental inoculation and was withdrawn). Five cows received a priming dose of 20 g of sulfadiazine Na and 4 g of trimethoprim (Diaziprim Forte®; Vitamed Ltd., Batyam, Israel) intramuscularly and additional intramuscular treatment of 10 g of sulfadiazine Na and 2 g of trimethoprim after 24 hours. Six cows were treated intramammarily, 6 times at 8 hours intervals, with a gaseous mixture generated as described herein) containing air and ozone applied to the inoculated quarters only. Prior to treatment it was ascertained that the ozonized air did not contain any noxious components such as nitrogen oxides. The gaseous mixture contained 7 ppm ozone (and was applied at a pressure of 2 atm. and a flow rate of 300 L per hour for 10 minutes. The concentration of ozone in gaseous mixture was measured using the UV Photometric Ozone Analytical Instrument model 1008-AH (Dasibi Environmental Corp., Glendale, CA, USA). The treatment started 12-h after inoculation when clear clinical signs of acute mastitis became evident. Veterinarians and animal technicians responsible for animal care, clinical examination and data collection were blind to animal group allocation and nature of treatment.

Clinical Observations

Systemic and local clinical signs were monitored throughout the study period. Rectal temperature, heart rate, respiratory rate and rate of primary rumen contractions were determined once daily for 3 days before infection, immediately before infection, 4, 8, 12, 16 and 24 h after infection and then twice daily (a.m. and p.m.) for 7 d and once daily for another week. Systemic signs and clinical status of inoculated and control quarters were graded clinically. Cows attitude and appetite, milk appearance and quarter size, quarter edema,

quarter pain and quarter temperature were graded as previously described (clinical mastitis score (CMS); 7-35 scale used).

Milk and Blood Samples

Duplicate quarter milk samples were aseptically collected from all quarters of each cow for bacteriological culture and SCC at 6 hours after infection, immediately pre-treatment time and 7 and 14 days post treatment. Bacteriological examination for udder pathogens was performed as previously described, using standard methods. Milk SCC were measured with Fossomatic instrument (Foss Electric, Hillerød, Denmark). Concurrently with the clinical examination, the California Mastitis Test (CMT) was performed and recorded using 0, 1, 2, 3, 4 scale.

Jugular blood samples were collected in plain and EDTA vacuum blood tubes once daily for two consecutive days before infection and 4, 12, 16 and 24 hours after udder inoculation and once daily for the following 7 days. Whole blood was analyzed for complete white blood cell counts (WBC), and hematocrit (Ht). Serum samples were analyzed for total calcium, total serum protein (TSP), aspartate serum transaminase (AST), urea, creatinine, inorganic phosphorus and sodium. The biochemical analysis was determined enzymatically by use of an automated analyzer (Kone Autoanalyzer).

RESULTS

Clinical Findings

All cows developed acute clinical mastitis as assessed by the Clinical Mastitis Score (CMS) and California Mastitis Test (CMT). CMS peaked for both treatment groups between 8 and 24 hours after infection, thereafter gradually returning to pre infection levels by two weeks. CMT peaked between 8 hours and 3 days after infection, thereafter declining to around levels of 1 for both groups. The disease was associated with typical systemic, hematological and blood biochemical changes. Rectal temperature peaked between 8 to 12 hours after infection and was associated with increased heart rate and respiratory rate, and decreased rumen motility. These changes were associated with decreased white cell counts, hypocalcemia and mild hypophosphatemia. Milk

production declined sharply up to 24 hours after infection and thereafter returned gradually to it's pre-infection levels for both treatment groups. All other parameters followed a similar pattern for both treatments groups and or failed to show significant deviations from pre infection levels.

One cow (number 362) was withdrawn from the ozone treatment group on day 3 after infection due to severe cystitis and nephritis. Signs of urinary tract disease were evident and recorded before the initiation of the ozone therapy and therefore could not be attributed to the effect of ozone. Data regarding this cow was not included in the analysis presented in this report.

No adverse drug reactions or any adverse events were observed following treatment with ozone intramammarily.

Bacteriological Findings

The bacteriological infection success rate was assessed by duplicate culture samples taken 6 hours post inoculation and at pretreatment time. The bacteriological cure rate was assessed by duplicate culture samples taken at days 7 and 14 post treatment. All samples taken from successfully infected quarters at a specific time should have been negative for *E. coli* to achieve bacteriological cure.

