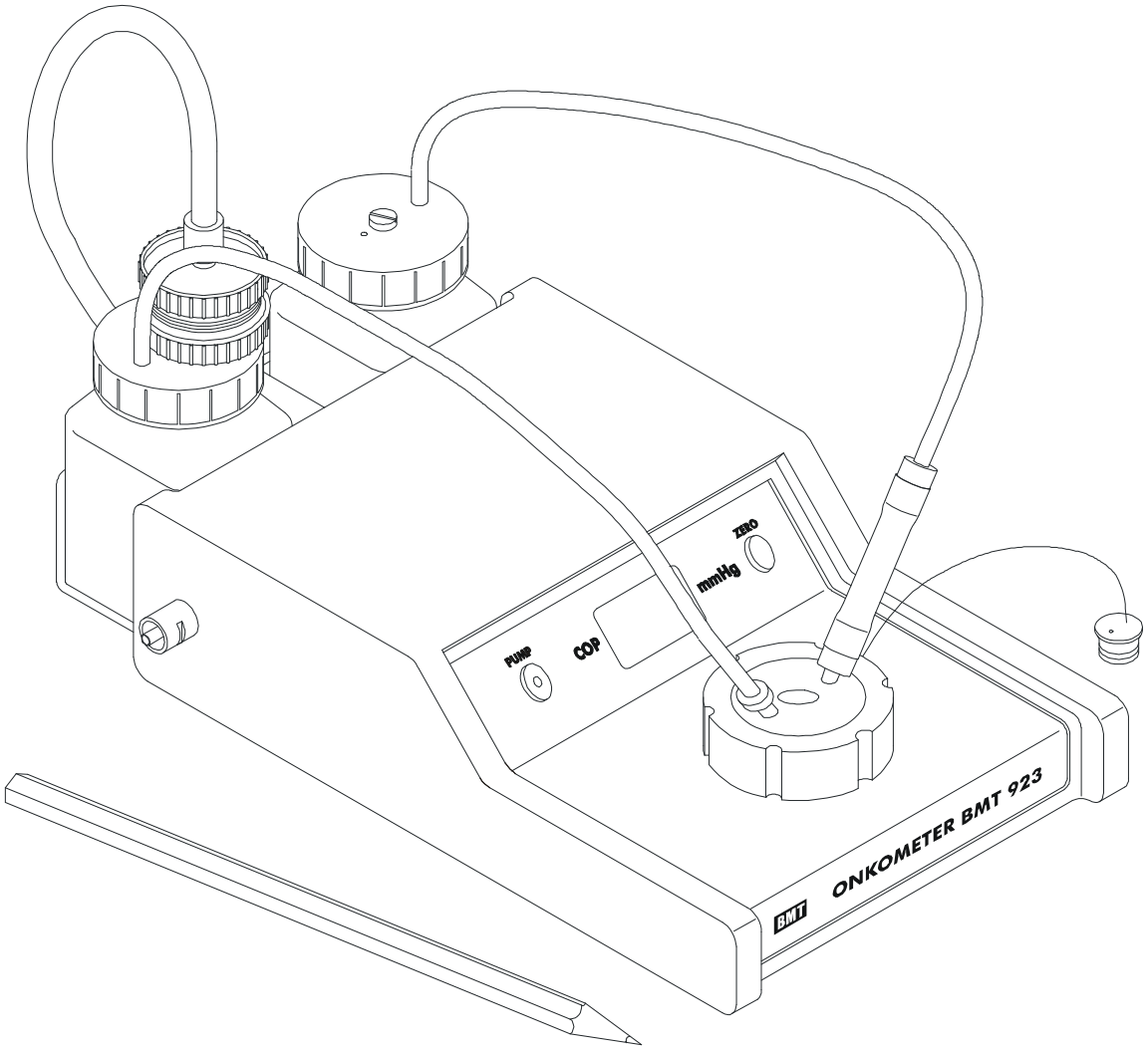
ONKOMETER BMT 923

Handbook

Rev. 05/2021



ONKOMETER BMT 923
Handbook

Contents

1. The Colloid Osmotic Pressure (COP)

The COP

The colloid osmotic pressure (COP) is a special case of osmosis. COP appears at semipermeable membranes which are well permeable for water and substances with molecular weights up to several thousands, but are impermeable for colloids, e.g. plasma proteins.

