ŽIVLJENJE TEČE DALJE
LIFE FLOWS ON

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LIFE FLOWS ON

Poročilo o transfuzijski dejavnosti v Sloveniji med epidemijo covida-19

The report on transfusion activity in Slovenia during the COVID-19 epidemic

2020–2021

KAZALO
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Obdobje epidemije covida-19 si bomo vsekakor zapomnili, saj je novi koronavirus korenito spremenil in posegel v naša življenje in delo, epidemija pa je izpostavila njune dobre in slabe strani. Preverila je vzdržnost, pripravljenost in pomanjkljivosti našega delovanja v kriznih situacijah. Pokazala nam je ogledalo našega življenja in ravnanja ter nas resno opozorila na že pozabljeno potrebo po povezanosti in soodvisnosti z ljudmi in naravo.

Epidemija, ki je povzročila ogromno žrtev in za seboj pustila boleče posledice, je bila hkrati izziv za iskanje boljših rešitev. Navade, vedenja in procese dela, ki se jih prej z dolgoletnimi napori ni dalo spremeniti, smo spremenili skoraj čez noč. Sprejeli in začeli smo uporabljati nove načine komunikacije, ki so morale zamenjati osebni stik. Naučila nas je, da je najbolj kritična »infrastruktura« osebje.

Še bolj kot pred epidemijo pa smo se zavedali pomembnosti in razpoložljivosti krvodajalcev za nemoteno preskrbo s krvjo.

Kljub izrednim razmeram smo zagotovili, da življenje teče dalje ...

The period of the Coronavirus pandemic will definitely be remembered as the virus that radically changed and affected our lives and work. The pandemic exposed our strengths and weaknesses in life and work. It checked our sustainability, our preparedness and our deficiencies in crisis situations. It showed us a mirror of our lives and actions and seriously reminded us of the already forgotten necessity of connection and interdependence between people and nature.

The pandemic, which claimed many victims and left painful consequences, was also a challenge to find better solutions. Habits, behaviours and work processes that previously could not be changed through years of effort were changed almost overnight. Overnight, we adopted and used new means of communication that had to replace personal contact. The pandemic leaves behind many improvements, good practices and experiences. It taught us that the most critical "infrastructure" is essentially the staff.

Now, even more than before the pandemic, we know the importance and availability of blood donors for a stable blood supply.

Despite the emergency, we provided that life flows on...

1.

PREDSTAVITEV TRANSFUZIJSKE MEDICINE V SLOVENIJI

PRESENTATION OF TRANSFUSION MEDICINE IN SLOVENIA

Osnovna naloga transfuzijske medicine je zdravljenje s krvjo, ki se vse od zgodnjih začetkov do danes ni spremenila. Prav tako ostajajo krvodajalci prvi in nenadomestljiv člen pri zdravljenju s krvjo.

The basic task of transfusion medicine is treatment of patients with blood, and this has not changed since it began. Blood donors remain the first and the irreplaceable link in blood treatment.

Četrti junij 1945 zaznamuje začetek transfuzijske medicine v Sloveniji, zato smo ta dan razglasili za dan krvodajalstva.

4 June 1945 marked the beginning of transfusion medicine in Slovenia, which is why this day was declared Blood Donor Day.

Zametki transfuzijske medicine v Sloveniji segajo v obdobje pred drugo svetovno vojno, ko je bilo zabeleženih nekaj primerov neposredne transfuzije krvi (iz vene krvodajalca v veno prejemnika). Četrti junij 1945 pa zaznamuje začetek transfuzijske medicine v Sloveniji, ko so na transfuzijskem oddelku v Ljubljani odvzeli in shranili prvih 18 steklenic krvi. Ta dan smo v Sloveniji razglasili za dan krvodajalstva.

Z razvojem transfuzijske medicine in širjenjem dejavnosti na področje diagnostičnih in terapevtskih storitev kot del interdisciplinarnega pristopa pri zdravljenju bolnikov danes zagotavljamo najboljše zdravljenje z ustrezno, kakovostno in varno krvjo, zdravili iz krvi, celicami in tkivi ter zdravili za napredno zdravljenje.

V Sloveniji dosega transfuzijska medicina evropske standarde in merila oskrbe, primerljive z najrazvitejšimi državami sveta.

The beginnings of transfusion medicine in Slovenia date back to the period before the Second World War, when a few cases of direct blood transfusion (from the donor's vein to the recipient's vein) were recorded. 4 June 1945 marked the beginning of transfusion medicine in Slovenia when the first 18 unit of blood were collected and stored in the Transfusion Department in Ljubljana. In Slovenia, this day was declared Blood Donor Day.

Today, with the development of transfusion medicine and the expansion of activities in diagnostic and therapeutic services as part of an interdisciplinary approach to the treatment of patients, we provide appropriate, high-quality and safe blood, cell and tissue products, plasma-derived medicinal products and advanced therapy medicinal products.

In Slovenia, transfusion medicine meets European standards and criteria for patient care similar to most developed countries in the world.

Transfuzijsko službo v Sloveniji sestavljajo organizacijsko in finančno ločene ustanove:

- **Zavod Republike Slovenije za transfuzijsko medicino (ZTM)** v Ljubljani s pripadajočimi centri za transfuzijsko dejavnost v Novem mestu, Trbovljah, Slovenj Gradcu, Izoli, Novi Gorici in na Jesenicah;
- **Center za transfuzijsko medicino Univerzitetnega kliničnega centra Maribor (CTM)** z enotama za transfuzijsko dejavnost (ETD) na Ptuju in v Murski Soboti;
- **Transfuzijski center Celje Splošne bolnišnice Celje (TC)**;
- **Bolnišnična krvna banka v Splošni bolnišnici Brežice**.