E.coli were cultured at 6 hours after inoculation and/or before treatment from 80% (8/10) and 100% (10/10) of inoculated quarters of ozone and STM treatment group cows respectively. The cure rate for the ozone treatment group was 62.5% (5/8) on day 7 post infection and 87.5% (7/8) on day 14 post infection. Four quarters (50%) of the successfully infected quarters were culture negative for *E. coli* on both post treatment samples. The cure rate for the STM treatment group was 100% (10/10) on day 7 and 100% (10/10) on day 14 post infection (see Table 2).

Table 2: Bacteriological infection rates and cure rates of infused quarters in the ozone and sulfatrimethoprim (STM) treatment groups.

Treatment group	Infection rate	Recovery rate (day 7 post infection)	Recovery rate (day 7 post infection)
Ozone	80 % (8/10)	62.5% (5/8)	87.5% (7/8)
STM	100% (10/10)	100% (10/10)	100% (10/10)

DISCUSSION

All cows of both treatment groups developed typical coliform mastitis with systemic signs and hematological and blood biochemical changes similar to those previously observed in both experimentally induced and field cases. Clinical recovery of the affected quarters and the return of systemic, hematological, biochemical and milk production to pre infection levels, was similar for both treatment groups.

The bacteriological cure rates were higher for the sulfadiazine trimethoprim treatment group in comparison to the ozone treatment group, however, these differences were not statistically significant.

CONCLUSIONS

The therapeutic effect of 7 ppm gaseous ozone in air mixture by intramammary administration was studied in experimentally induced *E. coli* mastitis in dairy cows. The course of the disease was similar for both treatment groups as well as recovery and return to pre infection milk production. No local or systemic adverse or toxic affects of ozone therapy were observed.

While the present invention has been particularly described with reference to certain embodiments, it will be apparent to those skilled in the art that many modifications and variations may be made. The invention is accordingly not to be construed as limited in any way by such embodiments, rather its concept is to be understood according to the spirit and scope of the claims which follow.

CLAIMS

1. A method for treating a disease of a body cavity tissue in mammals, wherein a gas containing an effective amount of ozone for treating such disease is introduced inside said body cavity, provided that where the mammals are AIDS patients, then the ozone is not introduced via the rectum.

2. A method according to claim 1, wherein said and said medicament is introduced via the teat canal, the rectum, the vagina, the uterus, the mouth or the larynx.

3. A method according to claim 2, wherein said disease is mastitis and said medicament is introduced via the teat canal.

4. A method according to claim 1, wherein said body cavity is the gastrointestinal tract, the peritoneal cavity, the bladder, the urethra or the urinary tract.

5. A method according to claim 4, wherein said body cavity is the bladder, the urethra or the urinary tract, and said disease is cystitis.

6. A method according to claim 1, wherein said gas is introduced by means of a catheter inserted into said body cavity.

7. A method according to claim 6, wherein said catheter comprises, for introducing said gas, an open-ended inlet tube, and a perforated outlet tube integral therewith for removing said gas.

8. A method according to claim 7, wherein said catheter comprises two coaxial tubes, namely an inner tube defining said inlet tube and an outer tube defining said outlet tube, the latter being perforated by a plurality of openings.

9. A method according to claim 1, wherein the mammals are humans and

said disease is sinusitis.

10. A method according to claim 1, wherein the mammals are non-human mammals and said disease is mastitis.

11. A medical apparatus for treatment of a disease of body cavity tissue by a flow of ozonized gas, which comprises:

means adapted for delivery of said flow of ozonized gas to body cavity tissue;

means for generating said flow of ozonized gas and conduit means for transferring said ozonized gas to said delivery means; and

means for providing unozonized gas and conduit means for transferring said unozonized gas to said generating means, said providing means being adapted, for example by use of an electrically driven compressor or pump, to supply gas at a pressure sufficient to drive said flow of gas after ozonization through said delivery means and into said body cavity.

