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## 2,783,180

TISSUE-HOLDER RECEPTACLES AND METHOD OF PREPARING TISSUE FOR MICROSCOPIC 5 EXAMINATION

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This invention relates to the preparation of human or animal tissue for microscopic examination and more particularly to containers or holders which are employed for holding the tissue specimens during their immersion in the various liquids, i. e., fixatives, dehydrants, infiltrating agents, clearing agents, etc., used in the preparation of the tissue.

Tissue processing apparatus of the type which may be used to advantage for immersing tissue in the various liquids is shown, for example, in Patents Nos. 2,341,197 and 2,341,198, granted to Edwin C. Weiskopf, United States Letters Patent No. 2,583,379, granted to Nelson G. Kling, and in United States Patent No. 2,741,221, granted to Edwin C. Weiskopf and Andres Ferrari, Jr. The aforesaid patents and patent application are owned by the assignee of the present application. In the operation of such apparatus the tissue holders are moved automatically into and out of each of a plurality of liquidcontaining receptacles, in succession, with intervening intervals during which said holders are positioned within the receptacles respectively for subjecting the tissue or 35 other material to the action of the various liquids provided in said receptacles, i. e. fixatives, dehydrants, clearing agents, infiltrating agents, etc.

One object of the invention is to prevent the curling or other distortion of tissue, for example intestines or other tubes or any other tissue specimens of thin wall section which is likely to curl up or become distorted by the fixative or other tissue processing liquids. In this connection it will be understood that if the tissue is allowed to curl or become distorted, it is difficult or impossible to cut a true representative section from the paraffin block in which the tissue is embedded. The object just stated is to eliminate this serious difficulty and disadvantage

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Another object is the provision of a tissue holder re- 50 ceptacle which enables the tissue specimen to be disposed in optimum condition for treatment by the various processing liquids.

A further object is the provision of a tissue-holder receptacle which facilitates the handling of the tissue by the pathologist or the technician in the laboratory.

A yet further object is generally to provide a tissue-holder receptacle which is inexpensive and at the same time superior in many respects to known tissue-holder 60 receptacles.

The above objects of the invention and other objects ancillary thereto will be fully understood from the following description considered in connection with the accompanying drawings, which are to be considered as illustrative of the invention but not in limitation thereof.

In the drawings:

Fig. 1 is a vertical sectional view, partly in elevation, illustrating part of an automatic immersion apparatus for practising the present invention;

Fig. 2 is a horizontal sectional view, on a larger scale,

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taken on line 2—2 of Fig. 1, the top part of one of the material holders being cut away for illustrative purposes;

Fig. 3 is a vertical sectional view taken on the line 3—3 of Fig. 2;

Fig. 4 is a perspective view of one of the material holders, its cover being removed;

Fig. 5 is a perspective view of the cover for the material holder; and,

Fig. 6 is a side view of two tissue holders, illustrating **10** a modification.

Referring first to Fig. 1, a plurality of material holders 10 are shown immersed in a beaker or other liquid receptacle 12, which is carried by the novel carrier 14 which is more specifically described and claimed in the co-pending application of Edwin C. Weiskopf and Andrés Ferrari, Jr., Serial No. 423,187, filed concurrently herewith, and owned by the assignee of this application. Carrier 14 and receptacles 12 are well adapted for use with automatic immersion apparatus 16, of the type shown in the aforesaid co-pending application of Nelson G. Kling and by the above mentioned patents.

Pursuant to the present invention provision is made in the tissue-holder receptacle for automatically holding the tissue specimen in flat condition so that it will not curl up or become distorted, and this result is accomplished by making the cover, in whole or in part, of the receptacle of a material to which the tissue specimen will self-adhere so that the tissue will stay flat while it is

processed in the various liquid agents.

Referring now to Figs. 2 to 5 in detail, which illustrates the presently preferred mode of practicing the invention, the body portion of the tissue holder receptacle is preferably non-metallic and can be formed, for example and not by way of limitation, of a plastic or of papier-mache, pressed paper, etc., and is generally cupshaped having a bottom 20, provided with a plurality of apertures 22 to provide access of the liquid to the tissue when the receptacles are immersed in the liquids in the beakers 12, and a peripheral side wall 24. Said side wall 24 includes a lower or main portion 26 and an integral upper portion 28 which is outwardly offset to provide a shoulder 30 as best illustrated in Fig. 3. The upper portion 28 is provided with an internal peripheral groove 32 adjacent shoulder 30 for inserting the peripheral marginal edge of a cover 34.