Vse enote transfuzijske službe oskrbujejo bolnike s komponentami krvi in izvajajo predtransfuzijsko testiranje. ZTM in transfuzijski centri opravljajo dejavnost zbiranja krvi v transfuzijskih ustanovah in na terenu. Predelava krvi v komponente se opravlja na ZTM v Ljubljani, CTM Maribor in TC Celje. Predelano kri vračamo v centre ali enote skladno s potrebami in načrtom za oskrbo bolnišnic na njihovem območju. Testiranje krvi izvajata ZTM v Ljubljani, CTM Maribor in TC Celje. Centralizirano za celotno Slovenijo se na ZTM v Ljubljani izvajajo testiranja krvi z metodo za neposredno ugotavljanje prisotnosti virusov (ang. *Nucleic Acid Techniques*, NAT).

Vse ustanove s pripadajočimi centri in enotami imajo vzpostavljeno **vodenje sistema kakovosti** in pridobljen certifikat ISO 9001, dovoljenje Javne agencije RS za zdravila in medicinske pripomočke za opravljanje dejavnosti preskrbe s krvjo in dovoljenje Ministrstva za zdravje RS za delo medicinskega laboratorija.

The Transfusion Service in Slovenia consists of organisationally and financially separate institutions:

- **The Blood Transfusion Centre of Slovenia in Ljubljana** with associated Blood Transfusion Units in Novo mesto, Trbovlje, Slovenj Gradec, Izola, Nova Gorica and Jesenice;
- **The Transfusion Medicine Centre at Maribor University Medical Centre** with associated Blood Transfusion Units in Ptuj and Murska Sobota;
- **The Transfusion Centre at the Celje General Hospital**;
- **Hospital Blood Bank at the General Hospital Brežice**.

All establishments of the Transfusion Service provide patients with blood components and perform pre-transfusion tests. The Blood Transfusion Centre of Slovenia (BTC) and Transfusion Centres with associated Units perform blood collection in transfusion facilities and on mobile sessions. Processing of blood into components is performed in the BTC in Ljubljana, the Transfusion Medicine Centre Maribor (TMC) and the Transfusion Centre Celje (TC). The processed blood is returned to the centres/units according to the needs and the plan to supply the hospitals in their area.

All institutions with their centres and units have implemented **a quality management system** and obtained ISO 9001 certification, the JAZMP (Agency for Medicinal Products and Medical Devices of the Republic of Slovenia) licence for the performance of blood supply activities, and the Ministry of Health authorisation for the work of the medical laboratory.

NAT blood tests (*Nucleic Acid Techniques*) are performed centrally at the BTC in Ljubljana for the whole of Slovenia.

Zavod RS za transfuzijsko medicino je **na državni ravni** odgovoren za strokovno raven preskrbe s krvjo in krvnimi pripravki ter povezovanje transfuzijske medicine z uporabniki storitev; strokovno usklajuje in povezuje transfuzijsko službo v nacionalno transfuzijsko mrežo; vodi sistem hemovigilance, enoten informacijski sistem, strokovno izobraževanje in razvojno-raziskovalno dejavnost ter sodeluje z mednarodnimi organizacijami, zvezami in sorodnimi zavodi v drugih državah.

At the national level, the Blood Transfusion Centre of Slovenia is responsible for the professional level of blood supply and blood products and for linking transfusion medicine with service users. It professionally coordinates and integrates the Transfusion Service into the national transfusion network, manages the haemovigilance system, the information system, professional training and research and development, and it cooperates with international organisations, associations and related institutions in other countries.

Krvodajalska pobuda
»Daruj energijo za življenje«
»Donate energy for life« campaign

2.

PREDSTAVITEV DEJAVNOSTI ZAVODA RS ZA TRANSFUZIJSKO MEDICINO

PRESENTATION OF THE ACTIVITIES OF THE BLOOD TRANSFUSION CENTRE OF SLOVENIA

PRESKRBA S KRVJO
BLOOD SUPPLY

Irena Razboršek

Vsak pacient v Republiki Sloveniji, ki potrebuje zdravljenje s krvjo, tudi prejme kakovostno in varno transfuzijo. To omogočajo krvodajalci, ki so osnovni pogoj za preskrbo s krvjo.

Every patient in the Republic of Slovenia who needs blood transfusion receives high-quality and safe blood. Blood donors are essential for blood supply.

V Sloveniji smo lahko ponosni na uspešno dolgoletno tradicijo krvodajalstva pod okriljem Rdečega križa Slovenije in krvodajalce, ki vsa leta zagotavljajo potrebno količino krvi, iz katere pripravimo komponente krvi in zdravila iz krvi, s katerimi omogočamo zdravljenje bolnikov.

Za pripravo komponent krvi so potrebni številni zahtevni zaporedni postopki, ki jih izvajajo zdravstveni delavci. Vsaka enota krvi je edinstvena, saj so v njej žive in neponovljive celice, ki zaradi bioloških značilnosti še vedno nimajo ustreznega nadomestka. Transfuzija krvi je transplantacija krvnih celic, s katerimi zdravimo bolezenska stanja in krvavitve, ki ogrožajo zdravje in življenje.

In Slovenia, we can be proud of a successful and long-standing tradition of blood donation and blood donors under the organisation of the Slovenian Red Cross (SRC). They provide the necessary blood units for blood components and plasma-derived medicinal products to fulfill patients' needs.

Preparing blood components requires complex, sequential procedures carried out by medical professionals. Each unit of blood is unique, as it contains living and unique cells for which there is no suitable substitute due to their biological properties. Blood transfusion is a transplantation of blood cells to treat diseases and haemorrhages that threaten health and life.

IRENA RAZBORŠEK
dr. med., spec. transf. med.
MD, Transf. Med. Spec.

Predstojnica Oddelka za preskrbo s krvjo
Head of the Blood Supply Department

Vsaka enota krvi je edinstvena, saj so v njej žive in neponovljive celice, ki zaradi bioloških značilnosti še vedno nimajo ustreznega nadomestka.