12. The apparatus of claim 11, characterized additionally by at least one of the following features:

(a) a filtering means and means for withdrawing used ozonized gas from said body cavity and for passing said withdrawn ozonized gas through said filtering means;

(b) a tubular housing having a tapering and conductive front end with the apex thereof forming an orifice and said housing having an open rear end, a coronizing electrode concentrically mounted in said housing upstream of said tapering front end and with its pointed front end extending towards said orifice, and a high voltage source having a potential of at least 2200 volts having a first terminal connected to said electrode and a second terminal connected to said conductive front end of said housing;

(c) said apparatus is adapted to deliver into said cavity gas containing about 1 to about 50 p.p.m. ozone;

(d) said apparatus is adapted for simultaneous treatment of a plurality of

mammals by connecting a plurality of said delivery means to said ozone generator.

13. The apparatus of claim 11 or claim 12, wherein said delivery means is selected from the group consisting of:

a catheter which comprises an inner open-ended inlet tube for introducing said gas and an outer perforated outlet tube for removing said gas integral and coaxial therewith, the outlet tube being perforated by a plurality of openings;

a hollow needle; and

a double lumen Foley catheter.

14. The apparatus of claim 13, wherein said body cavity tissues are accessible via a large opening such as the mouth, the apparatus comprising:

a tubular housing of a solid material having a tapering front end of a conductive and anti-corrosive material with its apex open in the form of orifice which is sufficiently small so that said orifice constitutes said delivery means;

a coronizing electrode concentrically positioned in said tube close behind the tapered front with its pointed front end extending towards said orifice, thus allowing flow of ozonized gas to be driven through said orifice thereby to contact the affected cavity tissue, and

an electric high-voltage generating means attached to said apparatus characterized by a potential of at least 2200 volts, said high-voltage generating means having its high-voltage terminal connected to said electrode and its zero terminal to said tapered front end.

15. The apparatus of claim 14, characterized additionally by at least one of the following features:

(i) a filtering means and means for withdrawing used ozonized gas from said body cavity and for passing said withdrawn ozonized gas through said filtering means;

(ii) the rear end of said tubular housing is of smaller or larger or of

substantially equal diameter to that of said orifice, said rear end being optionally partly or completely open, in order to allow ingress of air as said unozonized gas;

(iii) said apparatus is adapted to deliver into said cavity gas containing about 1 to about 50 p.p.m. ozone;

(iv) the entire tubular housing is made of a conductive and anti-corrosive material;

(v) said coronizing electrode is mounted inside said tubular housing by means of a cylindrical perforated support of a non-conductive material, permitting air to flow therethrough.

(vi) an motor-driven fan mounted inside said tubular housing and so disposed that it directs a flow of unozonized air in the direction of said electrode,

(vii) an at least partly hollow handle integral with said tubular housing and disposed generally transversely thereto

16. The apparatus of claim 15, still further characterized by at least one of the following features

(α) feature (vii) is present and said high-voltage generating means is positioned inside a hollow portion of said handle.

(β) features (I) and (vi) are present, the filtering means being disposed upstream of said fan.

(γ) feature (vi) is present, and both said electrode and said fan are mounted firmly inside tubular means of smaller diameter than and concentric with said tubular housing which has a closed rear end, thus providing an annular space between the tubular housing and the smaller diameter tubular means, whereby depending on the relative positions of said electrode and said fan, either (A) air is drawn from said orifice into the annular space and directed out via the inside of said tubular means and through said orifice, or (B) air is drawn from said orifice into the inside of said tubular means and directed out via the annular space and through said orifice, and when feature (i) is also present, then in case (A) said filtering means is disposed in said annular space and in case (B) said filtering means is disposed inside said tubular means upstream of said fan;

(δ) soft frusto-conical sleeve Is removably mounted on the front end of said

housing in order that it may be removed after each treatment.

17. Use of ozone in the manufacture of a gaseous medicament, for treating a disease of a body cavity tissue in mammals by introducing said medicament into said cavity, excluding introducing said medicament via the rectum where the mammals are AIDS patients.

18. Use according to claim 17, wherein said disease is mastitis and said medicament is introduced via the teat canal.

19. Use according to claim 17, wherein said disease is cystitis, and and said medicament is introduced via the bladder, the urethra or the urinary tract.

20. Use according to claim 17, wherein the mammals are humans and said disease is sinusitis.

21. Use according to claim 17, wherein the mammals are non-human mammals and said disease is mastitis.

22. Use of ozone in the manufacture of a gaseous medicament, for preventing a disease of a body cavity by introducing said medicament into said cavity.