In accordance with this invention, the tissue is mounted on the inner side of the cover 34, as indicated at T in Fig. 3, which shows a piece of the tissue mounted on the cover. In order to hold the tissue specimen in flat condition and prevent its curling up, or becoming distorted when treated by the fixative or other tissue processing liquids, said cover has an inner surface layer which is of such nature that the tissue will adhere to it, without the use of an extraneous adhesive, when placed in contact therewith. For this purpose the cover has an inner layer 46 formed of porous or absorptive material, such as for example the blotting surface layer of an ink blotter. The outer layer 48 of cover 34 may be relatively stiff and is preferably non-porous, such as, for example sized or calendered paper, so that the cover 34 will not readily disintegrate when wet. Portion 48 may be used as a label or to serve for identification purposes. The outer layer 48 of the disk or cover 34 may consist of paper which is similar to the smooth non-absorptive paper on the upper surface of a conventional ink blotter. Layers 46 and 48 are laminated and joined to each other in surfaceto-surface relation by a glue which is preferably insoluble in or resistant to water or in the agents in which the tissue is processed, such as for example a phenolic glue. The piece of tissue 49 is laid flat on portion 46 and automatically adheres to the surface thereof, the adhesion of

the tissue 49 to portion 46 being aided by the albumin normally present in the tissue. Perforations 50 may be provided in cover 34 in order to augment access of the tissue processing liquids to the tissue. However, these may be omitted from the cover. Also if desired wall 24 may be perforated.

In use, the tissue specimen in its moist or in a moistened condition is placed on layer 46 and will adhere thereto. The adhesion is enhanced by the action of the fixative on the albumin inherently present in the tissue, 10 as a result of which the albumin is coagulated by the formaldehyde fixative and there is a releasable bond between the tissue and the fibres of the porous material of layer 46. The fixative may be applied to the tissue specimen, for this purpose, as soon as the tissue is applied 15 to the cover, or after the cover is placed on the body portion of the receptacle 10. Thereafter a plurality of the receptacles with similar cover-carrying tissue are mounted on the carrier 14, as described in the application filed concurrently herewith, or may be placed in a perforated basket, as described hereafter, and in the course of the operation of the apparatus the tissue will be acted upon by the various liquids in the several beakers. The first liquid is the fixative and this will ordinarily be sufficient to improve the securement of the tissue to the cover 25 without a preliminary treatment of the tissue with the fixative when the tissue is first placed on the cover.

As illustrated in Fig. 6, the tissue-holder receptacles may have their lower peripheral edges corrugated as indicated at 52, for example, to prevent any possibility 30 of the liquids in which the holders are immersed from not passing freely into and out of the holders through the bottom thereof when the holders are mounted one on top of the other as illustrated in Figs. 1 to 3. Ordinarily however, the failure of an adequate quantity of 35 liquid to circulate freely into and out of the holders through the bottom openings is remote or negligible, especially so when the holders are used in processing machines of the type shown in the above mentioned Patent No. 2,741,221 according to which the tissue 40 holders are vertically reciprocated. The tissueholder receptacles shown in Fig. 6 and designated 10A are the same in all respects as holders 10 described above.

It will be understood that when the tissue 49 is applied to the surface 46 of cover 34, and then immersed in each 45 of the liquids including the paraffin baths, tissue specimens, such as pieces of intestines, tubes or any thin wall sections, or anything which is likely to curl up or become distorted after treatment by the fixative or the other tissue processing liquids, will hereafter when processed with the novel material holder 10 or 10A and cover 34 in accordance with the above technique as set forth in accordance with the present invention produce a substantially flat non-curled specimen. The tissue specimen produced in accordance with the present invention will be 55 imbedded in the paraffin block in a substantially flat condition whereby truly representative sections of the tissue specimen can then be cut from said paraffin block, after which the tissue specimens can be deparaffinized, stained and mounted on slides.

As clearly illustrated in Fig. 4, the upper peripheral edge of the upper portion 28 of wall 24 has an ear or extension member 36 having a portion 38 provided with an aperture as at 40. Member 36 is provided with a score line at 42, whereby the portion 38 may be severed from portion 44 of flange member 36, the purpose of which will be hereinafter further explained.

