

# Devices for Umbilical Cord Blood Collection

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**Abstract:** Umbilical cord blood (UCB) is an increasingly important and rich source of stem cells. These cells can be used for the treatment of many deadly diseases, including cancers, immune and genetic disorders. It also provides a readily available source of stem cells for transplantation purposes. In this paper, we review the literature published that reflects the designs of UCB collection apparatus in order to obtain stem cells.

**Keywords:** Placenta, umbilical cord blood collection, stem cells.

## INTRODUCTION

Since Gluckman *et al.*'s first work of successful haemopoietic stem cell transplantation using UCB as the source of marrow progenitors in 1988 [1], over 6000 UCB transplant procedures have been performed worldwide using UCB from related and unrelated donors into pediatric [2-5] and adult patients [6-8]. UCB provides a readily available source of stem cells for transplantation in many situations where bone marrow is used now. There are many advantages to use UCB instead of other sources of stem cells such as bone marrow and peripheral blood:

- There is no risk involved in UCB collection.
- UCB is much easier to collect and harvest without the risks of general anesthesia which is required to harvest bone marrow.
- UCB is readily available when needed if it is properly collected and stored at birth.
- UCB is more proliferate in nature and often more compatible when used in transplants.
- UCB has lower procurement costs.
- UCB has demonstrated broader potential clinical applications for improving neural repair and bone and tissue growth.

While the awareness of UCB capabilities was low among the public in the past, the UCB related industry is now a fast growing one. Many cord blood banks in many regions are being opened and governments in various countries are coming up with pro-policies to support the expansion of this industry. Currently, the patients have the option to store the UCB in either public and/or private cord blood banks. Published articles [8-10] provide an important insight into the clinical potential of UCB as a source of haemopoietic progenitor cells for transplantation.

The importance of UCB is widely recognized now. Blood centers worldwide now collect and store UCB after the delivery of a baby upon the parents' request. However, one problem associated with UCB is that its collection is a one-

time possibility and the amount of blood that can be collected is limited using conventional current ways of blood collection, which include syringe-assisted and gravity-assisted methods [11]. These methods are mainly manual operations. It is necessary to develop more efficient apparatuses to collect the blood. The aim of this article is to review the patents published which reflect the utility of UCB collection system in order to obtain stem cells and focused on new apparatus in this area. We will also discuss the working mechanisms of these devices which may lead in the near future to an integrated and comprehensive computer-controlled system for the whole process from placenta harvesting to cell separation and storage.

## BACKGROUND ON UMBILICAL CORD BLOOD AND STEM CELLS

It is well-known that the placenta is formed during pregnancy and the umbilical cord is a tube-like line that connects the developing baby to the placenta. It contains one or two major veins, buried within Wharton's jelly, for the exchange of nutrient- and oxygen-rich blood between the embryo and placenta. Usually, the umbilical cord develops after conception and becomes progressively longer until about 28 weeks of pregnancy, reaching an average length of 22 inches. As it gets longer, the cord generally twists around itself and becomes coiled. Following the birth of a baby, the umbilical cord, with the placenta is cut. It is not made up of any nerves or connective tissue so cutting it is not painful. There will also be no significant loss of either the baby or mother's blood while cutting the umbilical cord. Fig. 1 shows a placenta with umbilical cord collected.

Reports in [12-14] have verified that UCB collected from the umbilical cord is a rich and readily available source of stem cells. These results show that UCB contains an increased proportion of the earliest progenitors (i.e., CD34<sup>+</sup> and CD38<sup>+</sup>), and per nucleated cell UCB has approximately 10 times the repopulation potential of bone marrow. CD34<sup>+</sup> is one of the most important markers. It is used to 'see' in the hematopoietic pluripotential stem cell (PSC) which is the cell that is "wanted" in bone marrow or peripheral blood stem cell transplants. CD38 is a receptor that is found in lymphocytes.