23. Use according to claim 22, wherein said disease is mastitis in a cow, and said introducing serves to remove any milk residues from the udder of the cow.

24. A method according to claim 1, wherein there is used apparatus as defined in claim 11.

25. Use according to claim 17 or claim 22, wherein said treating or preventing, respectively, is carried out using apparatus a defined in claim 11.

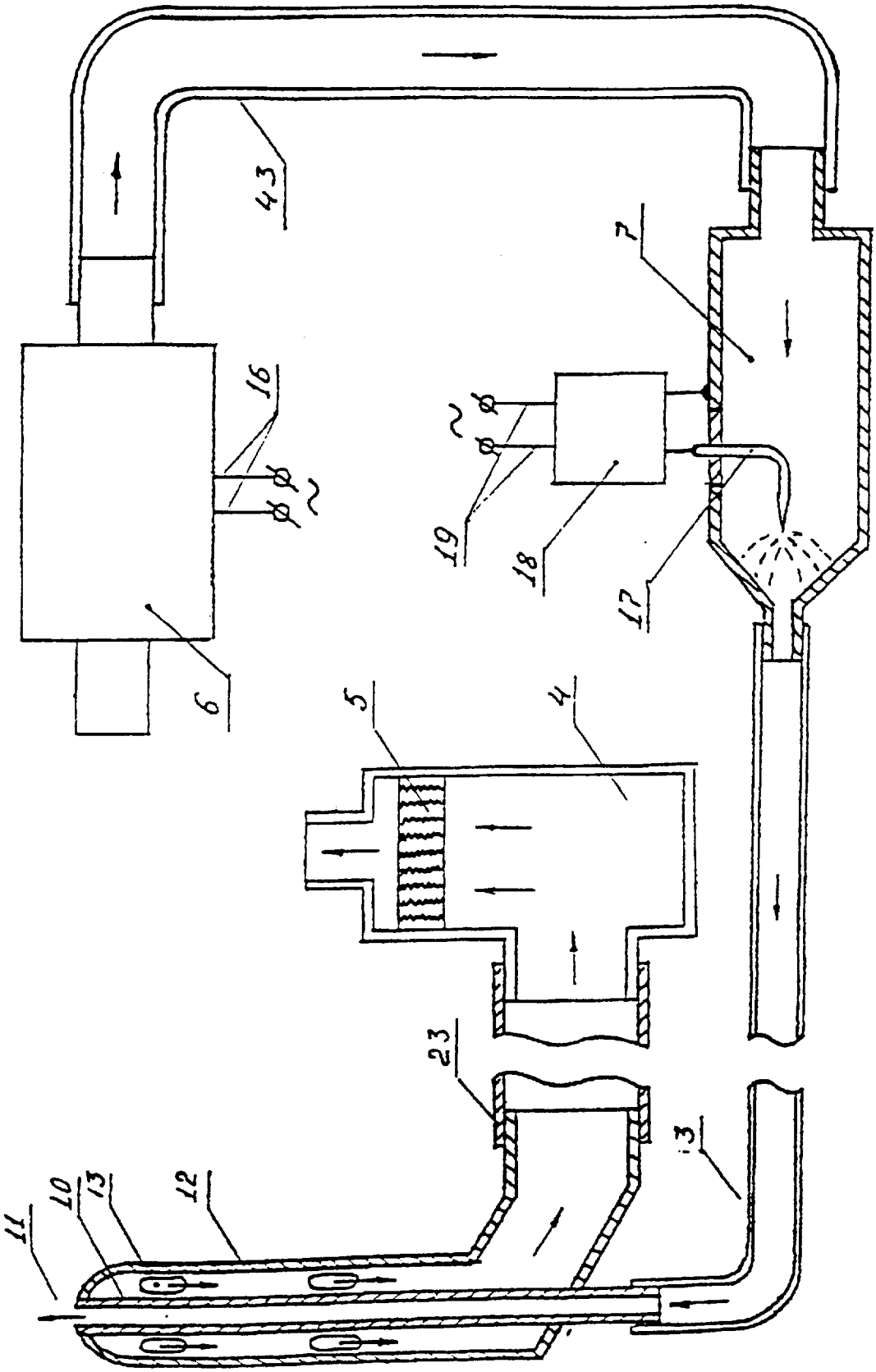

Fig 1