It will be understood that the tissue processing machines have a plurality of receptacles arranged in a circular row on one or more horizontal supports, indicated 70 herein at 62 and 64, and that the present drawings show only a part of a machine of the type shown by the above mentioned Kling patent and the Weiskopf and Ferrari Patent No. 2,741,221, further illustration or description

that in order to impart the various movements for processing the tissue specimens, such as the raising and lowering of the material holders 10 from the receptacles 12 containing the tissue processing liquids, and for imparting the vertical reciprocating movement to material holders 10, a conveyor 68 is provided. Said conveyor 68 includes the member or spider which is partially illustrated at 70, rods 71 and 72 suitably secured to spider 70 in any suitable manner. At the outer end thereof, each of the rods 71 and 72 is provided with a bracket or arm 74, 74 one end of which is provided with a sleeve 75 for securement to the free end of said rods. The carrier 14 is supported by a spindle 76 which has suitable provision for mounting on the other end of arm 74. Spindle 76 is mounted by means of member 78 which has an enlarged head. Mounted on the other end of spindle 76 is a channel shaped member 80 for carrying U-shaped member 82 of carrier 14, the leg portions of which are provided with pin projections 84, 84. The carrier 14 which is disclosed in the co-pending application of Edwin C. Weiskopf and Andres Ferrari, Jr., Serial No. 423,187, filed concurrently herewith, which is shown immersed in upper receptacle 12 also includes the supporting spindle 86 which is connected to cross-bar 88, said cross-bar being apertured at either end for receiving the pin projections 84. Also mounted on spindle 76 is a cover 90 for receptacles 12. As set out in the previously noted co-pending application which is filed concurrently herewith, said supporting spindle 86 comprises at least two portions in one modification, which can be readily disconnected from each other whereby to place material holders 10 or 10A thereon, after which said portions can again be connected whereby said material holders 10 or 10A when so placed on said supporting spindle 86 can be readily reciprocated within the liquids in said receptacles 12 and can also be readily moved from one receptacle to another.

As noted in Figs. 1 and 2, a plurality of the material holders 10 or 10A may be mounted on spindle 86, said material holders being mounted on said spindle by means of ear 36, and as noted previously, the lower portion of spindle 86 can be detached from the upper portion whereby the lower portion of spindle 86 can then be inserted through aperture 40, and then again attached to the upper portion of spindle 86, whereby the plurality of material holders 10 or 10A can be readily coupled to the carrier 14 for imparting to material holders 10 or 10A, the reciprocating movement required for the processing of the tissue specimen.

Pursuant to another feature of the present invention, material holders 10 or 10A may also be used with the basket type holder 92 by simply placing material holders 10 or 10A therein. As illustrated in Fig. 1, said basket type holder 92 is disposed within the lower receptacle 12, which is supported on the lower base 64. As illustrated in the aforesaid patents and as disclosed herein, said basket type holder 92 shown on the lower shelf 64, for illustrative purposes, is connected to and supported by the U-shaped member 82 by pins 84. As noted previously, flange 36 is provided with a score line at 42 whereby to sever portion 38 from 44. When material holders 10 or 10A are used with the basket type holder 92, there is no need for the portion 38, and therefore, portion 38 may be removed if desired.

In the aforesaid copending application filed concurrently herewith, Serial No. 423,187, a material holder carrier mechanism is disclosed and claimed, wherein tracks are provided on the carrier 14 by modifying the spindle portion 86. Flange 36 of material holders 10 or 10A may also be modified in accordance with the aforesaid copending application so as to have provided a complementary portion for engagement with the tracks.

As noted in Figs. 1 and 3, the material holders 10 or 10A are shown in stacked relation; however, as a result being unnecessary herein. However, it may be noted 75 of the reciprocating movement imparted to carrier 14 or

the basket type carrier 92 by the immersion apparatus 16, said material holders 10 will ordinarily have relative movement imparted thereto, as previously explained. Portion 38 has an aperture 40 which is of a slightly larger diameter than the diameter of supporting spindle 86 whereby to allow the material holders 10 or 10A to move relative to each other. The tissue processing liquids can flow through the apertured base 20 through apertures 22 so as to infiltrate tissue specimen.

While I have shown and described the preferred em- 10 bodiment of my invention, it will be understood that various changes may be made therein without departing from the underlying idea or principles of the invention within

the scope of the appended claims.