Wilhelm PFEFFER first described osmotic phenomena in plant cells (1877). He measured them with the first membrane osmometer ever built. Jacobus Hendricus VAN'T HOFF desribed them theoretically (1887). Ernest H. STARLING, the great physiologist, discovered the phenomenon of colloid osmotic pressure and its important role in balancing the capillary transmural fluid exchange (1896). It was Starling who built the first colloid osmometer with a sheep's peritoneal membrane, and he used it for the first measurement of colloid osmotic pressure in canine serum. Measurement took about three to four days.

COP is the "antagonist" of the intra-capillary hydrostatic pressure, both being equally important for interstitial fluid balance. But until recently, COP could not be measured in clinical diagnosis. Colloid osmometers simple and sturdy enough for the routine are available only since the 80's of the 20th century.

The ONKOMETER BMT 923 (with its predecessor BMT 921) is unsurpassed in simplicity of both measurement and maintenance. Measurement takes less than two minutes, and the instrument automatically holds the right steady state value of the displayed COP.

Clinical Impact of COP

COP of the capillary blood has to be judged in reference to the hydrostatic blood pressure in these capillaries and in the neighbouring venoles, to the hydrostatic pressure in the surrounding interstitial spaces, and to the COP of the interstitial fluid. Both of the latter can hardly be measured. Nevertheless knowledge of the COP, and namely knowledge of its trend, is important for clinical diagnosis. Some examples:

Intensive Care: COP has been used to monitor the infusion of human albumin, or artificial plasma expanders. The aim was to treat edema. It turned out that in some patients the resulting COP remained subnormal. Obviously in those patients proteins or starch were prone to leave the vascular system. In such situations infusion of albumin, or artificial colloids, is contraproductive because the development of edema is enhanced. Capillary leakages may be generalised, or prevail in one organ or a groop of organs. In any case the administration of macromolecules is contraindicated in such situations. The diagnostic tool of choice is to measure the colloid osmotic pressure.

Nephrology/Dialysis: COP is used to readjust the blood volume after dialysis. Oncometry is an easy and reliable method because total protein mass practically does not change during the setting for dialysis.

Gynecology/Obstetrics: In late pregnancy capillary leak syndrome is a frequent complication causing a more or less pronounced retention of water in the tissues. The transcapillary loss of proteins results in a progressive decrease in COP. When COP becomes too low dangerous eclampsia

(a brain edema) develops causing convulsion, a life-threatening complication. In such cases in some German hospitals birth is initiated intentionally when COP drops below about 13 mmHg. First warning is given by the pathologist when COP is down to 18 mmHg.

Open Heart Surgery/Heart Lung Machine: The priming volume in the extracorporeal circulation is monitored by measuring COP as an index for the degree of dilution of the blood. Only in dramatic cases COP is corrected by adding plasma.

The COP will gain additional interest when artificial proteins will come into clinical perspective. Many companies are working on the development of artificial proteins.

2. Sample Material

The best sample material for COP measurement is heparin plasma with up to 100 IE/ml heparin.

Heparinised whole blood can be used for measurement, but it is not recommended. In whole blood COP measurement needs much more time than in plasma. This is the reason why measurement sometimes is interrupted prematurely resulting in a false low result.

Attention: Only heparin may be used as the anticoagulant**!** Other anticoagulants, e.g. EDTA or sodium citrate, would lead to false high results.

Serum may be used for COP measurement, but also is not recommended. COP measured in serum principally is a bit lower than in plasma. But first of all the method of serum extraction can affect the COP significantly.

In case the trend of COP is of interest rather than the absolute value, the restrictions of serum mentioned above are less important. This also applies to heparinised whole blood.

COP is influenced by the position of the patient during withdrawal of the blood. The COP can be up to 15% lower when it is measured in the blood of a patient in supine position, compared with the upright position. For comparison of different measured values of the COP of one patient, or of several patients, the according positions must be indicated together with the COP values.

Immediately after withdrawal from the patient the blood sample should be centrifugated. Heparin plasma may be stored in a refrigerator at about +4 °C, but it must never be frozen. Correctly stored sterile plasma practically does not change its COP during one week, or even longer.

During storage of the plasma some decomposition occurs. Before COP measurement such samples should be homogenized by gently turning them several times (not by shaking).

3. The ONKOMETER BMT 923

The measuring chamber of the ONKOMETER BMT 923 is divided in two separate compartments: the reference chamber **5** and the sample chamber **6** (see sketch on page 6). Both compartments are separated from each other by the semipermeable membrane **1**.

This membrane (the measuring membrane) is supported by the cambered sieve plate **2** made of stainless, but magnetic steel. The sealing ring **3** (red silicone rubber) is sealing the upper, active surface of the asymmetric membrane from the reference chamber.