Each unit of blood is unique, as it contains living and unique cells for which there is no suitable substitute due to their biological properties.

PRESKRBA S KRVJO – IZDAJA KOMPONENT KRVI

Te edinstvenosti se še kako zavedajo izkušene usposobljene diplomirane medicinske sestre in diplomirani zdravstveniki, ki 24 ur na dan vse dni v letu sprejemajo naročila za komponente krvi. Skladno z naročilom in po opravljenih preiskavah skupaj z zdravnikom oskrbijo pacienta z ustrezno komponento krvi, ki je **skladna s pacientovimi krvnimi skupinami ABO, RhD in Kell**.

Potrebe po komponentah krvi različnih krvnih skupin so nepredvidljive in odvisne od bolnikov in njihovih krvnih skupin, v večini pa so podobne porazdelitvi krvnih skupin med prebivalstvom v Sloveniji. Pri nas sta najpogostejši krvni skupini A in 0 (**A približno 40 %, 0 pa 38 %**), krvne skupine **B je 15 %**, krvno skupino **AB** pa ima **približno 7 %** ljudi. **RhD-pozitivnih** je okoli **82 %** ljudi, **RhD-negativnih** pa le okoli **18 %**.

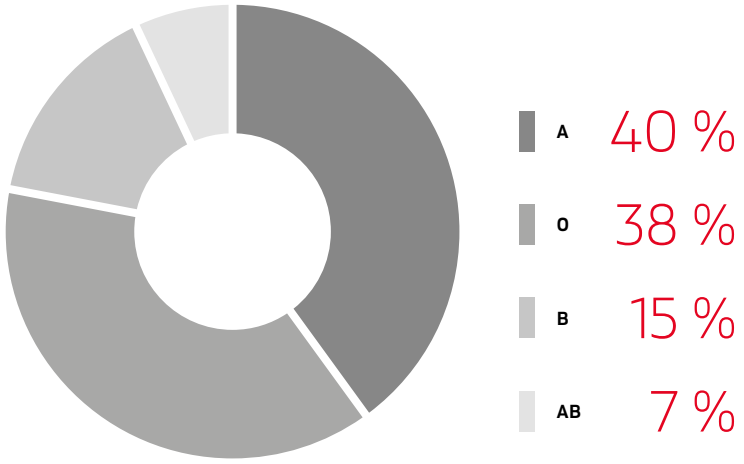
BLOOD SUPPLY – ISSUING AND DISTRIBUTION OF BLOOD COMPONENTS

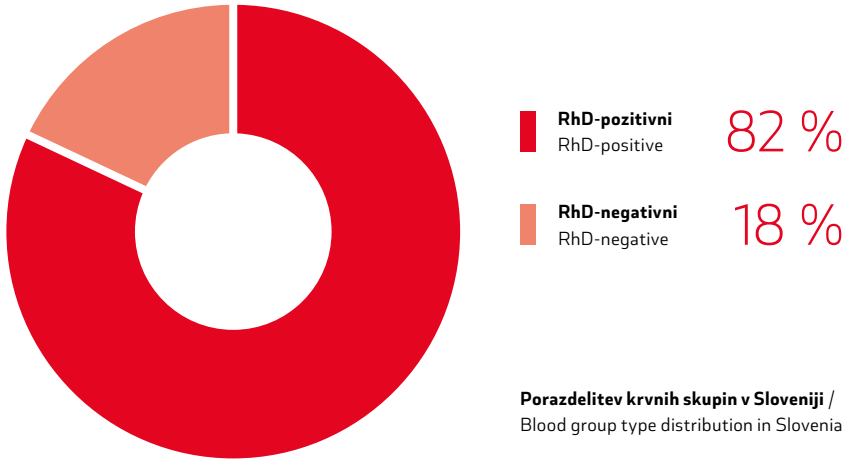
Experienced and qualified registered nurses who take orders for blood components 24/7, all year round, are aware of this uniqueness. According to the order and after the consultations with the relevant physician, they provide the patient with **the appropriate blood type ABO, RhD and Kell component**.

The need for blood components of different blood groups is unpredictable and depends on the patients and their blood group types. Usually, the distribution of blood group types among the population in Slovenia is similar. In Slovenia, the most common blood group types in the population are A and 0 (**A about 40%, 0 approximately 38%**), blood group type **B at 15%**, and blood group type **AB** belongs to about **7%** of people. About **82%** of people are **RhD-positive**, and only about **18%** are **RhD-negative**.

Skrbno vodenje zalog krvi po krvnih skupinah za ustrezno razpoložljivost komponent krvi na vseh lokacijah transfuzijske službe in izbira prave komponente krvi sta zahtevni nalogi.

Carefully managing blood stock by blood group types for proper availability of blood components at all Transfusion Service locations and selecting the right blood component is a challenging task.





Porazdelitev krvnih skupin v Sloveniji /
Blood group type distribution in Slovenia

Nujna naročila pomenijo, da pacient potrebuje transfuzijo takoj, zato se obravnavajo prednostno in se pacienta nemudoma oskrbi z ustreznimi enotami krvi. Nekajkrat na leto je izguba krvi pri pacientu tako huda, da se komponente krvi izdajajo po protokolu masivne transfuzije. To pomeni, da oskrbimo bolnika hkrati s petimi enotami eritrocitov, petimi enotami plazme in terapevtsko enoto trombocitov, ki ustreza pacientovi krvni skupini. Pošiljanje se ponavlja, dokler krvavitev pri pacientu ni ustavljena.

Za najmlajše, komaj rojene otroke in nedonošenčke se izberejo enote eritrocitov, ki so bile odvzete pred manj kot petimi dnevi. Priprava izmenjalne transfuzije za novorojenčka ali priprava opranih eritrocitov je zahteven in dolgotrajen postopek, pri katerem je potrebna izjemna natančnost, saj priprava poteka ročno.