Several reports in [15-17] support the viewpoints of the papers [18-20] that naive UCB lymphocytes are potentially

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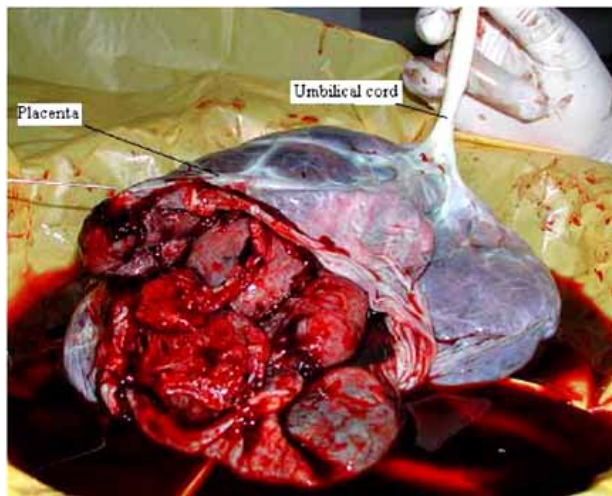


Fig. (1). Placenta with umbilical cord.

less immunologically active than those found in the blood or marrow and may therefore produce fewer problems with graft versus host disease (GVHD) than functionally mature lymphocytes harvested from live donors. Stem Cells comprises of the multi-potential stem cells that can be triggered to create bone, muscle and other tissues when cultured. The multi-potential stem cell can be subdivided into two main broad categories which are the lymphoid progenitor and the myeloid progenitor. Lymphoid Progenitor is the broad name for three types of white blood cells, namely the B-Cell, T-Cell and the NK Cell. Myeloid Progenitor is the broad name for cells that are normally found in the bone marrow that makes red blood cells, platelets, and some white blood cells (granulocytes and monocytes). More details on these can be found in the literature [18-20].

Stem cells harvested from UCB have unique features that lead to increasingly widespread usage in many transplant and blood related treatments. As described in [9], stem cells can be divide to create i) new red blood cells which carry oxygen to the brain; ii) new white blood cells used in the body's immune system; iii) new platelets which help blood clotting. As the development of new technologies, medical researchers believe that stem cell research has the potential to change the face of human disease since they are used to repair specific tissues or to grow organs. Still, there is general agreement that, "significant technical hurdles remain that will only be overcome through years of intensive research" [21]. Stem cells are available from a few sources, i.e., cord blood, adult, embryonic and cancer. In this paper, stem cells are obtained from UCB.

## METHODS AND DEVICES OF UCB COLLECTION

In view of the increasing importance and usage of the UCB, many devices have been invented for extracting and/or collection of UCB to yield useful volumes of UCB from a delivered placenta and/or umbilical cord. In the early stage, the methods for UCB collection can be broadly classified into two main categories, i.e., in utero and ex utero. The former method of UCB collection involves extracting the

blood from the umbilical cord while the placenta is still in the maternal womb. An example of such methods is the syringe-assisted collection method. In the latter method, the UCB is collected from the placenta which is outside the maternal womb. Usually, the collection of UCB is performed with the aid of a housing structure. Gravity-assisted methods are examples of such collection methods. In [22], a survey of the various works on UCB collection up-to 1994 is reported. The authors stated that the amount of blood that can be collected is limited using developed ways of blood collection, which include syringe-assisted and gravity-assisted methods. These methods are mainly manually carried out. Apart from being a tedious and difficult process, it is observed that the blood also inherit a high risk of unnecessary contamination using these methods.

To minimize the hazard of exposure to contaminated blood, a container as described in Fig. 2 may be used when taking fluid samples for the UCB collection. The device invented by Grossman *et al.* includes an upper receiving portion and a lower fluid discharge portion. The umbilical cord is placed into the upper portion of the container, allowing the blood to drain from the cord into the container due to gravity. This blood is then transferred to a second container. This transfer operation is achieved by a needle hood. During the collection, it is not necessary for the operator to touch the needle or the valve mechanism [23].