The pressure inside the funneled reference chamber is measured by the electronic pressure transducer **4**. The pressure at the bottom of the sample chamber is only the hydrostatic pressure of the sample (about 1.4 mm water column, or 0.1 mmHg). The pressure measured by the pressure transducer in the reference chamber thus practically is the pressure difference between both chambers.

The reference chamber is filled with physiologic saline. It must be absolutely free of air bubbles. The sample (about 100 µl) is filled into the sample chamber (direction **II**). Now the semipermeable membrane is separating the sample solution (in the sample chamber 6) from its solvent (in the reference chamber **5**). The sample "wants" to equilibrate the different colloid concentrations in both chambers, and "sucks" saline from the reference chamber upwards into the sample chamber. This is possible only until the resulting vacuum in the reference chamber has reached a certain limit which is the higher the more macromolecules are present in the sample. This limit pressure difference between the sample chamber and the reference chamber is the colloid osmotic pressure, or COP, of the sample. It is displayed by the ONKOMETER BMT 923 in millimeters of mercury (mmHg).

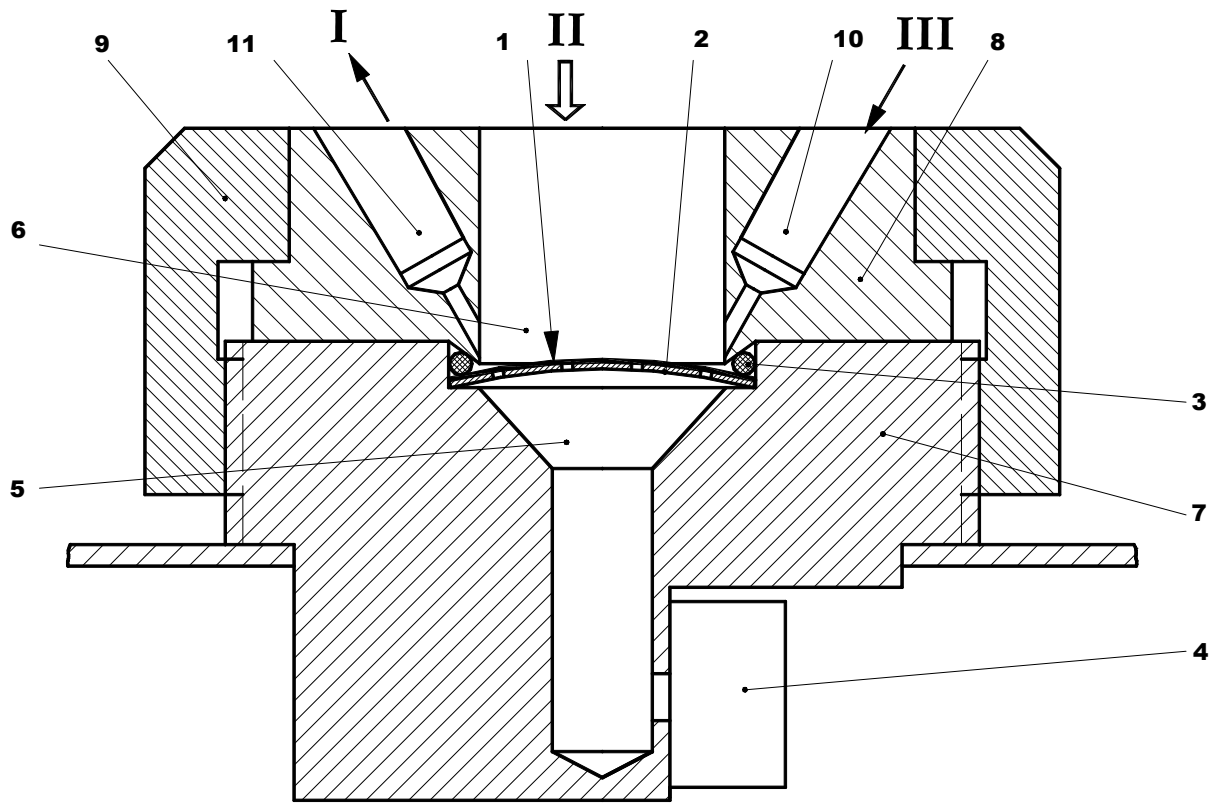
The salt (sodium chloride, molecular weight about 59) dissolved in the water has only little influence on the colloid osmotic pressure produced by the macromolecules (albumin has a molecular weight of about 66,300) because the salt can readily pass the semipermeable membrane. The influence of the salt is mainly dynamic: If the salt concentration in the sample is significantly different from that in the reference chamber a short pressure spike is displayed by the ONKOMETER BMT 923. This pressure spike is vanishing after a few seconds.