Za imunsko oslabljene paciente še bolj pozorno izbiramo komponente krvi in enote eritrocitov iz zaloge krvi, ne glede na dnevni čas, dodatno testiramo na prisotnost CMV (citomegalo virus).

Za paciente po transplantaciji krvotvornih matičnih celic (KMC) in tudi za tiste z nekaterimi resnimi bolezenskimi stanji vse celične komponente krvi tik pred izdajo obsevamo, da s tem dodatno preprečimo možne zaplete po transfuziji. Obsevanje komponent krvi se za vse bolnike v Sloveniji opravlja na ZTM v Ljubljani.

Za bolnike, ki so se zaradi prejetih transfuzij senzibilizirali in imajo v krvi protitelesa, z dodatnimi testi poiščemo ustrezne komponente krvi in tako zagotovimo optimalen učinek transfuzije.

Urgent orders mean that the patient needs a transfusion immediately. Therefore, orders are prioritised, and the patient is immediately supplied with appropriate blood units. Several times per year the patient's blood loss is so severe that blood components are administered according to the so-called "massive transfusion protocol". This means that five units of red cells (erythrocytes), five units of plasma, and one therapeutic unit of platelets compatible with the patient's blood group type are delivered to the patient simultaneously. The issuing and delivery is repeated until the patient's bleeding has stopped.

For the youngest, just-born infants and premature babies, red cell units collected less than five days-old are selected. Preparing an exchange transfusion for a newborn or preparing washed red cells are demanding, time-consuming procedures that require extreme care because the preparation is done manually.

For immunocompromised patients, blood components and red cell units are selected even more carefully as regardless of the time of day, additionally testing for CMV (cytomegalovirus) markers is performed.

All cellular blood components **for haematopoietic stem cell transplantation recipients** and patients with certain severe diseases are irradiated immediately before issuing to prevent further possible transfusion adverse reactions. Irradiation of blood components is performed for all patients in Slovenia at BTC in Ljubljana.

For transfusion-induced, sensitised patients who have antibodies in their blood, additional tests are carried out to find the appropriate blood components to ensure the optimal effect of the transfusion.

Neposredno pred izdajo zdravstveni delavec opravi še **zadnjo vizualno kontrolo in kontrolo podatkov** ter enoto krvi nato preda kurirju ali reševalcu. Pri oskrbi pacientov s krvjo je pomemben tudi njen **pravilen transport** med transfuzijskimi ustanovami in bolnišnicami. Od leta 2005 zagotavljamo ustrezno transportno verigo komponent krvi v validiranih zabojnikih z neprekinjenim temperaturnim nadzorom. Z uporabo cevne zračne pošte med UKC Ljubljana in ZTM v Ljubljani smo poenostavili dostavo in skrajšali čas transporta. Tudi v nekaterih regionalnih bolnišnicah se cevna pošta uporablja za transport krvi in vzorcev med transfuzijskim centrom in oddelki bolnišnic.

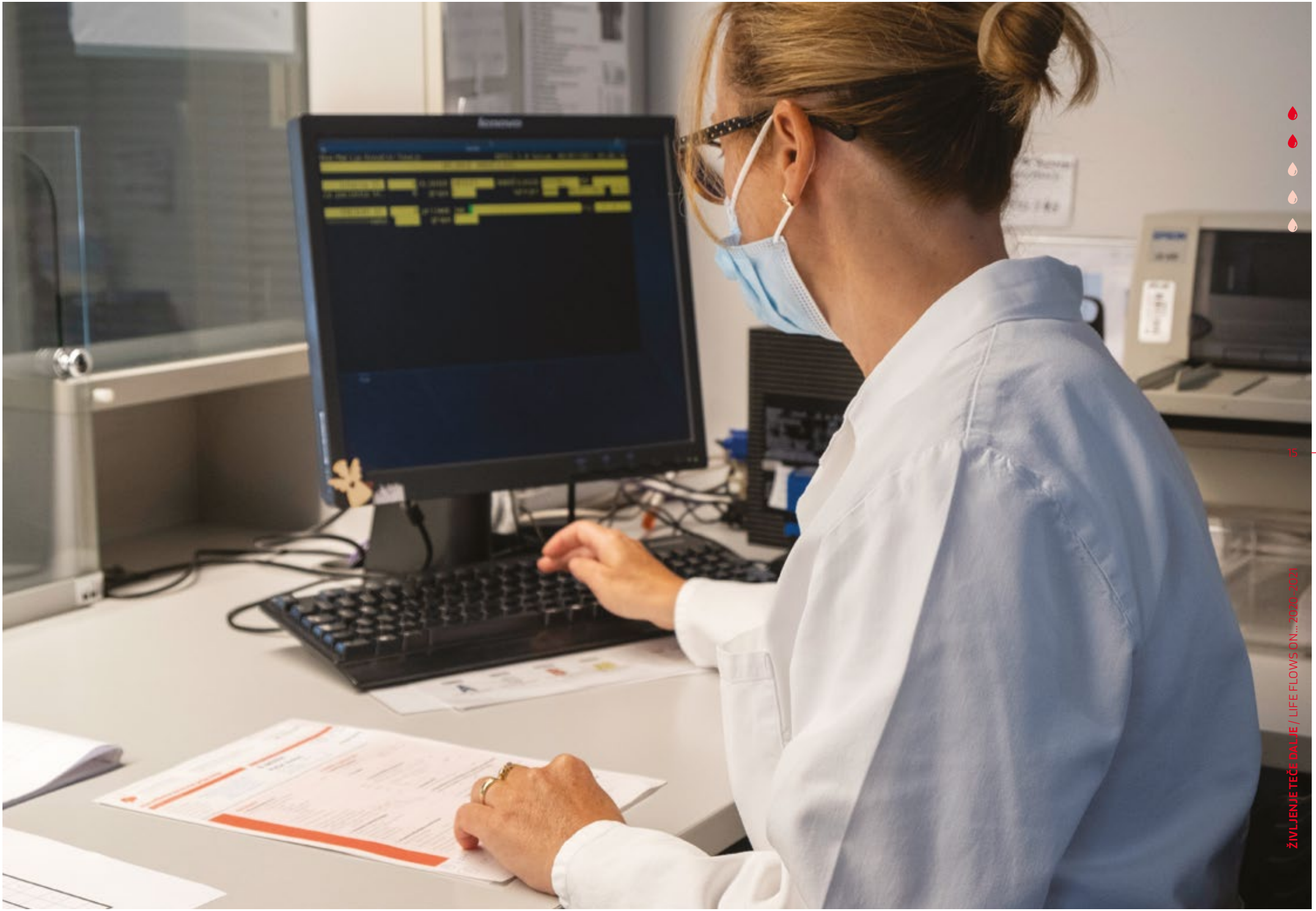
Največji porabniki krvi so bolniki z boleznimi krvi in krvotvornih organov, bolniki z rakom, bolniki, zdravljeni s transplantacijo organov in KMC, ponesrečenci ter bolniki, ki kri potrebujejo zaradi operativnih posegov.