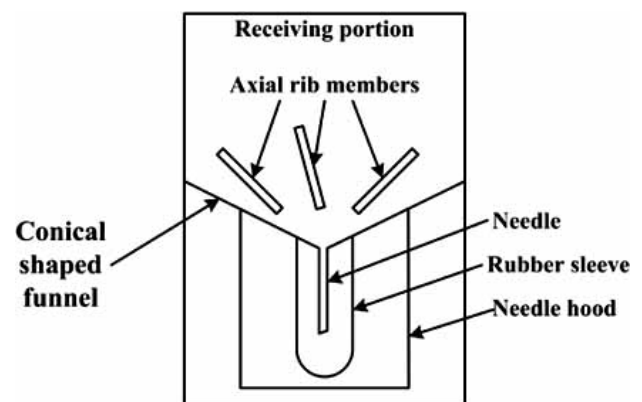


Fig. (2). Fluid sampler device Grossman *et al.* [23].

When collecting the blood using the designed apparatus, it is also quite important to consider the availability of UCB. According to the analysis given by [24], UCB collection typical yields 50-80 ml. Apart from obstetric factors such as infant weight and time of collection, the procedure involved and the equipment used to perform the collection affect the final yield. There is thus need for an UCB collection apparatus which can effectively yield an increased volume of blood from a delivered placenta when compared to some of the prior art known.

One way to increase the volume of the collection is to improve the syringe-assisted device, as shown in Fig. 3 [25]. This invention is an umbilical cord blood extractor which includes a lower tray for receiving the cord and an upper lid for squeezing the cord. The lower tray and upper lid are

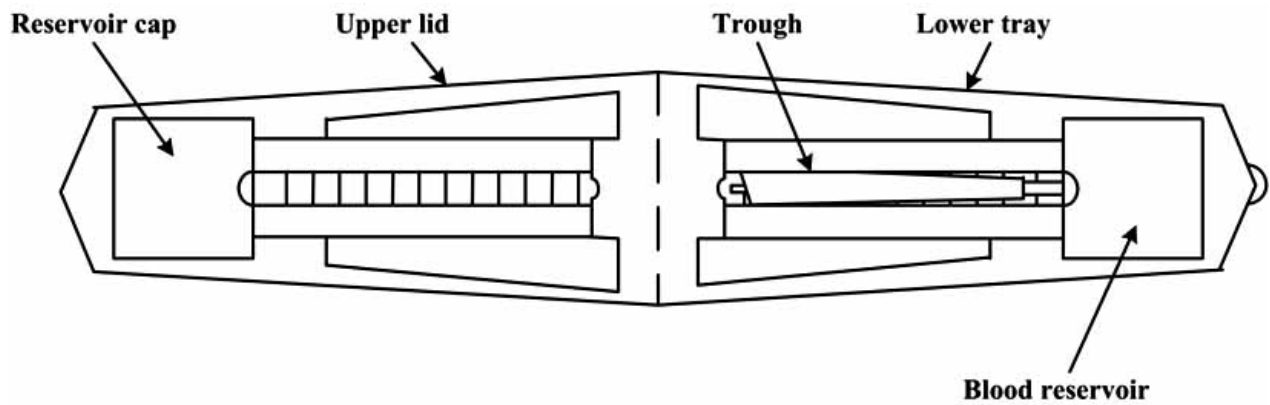


Fig. (3). Umbilical cord blood extractor [25].

connected by a live hinge, enabling the upper lid to rotate along the hinge from an open position upwards and toward the lower tray and to interlock with the lower tray in a closed position. The blood extracted from the cord collects in a distal blood reservoir. The apparatus can be seen as an expansion of syringe-assisted extractor and it can extract blood rapidly. However, it should be noted that the blood is extracted from a cut section of the umbilical cord after it is severed from the placenta. There are three drawbacks: i) only one piece of the umbilical cord is handled ii) the procedure may result in the blood leakage when cutting the umbilical cord iii) particular experience or training is required for its operation.