To zero the instrument the sample chamber is filled with pure saline (about 100µl, like the sample volume). Both chambers now contain only saline, and the COP displayed by the instrument has to be zero by definition. If the instrument does not display 00.0 the ZERO push button is pressed momentarily to zero the instrument.

In practice the sample chamber is filled twice, with two amounts of sample (approx. 100 µl each). Whole blood usually needs more than two amounts of sample.

Before the second amount of sample is filled into the sample chamber the first amount of sample is sucked out (with the internal electric vacuum pump), but the sample chamber of course may not be flushed! This practice of COP measurement guarantees that any residues of saline are completely removed from the sample chamber, namely from the large surface of the semipermeable membrane and from the sealing ring around the membrane.

After measurement the sample is sucked off the sample chamber via the capillary channel **11** (direction **I**). Via the other capillary channel **10** fresh saline now is pumped into the sample chamber (direction **III**). With the vacuum pump built into the ONKOMETER BMT 923 this saline then is removed. When this procedure is repeated several times the sample chamber is rinsed completely free of any macromulecular residues.



Measuring Chamber of the ONKOMETER BMT 923

1 Semipermeable membrane, asymmetrical cellulose triacetate membrane with a nominal retention rate (cut-off) of 20.000 daltons (molecular weight 20.000)

2 Sieve plate to support the membrane, stainless steel, ferromagnetic

3 Sealing ring, silicone rubber

4 Electronic pressure transducer for measuring the (negative) osmotic pressure in the reference chamber **5**

5 Reference chamber filled with physiological saline

6 Sample chamber into which the samples to be tested are filled from the top (**II**)

7 Lower part of measuring chamber with reference chamber **5**, PVDF (polyvinylidene fluoride)

8 Upper part of measuring chamber with sample chamber **6**, PVDF

9 Screw-ring to tighten upper part **8** of measuring chamber to lower part **7** of measuring chamber; when the ring is screwed down, the membrane is pulled tight, and at the same time the reference chamber and sample chamber are sealed

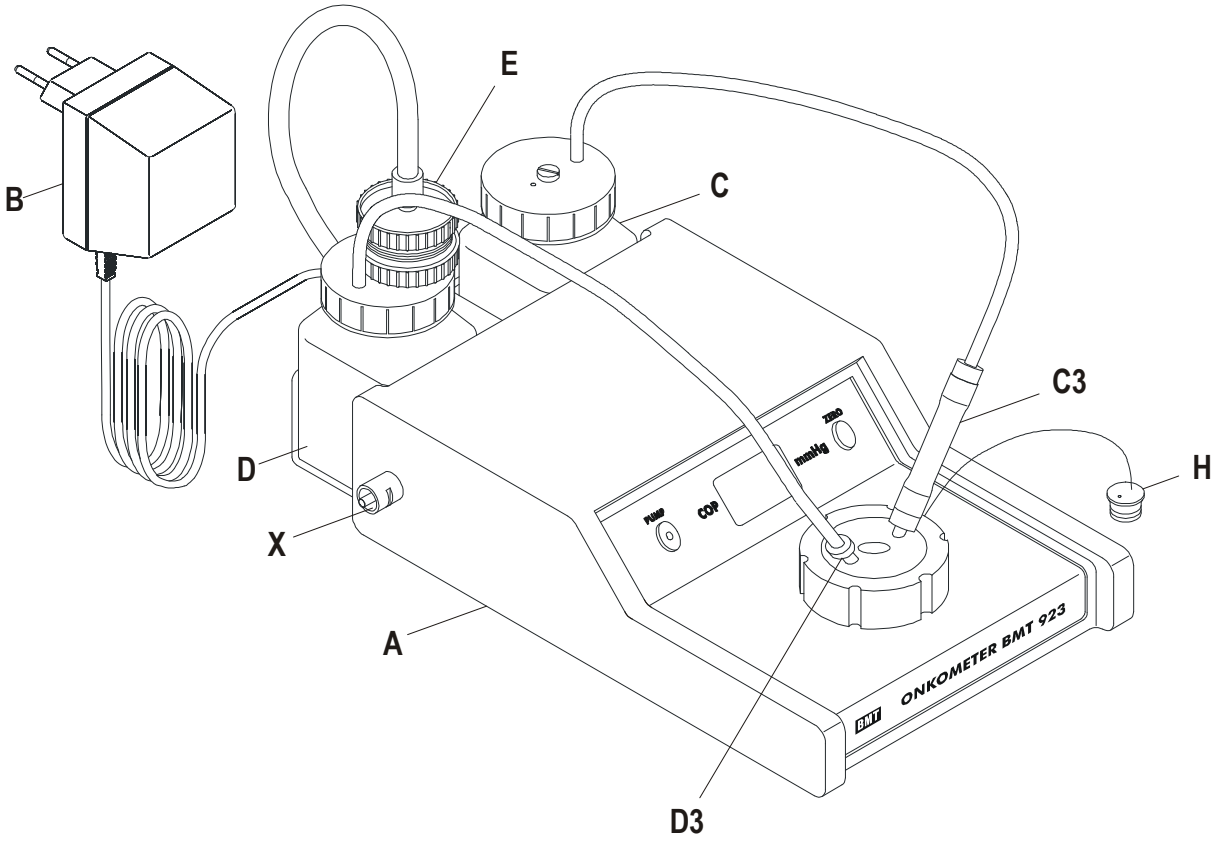
10 Luer bore and capillary channel for filling (**III** the sample chamber with saline using the hand-operated saline pump (not shown in sketch)