Transfuzijska medicina opravlja številne dejavnosti za zagotavljanje visokokakovostne in varne krvi in zdravil iz krvi. O varnosti in kakovosti komponent krvi nam daje informacije tudi **sistem hemovigilance**, s katerim na ravni države spremljamo neželene učinke pri prejemnikih transfuzije.

Immediately before issuing the blood component, the transfusion medicine staff perform **the final visual inspection and data check control**, then hand it over to the courier or paramedic. **Appropriate blood transport** between transfusion facilities/hospitals is also important for adequate blood supply. Since 2005, we have ensured an appropriate transport chain of blood components in validated containers with temperature control throughout the transport. We have simplified delivery and shortened transport duration of blood components and samples by using a pneumatic tube transport (mail) system between University Medical Centre Ljubljana and BTC in Ljubljana. In some regional hospitals this system is also used between the transfusion centre and the hospital wards.

The largest consumers of blood transfusion are patients with blood and haematopoietic diseases, cancer patients, organ transplant and haematopoietic stem cell (HSC) recipients, trauma patients and patients undergoing surgery.

Transfusion medicine carries out a range of activities to ensure a high level of quality and safety of blood and plasma-derived medicinal products. **The haemovigilance in the systematic surveillance** of adverse reactions and adverse events related to transfusion at a national level also provides information on the safety and quality of blood components.




DATEC

PRESKRBA S KRVJO – PRIPRAVA KOMPONENT KRVI

Zaradi nemotene preskrbe s krvjo in potrebe po stalnem obnavljanju zalog krvi odvzemi krvi potekajo vse dni v delovnem tednu na krvodajalskih akcijah na terenu ali v transfuzijskih ustanovah. Kri, odvzeta na različnih lokacijah, začne proti poldnevu prihajati v prostore za pripravo komponent krvi. Odvzeta kri počiva najmanj tri ure po odvzemu. Sledijo fizikalni postopki filtracije, centrifugiranja in ločevanja, ki s pomočjo celičnih ločevalcev omogočijo ločevanje krvi na celični in plazemski del. Čeprav so posamezni postopki avtomatizirani in je zagotovljena sledljivost postopkov in izvajalcev, gre vsaka enota nekajkrat skozi roke usposobljenih zdravstvenih delavcev, da jo označijo, določijo njen volumen in izvedejo vizualni pregled vsebine.

Priprava eritrocitov je zaključena že na dan odvzema. Shranjeni na optimalni temperaturi +4 °C bodo počakali na rezultate testiranja. Prav tako je na dan odvzema zaključena **priprava sveže zamrznjene plazme**, ki jo v osmih urah od odvzema globoko zamrznemo, da čim bolj ohranimo faktorje strjevanja krvi v njej. Shranjuje se pri temperaturi, nižji od –25 °C. Po testiranju je na razpolago za zdravljenje pacientov.

BLOOD SUPPLY – PREPARATION OF BLOOD COMPONENTS

To sustain a stable blood supply, blood collections take place every day of the working week at fixed blood donation sites and mobile sessions around the country. The collected blood units from various locations are delivered to the processing rooms around midday. The collected blood units need to rest for at least three hours after collection. Blood units are further divided through the processes of filtration, centrifugation and separation, which use cell separators to separate the blood into cell and plasma components. Although the individual procedures are automated, and traceability of procedures and qualified staff are ensured, each unit passes through the hands of professionals several times to label it, determine the volume of the unit and to visually inspect the contents.

Preparing the red cell units is completed on the day of collection. They are stored at the optimal temperature +4 °C where they await the test results. **Preparation of fresh frozen plasma** is also completed on the day of collection, and it is frozen within eight hours of collection to preserve blood clotting factors. It is stored below -25 °C. After the tests are completed, it is available for patient treatment.

Odvzemi krvi potekajo vse dni v delovnem tednu na krvodajalskih akcijah na terenu ali v transfuzijskih ustanovah.

Blood collections take place every day of the working week at fixed blood donation sites and mobile sessions around the country.