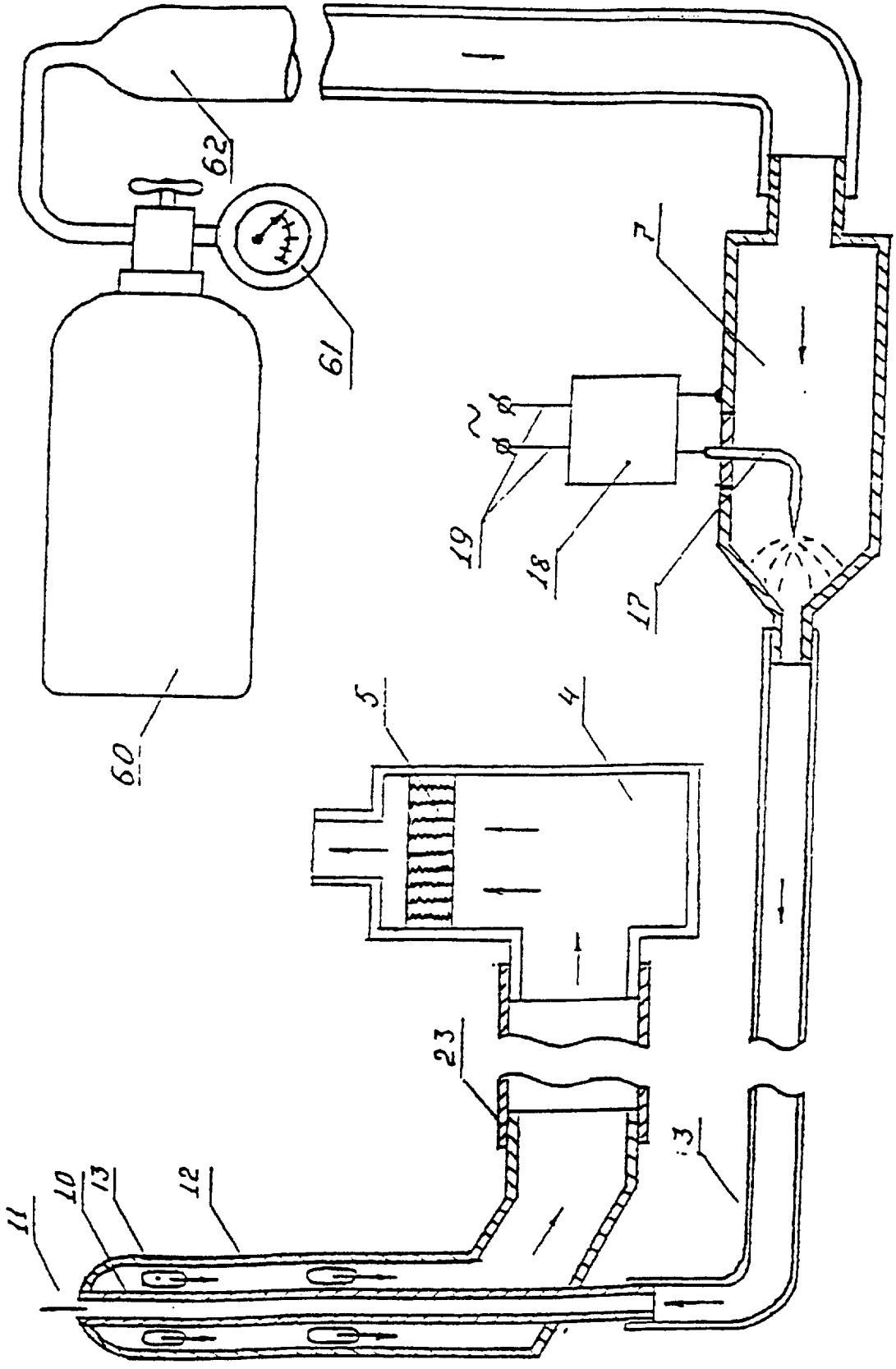

Fig 2

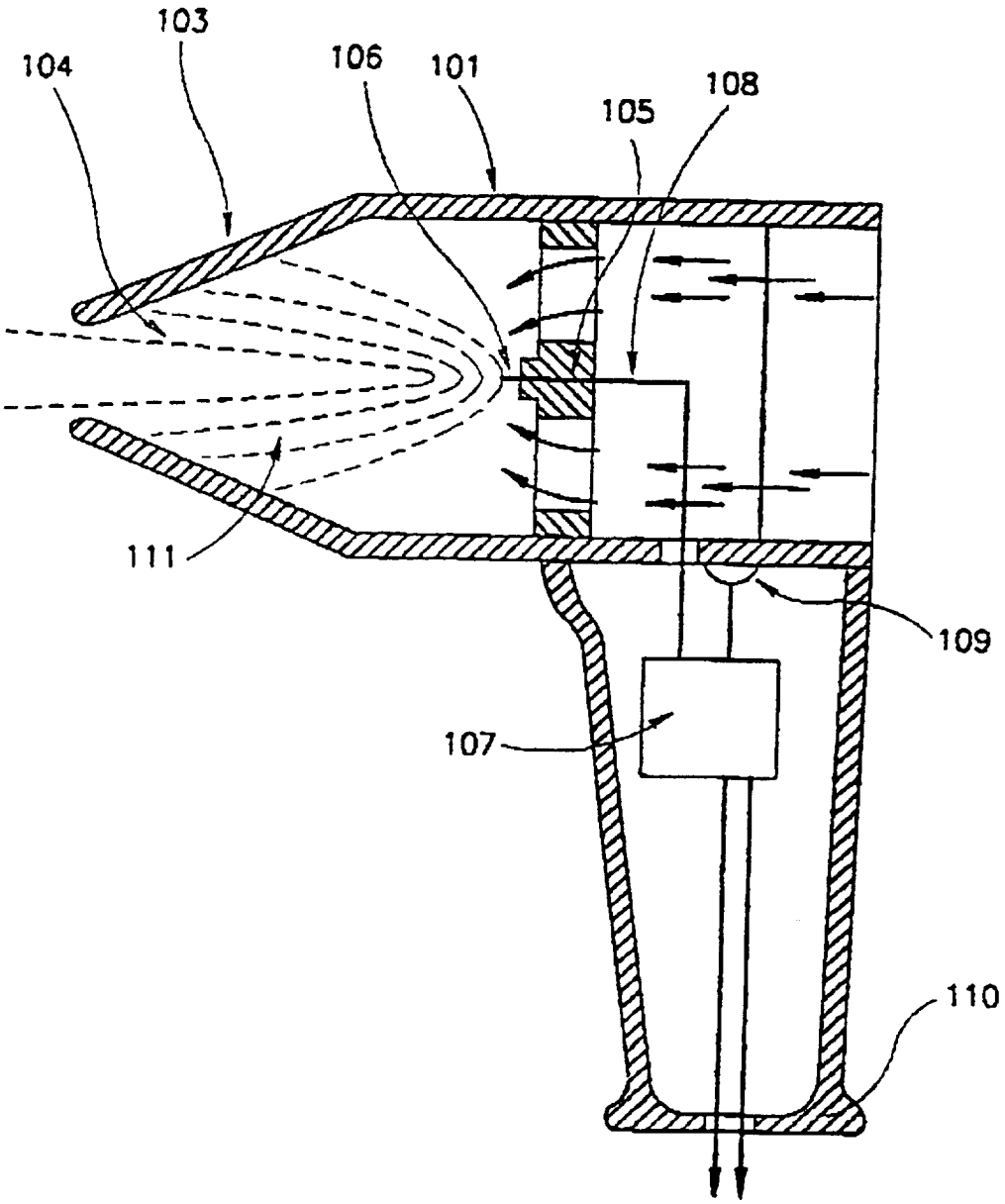

FIG.3A

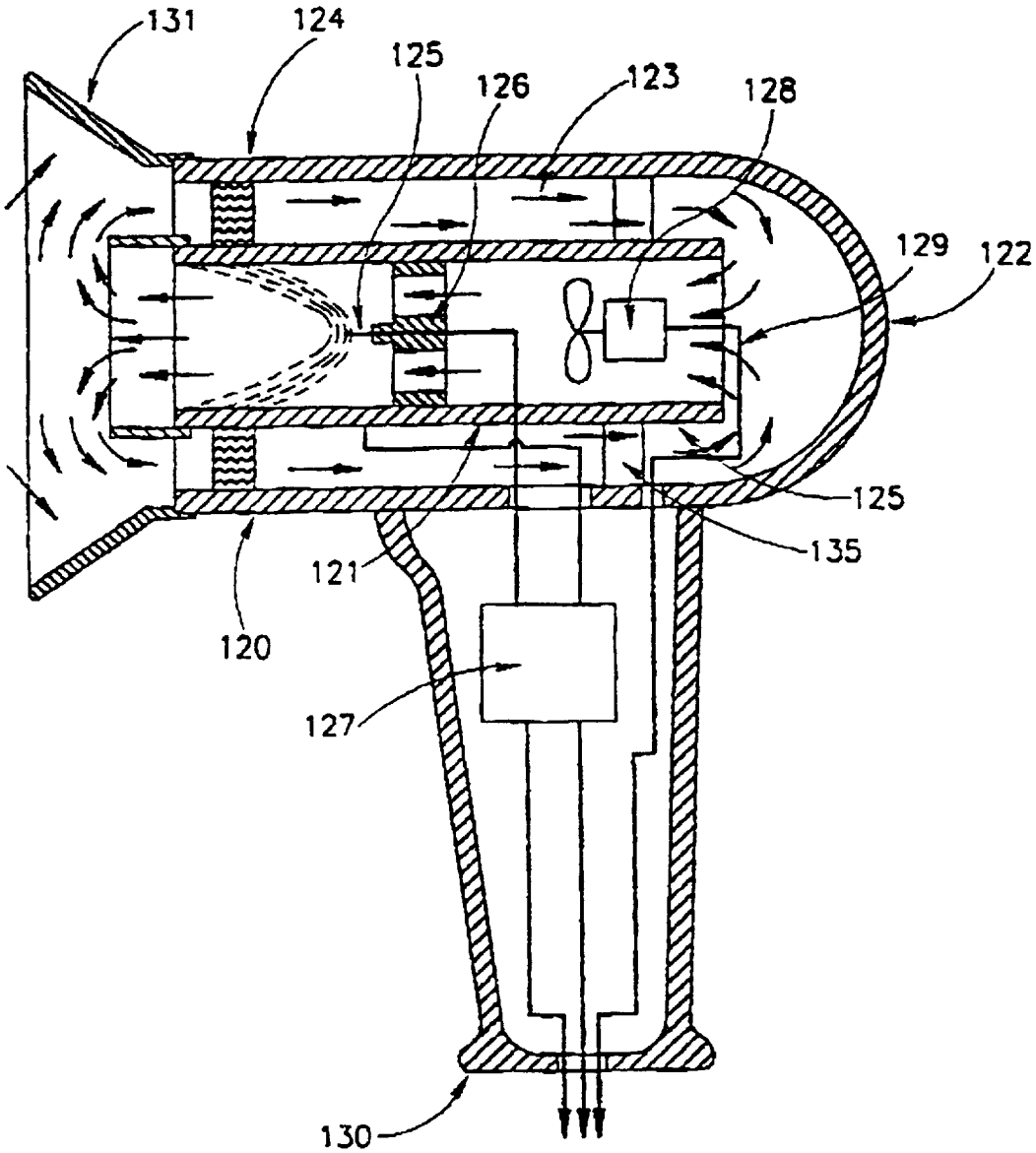

FIG.3B