11 Luer bore and capillary channel for drawing off (**I**) sample or rinsing solution (saline) from sample chamber using the electric vacuum pump built into the ONKOMETER BMT 923

4. Instrument Set-Up

The ONKOMETER BMT 923 (**A**) should be positioned at a place with sufficient light from above. It is important that the user can see the bottom of the sample chamber in good light.

The wall mount power supply (**B**) has to be plugged into a mains power outlet which is readily accessible (in case the power supply has to be suddenly disconnected from the mains in an emergency). The small black plug at the end of the cable coming from the power supply has to be plugged into the receptacle on the rear panel of the ONKOMETER BMT 923 (between the two plastic bottles).



The caps of the plastic bottles are different: The right cap (see sketch) is that of the rinse bottle (**C**) containig fresh saline. The other cap is that of the waste bottle (**D**) into which the waste from the sample chamber is sucked with the help of the internal electric vacuum pump when the push button PUMP is pressed. This cap has a Luer bore in which the air filter (**E**) is plugged in.

The hand-operated micro pump (**C3**) is connected with the cap of the rinse bottle. This micro pump has to be plugged into the right Luer bore on top of the measuring chamber. The Luer cone (**D3**) of the tubing which leads to the waste bottle has to be plugged into the left Luer bore. For left-handed users it is recommended to interchange the bottles and plug the hand-operated micro pump into the left Luer bore of the measuring chamber.

The thick tubing from the rear panel (leading to the internal vacuum pump) cannot be plugged directly into the Luer bore in the cap of the waste bottle. As a safety measure, the air filter is inevitably necessary to connect this tubing with the waste bottle.

The Luer-Lock connector (**X**) is the outlet of the internal electric vacuum pump. At this outlet a second air filter could be installed if desired.

5. Warning

The ONKOMETER BMT 923 may be used only for those purposes for which it has been designed and for which it is offered by the manufacturer.

6. Handling of the ONKOMETER BMT 923

Measuring

Prerequisites:
The instrument is connected to the mains via the wall mount power supply. The plug of the measuring chamber has been pulled out. The measuring chamber is filled with saline to about 100 µl. Tubings are connected.

- You need not wait for warm-up
- Display will be 00.0
- Press PUMP to remove saline from the sample chamber
- Fill in first amount of sample: approx. 100 µl of heparinised plasma or serum (or heparinised whole blood which, however, needs much more time for measurement)
- After about 15 seconds press PUMP again to remove the first amount of sample (do not flush!)
- Fill in the second amount of the same sample (approx. 100 µl)
- After about 30 seconds the display will have reached steady state value and automatically will be switched to hold, indicated by a beeping tone and a yellow flashing light. To delete the stored value press PUMP only very shortly and the display will show the momentary value again
- Flush chamber with the small hand-operated micro pump, and the electric vacuum pump built into the ONKOMETER BMT 923 (press PUMP)

Never leave the instrument after use without flushing the sample chamber, and filling it to one third with saline, and closing the sample chamber with the plug to prevent the membrane from drying out!

Changing the membrane

- Soak a fresh membrane in saline until white spots have disappeared (approx. 15 minutes)
- Press PUMP to empty sample chamber, remove tubings

Attention: Now safety gloves are recommended!