NASLEDNJE KRVODAJALSKE AKCIJE
KOLEDAR DOGODKOV

Svežo zamrznjeno plazmo od prostovoljnih neplačanih krvodajalcev, ki smo jo pripravili iz polne krvi ali s postopkom plazmafereze in je nismo uporabili za klinično zdravljenje bolnikov, **uporabimo za izdelavo zdravil iz krvi**. Tako ravnamo že vse od leta 1992. Plazma, zbrana v Republiki Sloveniji za izdelavo zdravil, se po predpisanih postopkih predela v polispecifične imunoglobuline, albumin in faktorje strjevanja krvi pri izbranem izvajalcu v tujini na podlagi evropskega razpisa. Zdravila iz krvi so registrirana in proizvedena skladno z načelom dobre proizvodne prakse in Evropske farmakopeje. Z njimi pokrivamo med 55–60 % potreb v Sloveniji. Z načrtom povečanja števila opravljenih plazmaferez smo del evropske strategije (EU) za doseganje strateške neodvisnosti v regiji. Še vedno je 70 % zdravil iz krvi, ki se uporabijo v EU, proizvedenih iz plazme, zbrane v Ameriki.

ZTM oskrbuje zdravstvene ustanove v Sloveniji z **zdravili iz krvi** in nekaterimi rekombinantnimi zdravili. Dejavnost prometa z zdravili na debelo je pomemben del aktivnosti ZTM, ki ga izvaja Center za oskrbo in promet z zdravili in medicinskimi pripomočki (COPZMP).

Postopek **priprave trombocitov** iz polne krvi se začne s pripravo vmesnega proizvoda, bogatega s trombociti (ang. *buffy coata*), nadaljuje pa se z združevanjem petih enot vmesnega proizvoda iste krvne skupine, in tako s postopkom centrifugiranja pridobimo komponento z visoko koncentracijo trombocitov. Sledi še postopek patogene inaktivacije – uničenja virusov, bakterij in drugih povzročiteljev bolezni. S tem dosežemo še višjo kakovost komponente in stopnjo varnosti za bolnika, ker lahko tako preprečimo prenos bolezni, za katere nimamo na voljo specifičnih preiskav.

Popoldne in čez noč se v laboratorijih za testiranje krvi krvodajalcev zaključi **testiranje na vse zakonsko določene bolezni**, ki se lahko prenesejo s krvjo (HIV, virus hepatitisa B in C ter sifilis, med aktivnostjo komarjev lahko tudi na virus Zahodnega Nila). Vsaka komponenta krvi se še računalniško preveri z dobljenimi rezultati opravljenih testov. Samo komponente krvi, ki izpolnjujejo vse zahtevane standarde, prejmejo zaključno nalepko in so na voljo za oskrbo pacientov.

Fresh frozen plasma collected from voluntary, non-remunerated whole blood or by plasmapheresis blood donors, and not used for the clinical treatment of patients, **is used to make plasma-derived medicinal products**. This process is used and has been in place in Slovenia since 1992. Collected plasma is processed into polyspecific immunoglobulins, albumin and blood coagulation factors by a selected contractor abroad based on a European tender under the prescribed procedures. The plasma-derived medicinal products are registered and manufactured by following the principle of good manufacturing practise and European Pharmacopoeia. They cover 55–60 % of the demand for these medicinal products in Slovenia. With our plan to increase the number of plasmaphereses performed, we are part of the European strategy (EU) to achieve strategic independence in the region. However, 70 % of plasma-derived medicinal products used in the EU are made from plasma collected in America.

BTC supplies health care institutions in Slovenia with **plasma-derived medicinal products** and also with some recombinant medicinal products. The activity of wholesale distribution of medicinal products is an important part of BTC's activities that are provided by the Center for the Supply and Distribution of Medicinal Products and Medical Devices.

In the **production of platelets** from whole blood, an intermediate product rich in platelets is produced (buffy coat) first. The pooling of five units of the intermediate product of the same blood group is continued. Thus, a component with a high concentration of platelets is obtained by centrifugation. The pathogen inactivation technology – the destruction of viruses, bacteria, and other pathogens – is applied. This results in an even higher quality of the component and safety for the patient because, in this way, we can prevent the transfusion transmitted infections for which there are no specific tests.

In the afternoon and at night **all legally required screening tests for transfusion-transmitted agents** (HIV, hepatitis B and C virus and T. Pallidum/syphilis, and West Nile virus during mosquito season, if necessary) are performed in the donor blood testing laboratories. Each blood unit has to pass computerised validation of the tests results. Only blood components that meet all required standards receive a final label and are available for patient treatment.

Žive celice, skrbno shranjene na optimalni temperaturi, imajo rok uporabe. Rdeče krvničke ali eritrocite lahko za zdravljenje uporabimo do 42 dni, krvne ploščice ali trombocite samo 5–7 dni, samo svežo zamrznjeno plazmo pa lahko uporabimo več mesecev po odvzemu.

Live cells that are carefully stored at optimal temperature have their own shelf life. Red blood cells or erythrocytes can be used for treatment up to 42 days, platelets or thrombocytes for only five to seven days, and only fresh frozen plasma can be used several months after collection.

Komponente krvi morajo dosegati visoke standarde kakovosti, zato že med pripravo poteka vzorčenje za kontrolo kakovosti.

Blood components must meet high-quality standards; therefore, quality control testing takes place during preparation.

PRESKRBA S KRVJO – ZBIRANJE KRVI

Preskrba s krvjo se začne z **zadostnim številom odgovornih in varnih krvodajalcev**, ki so pripravljeni darovati kri. Dnevno jih v Sloveniji potrebujemo okoli 350 in prav zaradi njihove pomembne in nenadomestljive vloge so pomemben del zdravstvenega sistema.

Krvodajalci lahko kri darujejo v transfuzijskih ustanovah in na terenskih krvodajalskih akcijah, v okviru organiziranih akcij ali pa se, kot to počnejo vse pogosteje, za prihod odločijo na podlagi objavljenih zalog krvi na spletni strani ZTM (ztm.si). S spremljanjem zalog krvi in prihodom glede na potrebe aktivno sodelujejo pri njihovem uravnavanju.