Comparing with the prior art system [25], Knippscheer [26] provides an apparatus to apply a on/off compression on the umbilical cord. This invention is not mentioned in [22]. As illustrated in Fig. 4, this apparatus can extract blood fluids from a placenta and umbilical cord, especially in the balloon design which generates the pressure softly to the placenta. The apparatus has a funnel-shaped compartment for holding the placenta in place. A compressor is attached to the cover member and inflates a balloon disposed inside the compartment. The centrifugal force is employed in this apparatus assisting in the collection of the fluid from the placenta and the umbilical cord. The mechanism is well known and it is believed that the pressure generated by the compressor will allow the cord blood to flow out of the placenta.

Another apparatus of the inventions related to the method and apparatus for extracting fluids is by Paderni [27]. This device uses the same idea as in Fig. 4. The placenta and the umbilical cord are placed on a supporting plate and pressure is applied to the upper side of the placenta by a flexible membrane. The pressure can be generated by pneumatic, electric or other means. Here, a variety of pressure sources can be used in the disclosed device and using a liquid to apply pressure would be an obvious design choice to a person skilled in the art. A fluid collection means may be provided at the lower end of the apparatus. A collection method integrated with [28] is also patented by the same author (see [27]). The objective of the invention is to ensure maximum sterility of the sample by applying a procedure and using an apparatus which minimizes contact of the blood

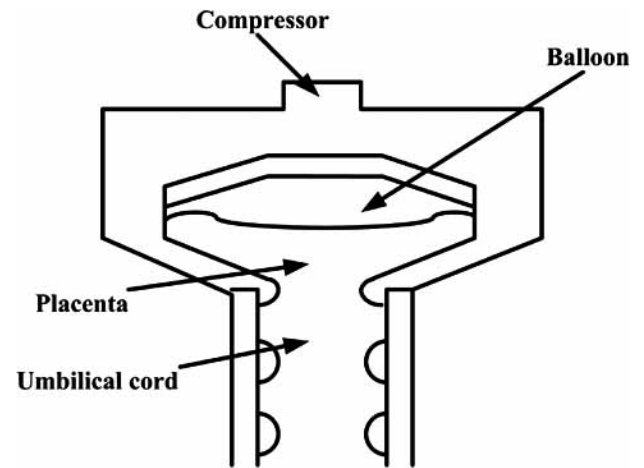
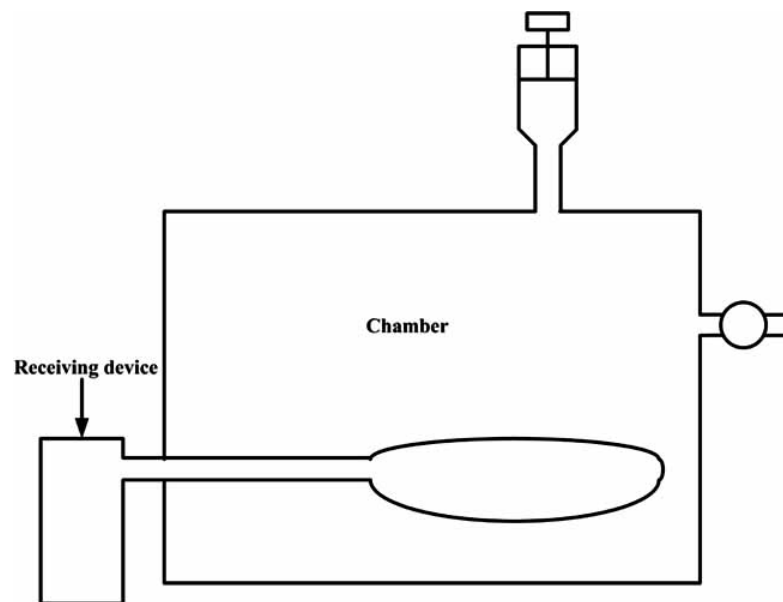


Fig. (4). Method and apparatus for extracting fluid.

with potentially contaminated external factors [28]. The method suggested that the procedure for collecting blood from a placenta will begin through the cut end portion of the umbilical cord to a collection apparatus and then applying pressure to the placenta. Application of negative pressure is another option to improve placental blood collection.