- Screw off the screw-ring (counter-clockwise) and remove it
- Remove the upper part of the measuring chamber (including sample chamber)
- Take the sieve plate, together with the semipermeable membrane and the red sealing ring, out of the lower part of the measuring chamber using the white magnetic pin (accessories kit, **G2**)

Attention: Used membranes to be treated as infectious material!

Attention: The parts: sieve plate, sealing ring, upper part of chamber, screw ring, may be sterilized using 70% alcohol, or ethylene oxide, or plasma

- Remove the saline from the funnel-shaped lower part of the measuring chamber using the red nozzle (accessories kit, **G3**) and the internal vaccum pump by pressing PUMP
- Now introduce the red nozzle, mounted on top of the hand operated saline pump (**C3**), completely into the bore hole at the bottom of the funnel and fill the lower part of the measuring chamber flat with saline until it flows over the edge of the funnel. Make sure that no air bubbles are left on the wall of the funnel, (any air bubble in the lower part of the chamber will dramatically retard measurement and will lead to incorrect measurement)
- Use the tweezers (accessories kit, **G1**) to place the sieve plate into position with the curvature facing upwards, tap gently on the sieve plate with the tweezers so that air bubbles disappear
- Lay the wet membrane onto the sieve plate so that the black spot is facing up
- Lay the red sealing ring on the membrane and press it down slightly
- Fit the upper part of the measuring chamber on the lower part carefully placing the two pins into the two holes
- Position the screw-ring and screw on slowly
- Reattach the tubings
- Take sample measurements with albumin solution: human albumin (5%) for infusion purposes will show a COP of approx. 19.5 mmHg (18 to 21, see 8.). The membrane is O.K. if the display will reach a stationary value. If the displayed value will drop continuously, the membrane is defective, or it is not positioned correctly. In this case repeat the procedure with a new membrane.

7. Maintenance

- Empty and clean waste bottle (**D**) daily, or on a regular basis

Attention: The waste fluid contains blood components. Be careful !

- Replace air filter insert weekly, at least monthly.
  Open filter holder (**E**) and replace filter insert (**E2**)
- Replace the semipermeable membrane monthly
- Rub the Luer cones of the hand operated saline pump (micro pump) and of the suction tube gently with silicone paste (accessories kit, **G6**) once a month to prevent salt crystals forming at the seam
- Rub the red sealing ring of the chamber plug (**H**) with silicone paste once a month
- Clean the thread of the screw-ring and of the lower part of the chamber about twice a year and rub the thread with a thin layer of silicone paste, use the small brush (accessories kit, **G7**)

8. "Standard" Protein Solutions, Calibration

A membrane osmometer, especially a colloid osmometer, has to measure and display the physical quantity pressure, nothing else. It cannot be "calibrated" with a substance.

The ONKOMETER BMT 923 of course is calibrated during production with a precise reference pressure meter. The electronic semiconductor pressure transducers in the ONKOMETER BMT 923 are so stable that we never have seen a calibration deviation of more than 0.2 mmHg.

The pressure transducer of course can be destroyed, or it can be damaged by proteins which had been injected directly into the reference chamber. But such a situtation cannot be overlooked because the instrument can no more be zeroed. It has to be sent-in for repair.

9. Typical Problems: Reasons and Remedies

- **Measurement is too slow**

  Not any air bubble may be enclosed in the reference chamber! Even a tiny bubble which can hardly be seen with the naked eye, would make COP measurement dramatically slow. During membrane replacement it can happen that a small air bubble sticking inside the funnel is overlooked, or a bubble was so deep inside the funnel that it was invisible.
  Remedy: The reference chamber has to be filled again, eventually after it has been wetted inside with a few drops of alcohol.

  But air can enter the reference chamber "spontaneously". This can happen when Somebody had left the sample chamber open and had let it dry out. The instrument then had startet to beep and thus signalled the situation. Mr. Somebody now has filled saline into the sample chamber, and the warning beep disappeared. But the instrument still is not in order! Water has evaporated through the membrane from the reference chamber to the ambient and a slight vacuum now appeared in the reference chamber (this was the reason for the warning beep). This vacuum usually sucks some air into the reference chamber which leads to a very slow COP measurement.
  Remedy: The reference chamber has to be filled again.