Ustrezne zaloge krvi zagotovimo z natančno načrtovanimi krvodajalskimi akcijami ter dobro obveščenimi in odgovornimi krvodajalci. Rdeči križ Slovenije letno organizira okoli 1150 krvodajalskih akcij, od tega več kot 370 terenskih. Vsako leto se na odvzem krvi prijavi okoli 100.000 krvodajalk in krvodajalcev, kar pomeni, da oskrbimo vse bolnike, ki kri potrebujejo. ZTM opravi okoli 66 % vseh odvzemov v Sloveniji, od tega v Ljubljani s svojo terensko ekipo kar dve tretjini.

Uravnavanje zalog krvi je kompleksno, zato sta potrebna stalna spremljanje in ukrepanje transfuzijske službe. Zaloge krvi niso odvisne samo od krvodajalcev in zbrane krvi, ampak tudi od njene porabe. Ta je nepredvidljiva tako glede na potrebne količine in krvne skupine komponent krvi.

BLOOD SUPPLY – BLOOD COLLECTION

The blood supply starts with a **sufficient number of responsible and safe blood donors** who are willing to donate blood. In Slovenia we need about 350 blood donors per day. Precisely due to their important and irreplaceable role, blood donors are an important part of the health care system.

Blood donors can donate blood at organised sessions located in fixed transfusion sites and mobile drives. Lately and more often, they decide to donate based on the published blood stocks on the BTC website (ztm.si). They actively participate in monitoring blood stocks and sustainable blood supplies.

Adequate blood supplies are ensured through carefully planned blood drives and well-informed and responsible blood donors. The Slovenia Red Cross organises about 1,150 blood sessions annually, of which over 370 are mobile blood drives. Every year, about 100,000 blood donors are registered to donate and thus to cover all patient needs. BTC performs about 66 % of all blood unit collections in Slovenia, two thirds are performed from BTC in Ljubljana and its mobile drive team.

The blood stock management is complex, requiring continuous monitoring and actions by the Transfusion Service. The blood stock depends not only on the blood donors and the collected blood units but also on the blood consumption. This is unpredictable in terms of the quantities and blood group types of blood components required.

Dnevno v Sloveniji potrebujemo okoli 350 krvodajalcev.

In Slovenia we need about 350 blood donors per day.

DIAGNOSTIČNE STORITVE
DIAGNOSTIC SERVICES

— *Irena Bricl*

Preiskave Oddelka za diagnostične storitve so pomemben del dejavnosti ZTM. Preiskave opravljamo tako za krvodajalce kot za paciente.

The Diagnostic Services department performs a great number of laboratory testings and is thus an important part of BTC's activities. The laboratory diagnostics are performed in blood donors as well as in patients.

KRVODAJALCI IN ZAGOTAVLJANJE VARNE KRVI

Med postopki predelave odvzete krvi istočasno potekajo **laboratorijski postopki različnih presejalnih testiranj krvi na označevalce okužb**, ki se prenašajo s krvjo, in določitve krvnih skupin.

Vsako enoto odvzete krvi testiramo na povzročitelje aidsa, sifilisa in hepatitisa tipa B in C. Uporabljene metode testiranja so najsodobnejše, licencirane po najstrožjih mednarodnih merilih in popolnoma avtomatizirane. Ovira pri zagotavljanju popolne varnosti je samo diagnostično okno – obdobje od trenutka okužbe do pojava označevalcev te okužbe, ki ga iščemo s specifičnim testom.

BLOOD DONORS AND PROVIDING SAFE BLOOD

During the processing of the collected blood, **laboratory procedures of various blood screening tests for markers of transfusion transmitted infectious agents** and blood-group typing procedures are performed simultaneously.

Each collected blood unit is tested for markers of HIV, syphilis and hepatitis B and C. State-of-the-art testing methods are used, licensed in accordance with the strictest international criteria and are completely automated. The most important barrier in ensuring complete blood safety is »diagnostic window« – the period from the moment of infection to the appearance of infection markers, which we look for with a specific test.

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Predstojnica Oddelka za diagnostične storitve
Head of the
Diagnostic Services Department

Zato smo leta 2007 na Zavodu Republike Slovenije za transfuzijsko medicino v Ljubljani – centralizirano za vso Slovenijo – dodatno uvedli presejalno testiranje posameznih odvzetih enot krvi za transfuzijo z metodo za neposredno ugotavljanje prisotnosti virusov (ang. *Nucleic Acid Techniques*, NAT). Z njim močno skrajšamo diagnostično okno, saj lahko okužbo zaznamo veliko pred pojavom posrednih seroloških označevalcev okužb. Kri, testirana po metodi NAT, je varnejša tudi zato, ker je metoda izjemno občutljiva, saj omogoča tudi zaznavanje okužb z nizkim virusnim bremenom.

Vsaki odvzeti enoti krvi določimo še **antigene krvne skupine AB0 in RhD** ter **antigene sistemov Rh (C, c, E, e)** in **Kell**. Da bi preprečili prenos in škodljivo delovanje nepričakovanih eritrocitnih protiteles iz plazme krvodajalca na prejemnika, iščemo **eritrocitna protitelesa** v vseh enotah z **Indirektnim (posrednim) Coombsovim testom**. Če jih zaznamo, teh enot ne uporabimo za transfuzijo.

Therefore, in 2007 we introduced at the Blood Transfusion Centre of Slovenia (BTC) in Ljubljana, additional screening tests of individual blood units taken for transfusion with methods for direct detection of viruses (Nucleic Acid Techniques – NAT). NAT testing is centralised for the whole country. This method shortens the diagnostic window period considerably, as the infection can be detected much earlier and before serological markers of infection appear. Blood tested according to the NAT method is much safer because the method is extremely sensitive, i.e. it enables the detection of low viral burden.