Having thus described my invention, what I claim and 15

desire to secure by Letters Patent, is:

1. A tissue-holder receptacle for use in treating the tissue with a processing liquid in the preparation of the tissue for microscopic examination, comprising a container having an internal surface part thereof formed of 20 porous fibrous material for mounting the tissue thereon in position for access thereto of processing liquid within the container, said porous fibrous material having a plurality of openings therethrough for access of said liquid to the tissue.

2. A tissue-holder receptacle for use in treating the tissue with a processing liquid in the preparation of the tissue for microscopic examination, comprising a container having a wall provided with a plurality of openings therethrough for the pasasge of said liquid into and out of the container, said container having an internal surface part thereof formed of porous fibrous material for mounting the tissue thereon in position for access thereto of processing liquid entering said container through said openings, said container having a part confronting said internal surface part in spaced relation thereto and defining therewith a space for the tissue mounted on said porous fibrous part.

3. A tissue-holder receptacle for use in treating the tissue with a processing liquid in the preparation of the tissue for microscopic examination, comprising a container having a internal surface part thereof formed of porous fibrous material for mounting the tissue thereon in position for access thereto of processing liquid within the container, said container having a removable cover

provided with said internal fibrous surface.

4. A tissue-holder receptacle for use in treating the tissue with a processing liquid in the prepartion of the tissue for microscopic examination, comprising a container having an internal surface part thereof formed of 50 porous fibrous material for mounting the tissue thereon in position for access thereto of processing liquid within the container, said container having a removable cover provided with said internal fibrous surface, said cover having a moisture-resistant outer surface.

5. A tissue-holder receptacle for use in treating the tissue with a processing liquid in the preparation of the tissue for microscopic examination, comprising a perforated container having an internal surface part thereof formed of porous fibrous material for mounting the tissue thereon in position for access thereto of processing liquid, entering said container through the perforations provided therein, said container having a removable cover pro-

vided with said internal fibrous surface.

6. A tissue-holder receptacle for use in treating the tissue with a processing liquid in the preparation of the tissue for microscopic examination, comprising a perforated container having an internal surface part thereof formed of porous fibrous material for mounting the tissue 70 thereon in position for access thereto of processing liquid, entering said container through the perforations provided therein, said container having a removable cover provided with said internal fibrous surface, said cover having a moisture-resistant outer surface.

7. A tissue-holder receptacle for use in treating the tissue with a processing liquid in the preparation of the tissue for microscopic examination, comprising a container having a internal surface part thereof formed of porous fibrous material for mounting the tissue thereon in position for access thereto of processing liquid within the container, said container having a removable cover provided with said internal fibrous surface, said container having a wall thereof provided with perforations for the

passage of liquid into and out of the container.

8. A tissue-holder receptacle for use in treating the tissue with a processing liquid in the preparation of the tissue for microscopic examination, comprising a container having an internal surface part thereof formed of porous fibrous material for mounting the tissue thereon in position for access thereto of processing liquid within the container, said container having a removable cover provided with said internal fibrous surface, said container having a bottom wall provided with perforations for the passage of liquid into and out of the container, said cover having an inner layer of porous paper providing said internal porous surface part of the container, an outer layer joined to said porous layer, and a layer of water insoluble adhesive interposed between said inner and outer layers securing them to each other and preventing the passage of moisture from said inner layer to said outer layer.

9. A tissue-holder receptacle for use in treating the tissue with a processing liquid in the preparation of the tissue for microscopic examination, comprising a container having an internal surface part thereof formed of porous fibrous material for mounting the tissue thereon in position for access thereto of processing liquid within the container, said container having a removable cover provided with said internal fibrous surface, said cover having an inner layer of porous paper providing said internal porous surface part of the container, an outer layer joined to said porous layer, and a layer of water insoluble adhesive interposed between said inner and outer layers securing them to each other and preventing the passage of moisture from said inner layer to said outer layer.

10. A tissue-holder receptacle for use in treating the tissue with a processing liquid in the preparation of the tissue for microscopic examination, comprising a container having a body portion provided with perforations, the upper part of said body portion having an internal cover-seat, and a cover for the top of container releasably secured on said internal cover-seat of said body portion, said cover having an internal fibrous surface for carrying the tissue thereon.