- **Zeroing is impossible, display is unstable**

  In every clinic a specialist exists who comes to the ONKOMETER with a syringe in his hand, and now tries to inject the sample into the measurement chamber like he would inject it into a patient: He punctures the membrane with the canula. The instrument now is no more operative. Since such specialists usually leave the place without a word, the next user maybe will suspect a defective membrane and will replace it by a new one. But he does not know that the reference chamber and the pressure transducer have been soiled with protein. After replacement of the membrane the instrument will still not function sufficiently.
  Remedy: The ONKOMETER has to be sent in (see chapter 10.) for protein removal, cleaning, and recalibration.

- **Readout initially rising, but then continuously falling**
  When the semipermeable membrane has a leak, even a very small one, no stable colloid osmotic pressure difference can build up between the sample chamber and the reference chamber. More and more protein passes the leak until the protein concentration in the reference chamber is the same as in the sample chamber.
  Remedy: The measurement chamber has to be opened, the reference chamber must be flushed thoroughly, and a new membrane has to be installed.

10. Technical Assistance, Repairs

If you have any queries about the ONKOMETER BMT 923, or if your instrument has to be serviced or repaired, please contact the manufacturer

BMT MESSTECHNIK GMBH
Hamburger Strasse 19
D-14532 Stahnsdorf
Germany

Tel. +49-3329-69677-0
Fax +49-3329-69677-29
service@bmt-berlin.de
www.bmt-berlin.de

11. Power, Consumables

The ONKOMETER BMT 923 needs mains voltage 230 or 115 VAC (to be specified with the order). Power consumption is 2.5 W (standby) and 12.5 W (when the internal vacuum pump is running for about 5 seconds). Consumables are

- physiologic saline
- semipermeable membranes
- air filter inserts

Semipermeable membranes and air filter inserts can be ordered from the manufacturer BMT MESSTECHNIK GMBH (see chapter 10.).