In [26-28], various materials are suggested to be used for transmitting the pressure to the placenta. In [29], a collecting device and method for recovering blood from an umbilical cord is proposed by Zimmermann *et al.*. They do not use any circular pads made from various materials to press the placenta, only air pressure generated by a compressor is used (see Fig. 5). It is observed from the figures in the patent that the umbilical cord is subjected to pressure inside a chamber. The blood flows from the cord into a receiving device. Fluid pressure can be provided by a gas bottle or line. A pressure regulating mechanism is provided to control the pressure within the chamber.

A novel UCB collection system [30], which ensures an automated and efficient collection of UCB from delivered placentas, is developed. This is a device for extracting and collecting blood from a delivered placenta comprising of a compartment to locate and support a delivered placenta and



**Fig. (5).** Device for recovering blood from an umbilical cord [29].

umbilical cord. The compartment includes a flexible membrane which can be displaced under the influence of a fluid pressure differential between the compartment side and the non-compartment side of the membrane to impart onto the placenta a controllable pressure to encourage and facilitate the displacement of the blood carried by the placenta towards the umbilical cord. The compartment includes the required number of outlet openings via which the umbilical cord can extend, in a sealed manner, to allow the flexible membrane pressure induced flow of blood carried by the placenta to displace from the compartment for external to the compartment collection of the fluid.

The automated approach outperforms the current means through a novel patented placenta manipulation system under the computer control to meet the stringent requirements of compactness, robustness, ease in development, use and maintenance, as well as operability under diverse and tough ambient conditions.

The system comprises of mainly four modular components which can be modified or replaced, while the other components remain functional. Collectively, the four components form an electro-mechanical apparatus which is able to manipulate the placenta via a combination of high frequency vibration and controlled pneumatic pressure, to maximize the flow of blood from the placenta to a collection tube. In addition, all the key components which may be directly or indirectly in contact with the placenta can be readily sterilized and are also designed to filter contaminants from the collected blood. The hardware architecture and the pictorial diagram of the UCB collection system are shown in Figs. 6 and 7, respectively.

The placenta tray serves as the support base for the placenta, with the maternal side facing upward, the fetal side facing downward, and the umbilical cord, originating from the fetal side, passing through the ventura of the funnel-shaped element which is formed by a plastic umbilical cord

positioner. A variable thickness silicon pressure pad (i.e., which is inside the placenta tray) with an integral sealing ring can be snapped into position above the maternal side of the placenta in placenta tray. It serves to keep the slippery placenta in place within an air-sealed space. The pneumatic application system is employed to apply the massaging effect on the placenta. The pressure within the chamber is regulated via a pressure sensor. The stainless steel structure is integrated with a vibrator which generates high frequency vibration to the entire structure. Bottlenecks and clots impeding blood flow can be reduced. The amount of vibration is adjustable via the vibration controller.

The various parts and functions of the UCB collection device require a high performance and compact control system to fulfill, coordinate and synchronize. As the collection of UCB is a one-time possibility, there is no room for malfunction in control. UCB clogs after minutes unless the placentas are preserved under low temperature. Contamination is another critical issue here, as the tolerance for contamination is extremely low, as far as the possible applications of UCB are concerned. To this end, the control unit has to be compact, robust and lends itself to diverse conditions encountered during heated sterilization and clinical tests. Above all, due to the short time span permissible to complete the operation, it has to be easy to use, easy to test and easy to maintain. This modular system has been tested clinically and ever ready to be employed in delivery rooms.