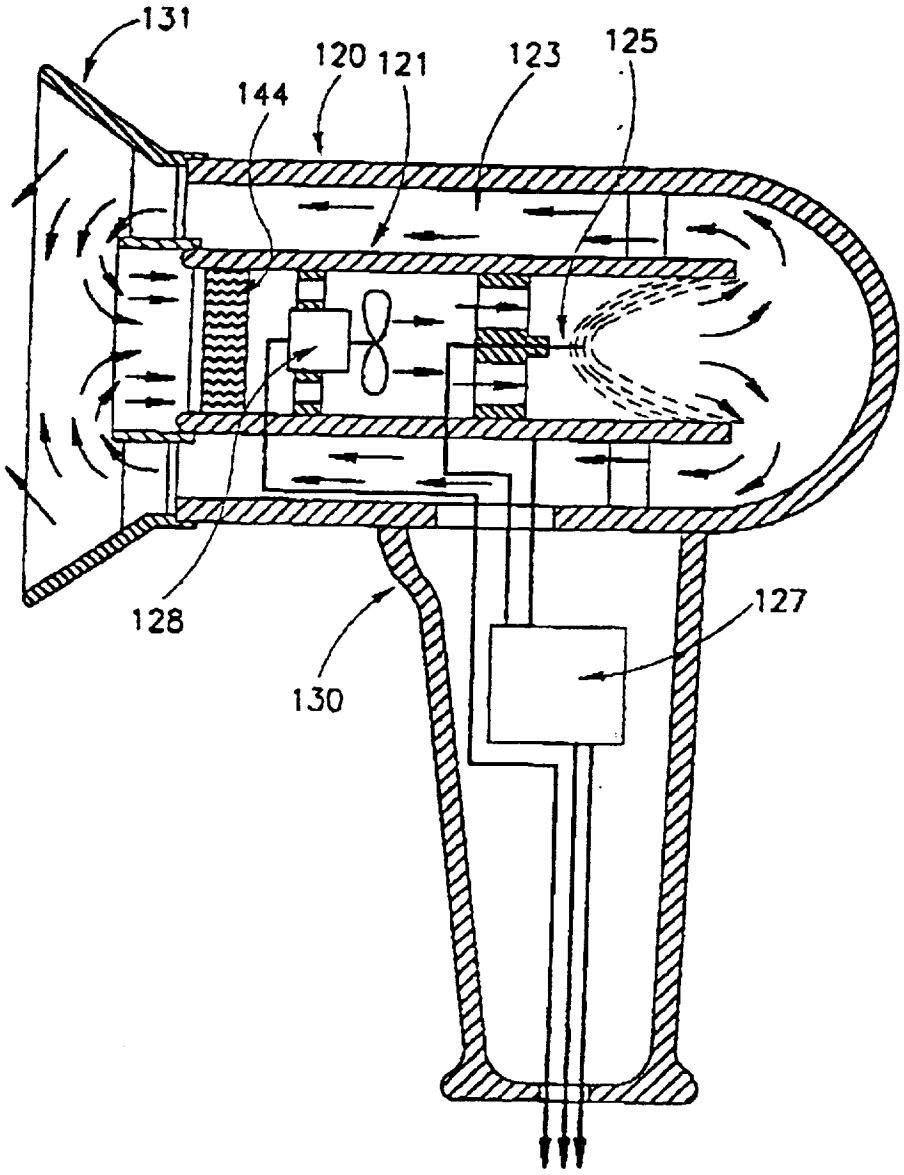

FIG.3C

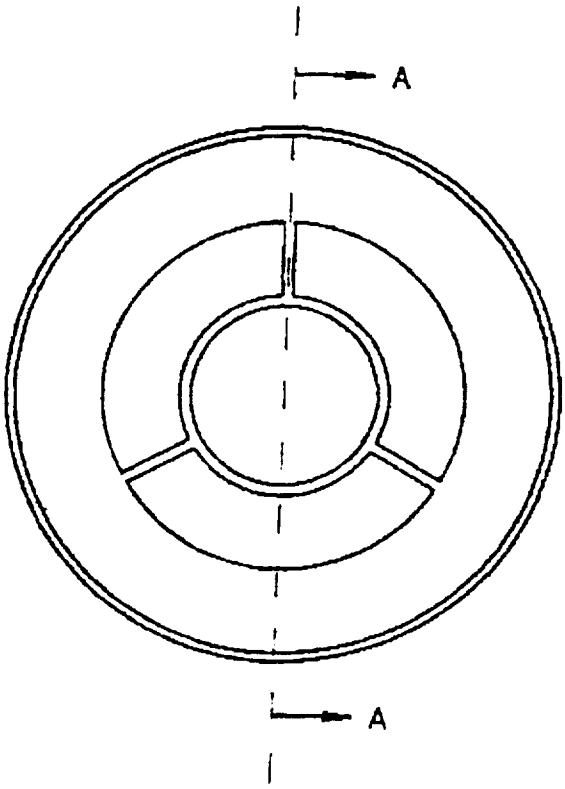

FIG.4

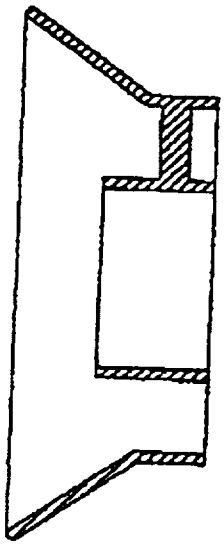

FIG.5