11. A tissue-holder receptacle for use in treating the tissue with a processing liquid in the preparation of the tissue for microscopic examination, comprising a container having a body portion provided with perforations. the upper part of said body portion having an internal cover-seat, and a cover for the top of container releasably secured on said internal cover-seat of said body portion, said cover having an internal porous fibrous surface for mounting the tissue thereon in position for access thereto

of processing liquid within the container.

12. A tissue-holder receptacle for use in treating the tissue with a processing liquid in the preparation of the tissue for microscopic examination, comprising a container having a body portion provided with perforations, the upper part of said body portion having an internal cover-seat, and a cover for the top of container releasably secured to said internal cover-seat of said body portion, said cover having an internal porous fibrous surface for mounting the tissue thereon in position for access thereto of processing liquid within the container, and a lateral extension on said body portion externally thereof having a formation for mounting the tissue holder in a tissue processing machine.

13. The method of preparing tissue for microscopic

examination according to which the tissue is immersed in a processing liquid, comprising mounting the tissue specimen in flat condition on a member having a porous fibrous surface to which the tissue adheres and immersing said mounted tissue specimen in the processing liquid.

14. The method of preparing tissue for microscopic examination according to which the tissue is immersed in a processing liquid, comprising mounting the tissue specimen in flat condition on a member having a porous said mounted tissue specimen in a liquid fixative for coagulating the albumin in the tissue and thereby increasing the adhesion of the tissue to said surface.

15. The method of preparing tissue for microscopic a processing liquid, comprising mounting the tissue specimen in flat condition on a member having a porous fibrous surface, and applying a coagulant to the tissue on said member to form a releasable adhesion of the

tissue to said surface.

16. A tissue-carrier for use in treating the tissue with a processing liquid in the preparation of the tissue for microscopic examination, comprising a member having a porous surface to mount the tissue specimen in selfadhering relation thereon and having provision for the passage of liquid therethrough for exposing the tissue to the processing liquid for action of said liquid thereon.

17. A tissue-carrier for use in treating the tissue with a processing liquid in the preparation of the tissue for microscopic examination, comprising a member having 30a porous surface to mount the tissue specimen in selfadhering relation thereon and exposed to the processing liquid for action of said liquid thereon, and a receptacle member adapted to enclose the tissue and provided with said first mentioned member.

18. A tissue-carrier for use in treating the tissue with a processing liquid in the preparation of the tissue for microscopic examination, comprising a member having a porous surface to mount the tissue specimen in self- 40 adhering relation thereon and exposed to the processing liquid for action of said liquid thereon, and a receptacle member adapted to enclose the tissue and provided with openings for the passage of said liquid to the tissue on said first mentioned member, one of said members having a lateral extension provided with means for mounting the tissue carrier on a support.

19. A tissue-carrier for use in treating the tissue with

a processing liquid in the preparation of the tissue for microscopic examination, comprising a member formed of sheet material and having a porous surface to mount the tissue specimen in self-adhering relation thereon, said member having provision for exposing opposite surfaces

of the tissue to the processing liquid.

20. A removable cover for a tissue-holder receptacle for use with a processing liquid in the preparation of the tissue for microscopic examination, said cover comprising fibrous surface to which the tissue adheres and immersing 10 a member formed of sheet material and having an internal surface part formed of fibrous material for mounting the tissue thereon, and said cover being perforated to provide for access of the processing liquid to said tissue.

21. A removable cover for a tissue-holder receptacle examination according to which the tissue is immersed in 15 for use with a processing liquid in the preparation of the tissue for microscopic examination, said cover comprising a member formed of sheet material and having its internal surface formed of fibrous material for mounting the tissue thereon and its external surface formed of relatively moisture resistant material, and said cover being perforated to provide for access of the processing

liquid to said tissue.

22. A tissue-holder receptacle for use in treating the tissue with a processing liquid in the preparation of the 25 tissue for microscopic examination, comprising a body portion and a cover therefor, said receptacle body and cover providing a tissue enclosing and retaining chamber, and having an inner porous surface portion for attaching the tissue thereto within said chamber, said receptacle having provision for the passage of liquid into and out of said chamber for access of the processing liquid to the tissue therein.

23. A tissue-carrier for use in treating the tissue with a processing liquid in the preparation of the tissue for openings for the passage of said liquid to the tissue on 35 microscopic examination, comprising a paper disk having a porous surface to mount the tissue specimen in selfadhering relation thereon, said disk having perforations therethrough to provide access of the processing liquid to the adhered surface of the tissue.

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