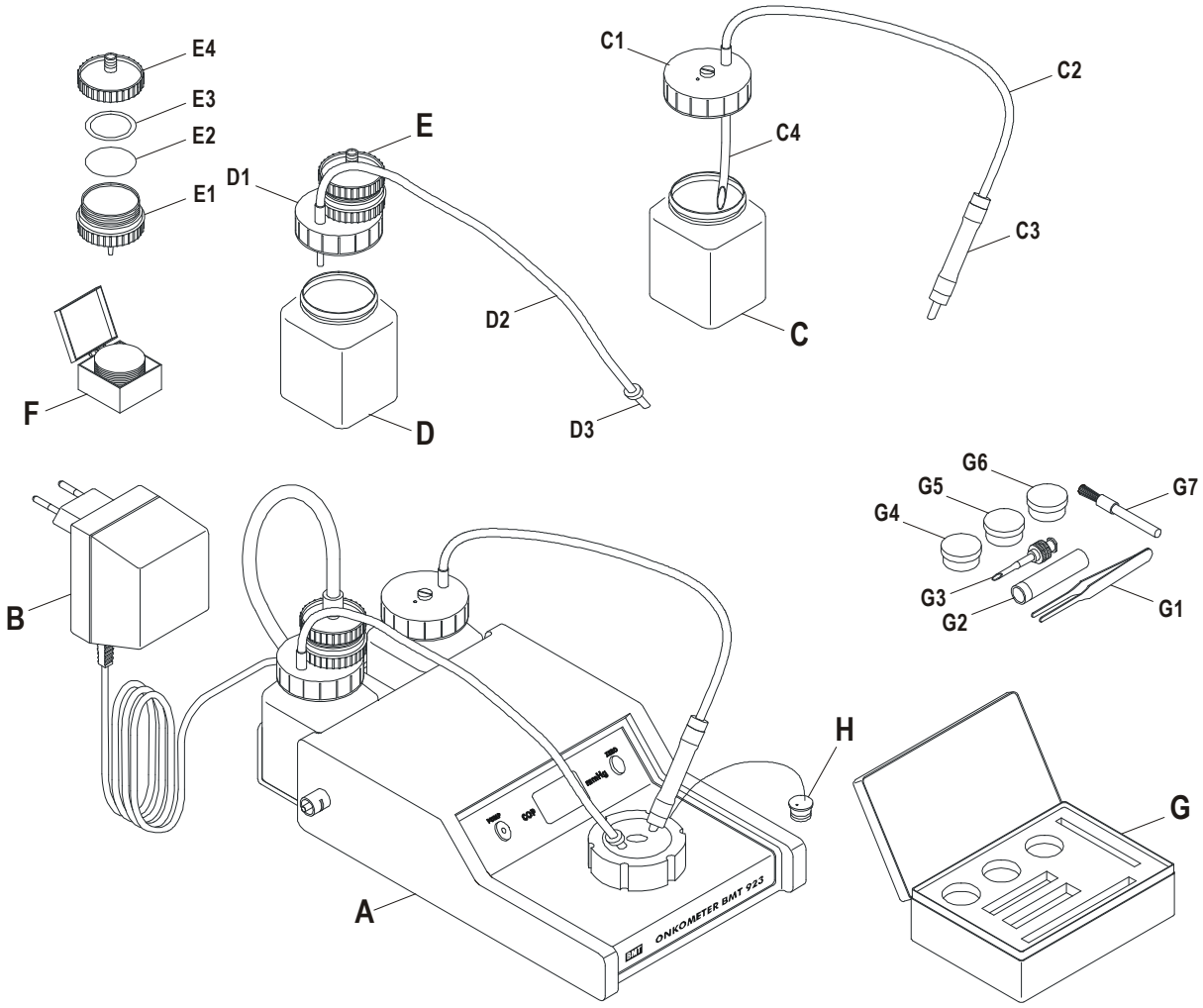
12. Disposal of an old instrument

The ONKOMETER BMT 923 does not contain hazardous substances. Disposal is not critical. But we recommend that old instruments be sent back to us, BMT MESSTECHNIK GMBH (see chapter 10.) instead of being locally discarded.

13. Technical Data

measuring range	99.9 mmHg
semipermeable membrane	cellulose triacetate 20,000 daltons (others on request)
sample volume	2 x 100 µl
solvent	physiologic saline (0.9 % NaCl)
measuring time	1 to 2 minutes
error of pressure measurement	0.2 mmHg max
zeroing of pressure display	semi-automatic
flushing of sample chamber	hand-operated saline pump & internal electric vacuum pump
storage of measured value	automatic, when plateau has been reached
power consumption	2.5 W (12.5 W during vacuum pumping)
power supply	12 VAC via wall mounted power supply (230 or 115 VAC)
dimensions	14 x 9 x 25 cm (W x H x D)
weight	1 kg (main instrument), 0.6 kg (power supply)
CE	DIMDI registration number: DE/CA73/44319-01

14. Scope of delivery of the ONKOMETER BMT 923



A main instrument

B wall mount power supply

C rinse bottle
- C1 cap (rinse bottle)
- C2 tubing
- C3 micro pump (saline pump)
- C4 internal suction tubing

D waste bottle
- D1 cap (waste bottle)
- D2 tubing
- D3 Luer cone

E filter holder (air filter)
- E1 lower shell
- E2 filter insert
- E3 silicone ring
- E4 upper shell

F box with filter inserts (50 pcs.)

G accessories box
- G1 tweezers
- G2 magnetic pin
- G3 nozzle
- G4 semipermeable membranes (10 pcs.)
- G5 sieve plate
- G6 silicone paste
- G7 brush

H chamber plug

15. Literature about the COP

At the end of this manual we have enclosed a CD with several publications about the COP, and a wealth of literature recommendations. If this CD has already gained the interest of another reader, please contact us. We will be glad to send you another copy of this CD. You will find our address in chapter 10.

The contents of the CD is as follows:

Colloid Osmotic Pressure - Some Publications

1. History: Discovery of COP by Ernest H. Starling in 1895
2. Pulmonary Capillary Pressure and Permeability
3. Colloid Osmotic Pressure as a Prognostic Indicator of Pulmonary Edema and Mortality in Critically Ill
4. Postoperative Albumin Infusion Therapy Based on Colloid Osmotic Pressure
5. Perfusion Related Factors of Endotoxin Release during Cardiopulmonary Bypass
6. Reduction in Prime Volume Attenuates the Hyperdynamic Response after Cardiopulmonary Bypass
7. Mechanisms for Reduced Colloid Osmotic Pressure in Preeclampsia
8. Postnatal Changes in Colloid Osmotic Pressure in Premature Infants
9. Calculated Capillary Hydrostatic Pressure in Normal Pregnancy and Preeclampsia
10. Extreme Hyponkose bei postpartaler Eklampsie
11. In-vitro Colloid Osmotic Pressure of Commonly Used Plasma Expanders and Substitutes
12. Fluid Distribution and Tissue Thickness Changes in 29 Men during 1 Week at Moderate Altitude (2315 m)
13. COP Literature (from Adolf Grünert "Onkometrie" ISBN 3-17-009068-2)
14. Literature Survey 1990 - 2002 (306 records)