## CURRENT & FUTURE DEVELOPMENTS

UCB studies mentioned above have shown that UCB collection systems utilize air or other fluid pump systems to apply pressure on the placentas to extract the UCB. Some use human hands to implement this function for UCB collection [23,25] while others develop machines [26-29] or computer controlled systems [30] for this purpose. The current trend in the industry is such that the UCB collection

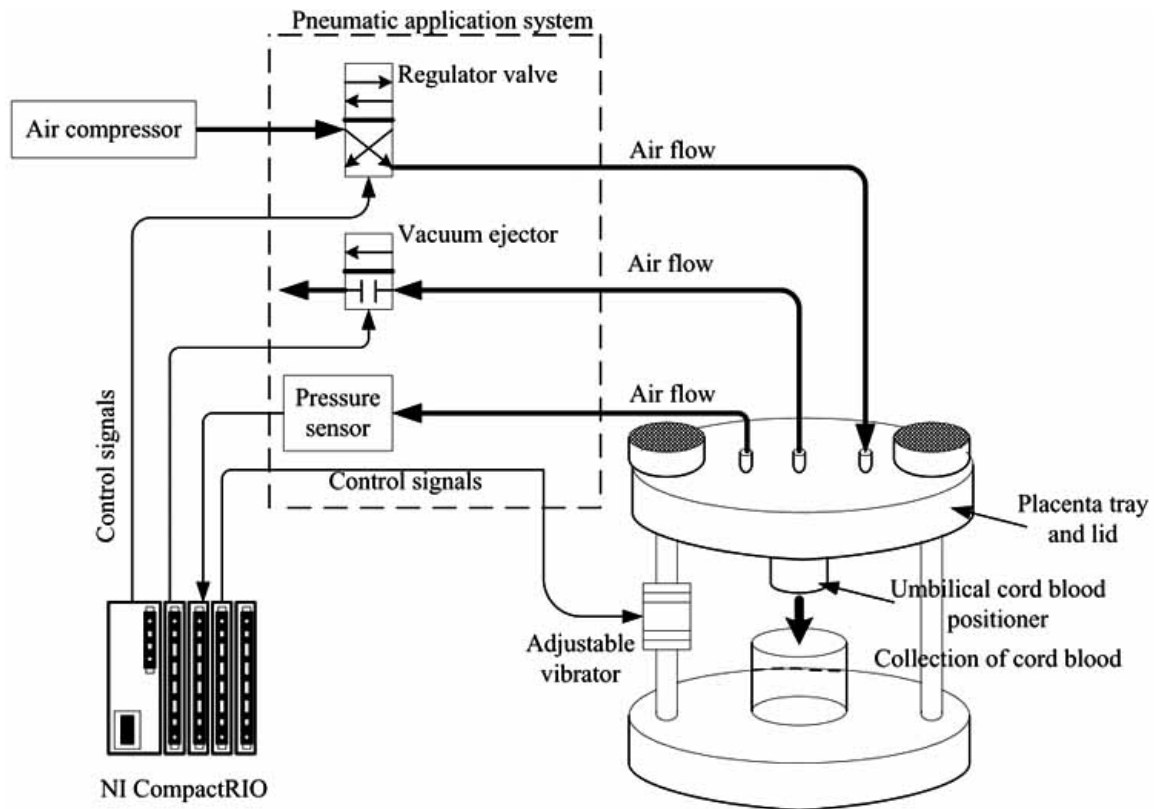


Fig. (6). Schematic hardware setup of the UCB collection system.



Fig. (7). Pictorial diagram of the UCB collection system.

system incorporates advanced computer technology and intelligent sensors in UCB collection methods in order to enable an efficient and automated process. The patented file [30] has proved this comment. In addition, to prevent contamination from the external environment, it is observed

that an enclosed housing that minimizes contamination of the UCB from the external environment would be very advantageous for this purpose. Current work is undertaken to design the mechanical part for this purpose.

On another note, another future development of UCB systems is to incorporate the automated UCB collection system into the whole process, beginning from placenta harvesting to cells isolation and storage. In this aspect, hierarchical control architecture and advanced system diagnostic tools may provide good solutions to realize an integrated and comprehensive solution.

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