AB0 and **RhD typing** is performed in each collected blood unit. **Antigens of the Rh (C, c, E, e)** and **Kell** systems are determined at the first and the second donation. To prevent the transmission and harmful effect of unexpected red blood cell antibodies from donor plasma to the recipient, we perform antibody screening in all units using the **indirect antiglobulin (Coombs) test**. If such antibodies are detected, those units are discarded.


ARCHITECTPLUS
STOJALA
ERGOTRON
Alinity

BOLNIKI IN NOSEČNICE

Ustreznost krvi bolnikom zagotavljamo z imunohematološkimi preiskavami, ki omogočajo varno transfuzijo krvi in presaditev organov, celic in tkiv ter preprečujejo nekatere neželene imunske pojave po transfuziji, transplantaciji in med nosečnostjo.

V idealnih okoliščinah bi bolniku transfundirali kri, ki je pri bolniku in krvodajalcu enaka v vseh eritrocitnih antigenih, s čimer bi dodatno zmanjšali možnost imunskega odziva s tvorbo protiteles – senzibilizacijo. Zaradi raznolikosti teh antigenov in s tem možnih kombinacij se trudimo transfundirati najbolj skladne enote krvi. Skladnost za vsakega bolnika posebej z vsako enoto eritrocitov preverjamo z **navzkrižnim preizkusom**. Da bi preprečili neželen transfuzijski odziv zaradi nepričakovanih eritrocitnih protiteles v plazmi prejemnika, te iščemo z Indirektnim Coombsovim testom, ki ga naredimo pri vsakem bolniku.

Največji porabniki krvi so bolniki z boleznimi krvi in krvotvornih organov, bolniki z rakom, bolniki, zdravljeni po transplantaciji organov in krvotvornih matičnih celic (KMC), ponesrečenci ter bolniki, ki potrebujejo kri zaradi operativnih posegov.

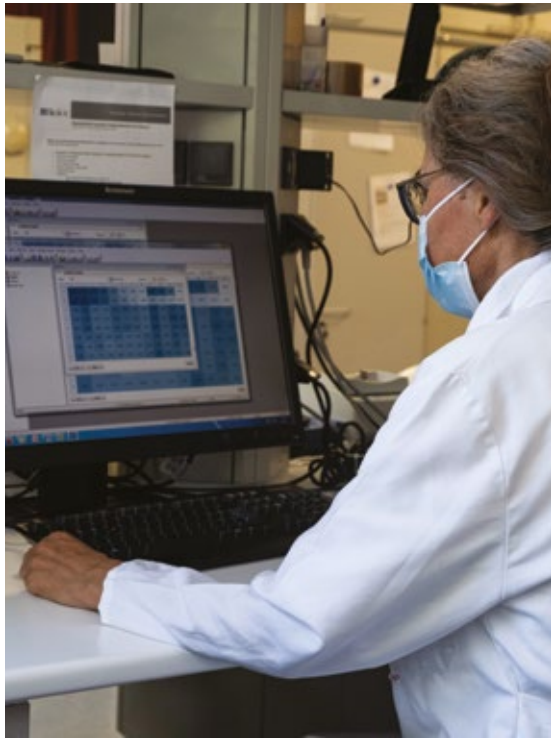
Za zagotovitev varnega in učinkovitega zdravljenja bolnikov z eritrociti je treba pri določenih bolnikih izbrati kri, skladno v imunsko pomembnih antigenih.

PATIENTS AND PREGNANT WOMEN

Blood compatibility is ensured by performing immunohaematological tests, which allow safe blood transfusion and transplantation of organs, cells and tissues and prevent some adverse immune reactions after transfusion, transplantation and during pregnancy.

Ideally, the patient would receive blood from a blood donor who is identical in all clinically important erythrocyte antigens, further reducing the possibility of an immune reaction with the formation of antibodies – sensitisation. Due to the large number of antigens and their possible combinations, we strive to transfuse the red blood cells units with the best match, routinely compatible in AB0, RhD and Kell antigens. To ensure safe and effective treatment of sensitised patients it is necessary to select identical/compatible blood in additional antigens. Compatibility is examined with **a compatibility test "cross-match"** for each unit of red blood cells. To prevent an adverse transfusion reaction due to unexpected red blood cell antibodies in the recipient's plasma, every patient is screened for their presence with an indirect antiglobulin test.

The largest consumers of blood components are patients with blood and haematopoietic diseases, cancer patients, patients after organ transplantation and haematopoietic stem cell (HSC) transplantation, trauma patients and surgery patients.



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Preiskave, ki jih opravljamo, so glede na metodo izbora **enostavnejše, serološke** ali **nekoliko zahtevnejše – molekularno biološke preiskave**.

Opravljamo **eritrocitne**, **trombocitne**, **granulocitne preiskave**, **preiskave tkivne skladnosti** in **določanje označevalcev okužb** pri pacientih.

Serološke preiskave za določanje eritrocitnih, trombocitnih in granulocitnih antigenov, molekularno biološke preiskave ter ugotavljanje trombocitnih in granulocitnih protiteles in njihove specifičnosti opravljamo samo na ZTM.

ZTM je v slovensko transfuzijsko službo uvedel **nacionalni telemedicinski sistem**, ki uspešno deluje že od leta 2005 in omogoča delo specialistov transfuzijske medicine na daljavo. Z uporabo telemedicine vsako predtransfuzijsko preiskavo na daljavo odčita specialist transfuzijske medicine, s čimer smo zmanjšali stroške v transfuzijski službi in omogočili enako specialistično transfuzijsko obravnavo bolnikov po celi Sloveniji.

Transfuzijska služba sodeluje tudi v programu **vodenja nosečnosti** z imunohematološkimi preiskavami in svetovanjem pri zaščiti RhD-negativnih nosečnic oz. ob odkritju prisotnosti nepričakovanih eritrocitnih protiteles pri njih. S temi preiskavami in z zaščito s posebnimi protitelesi se je močno zmanjšala umrljivost plodov med nosečnostjo in novorojenčkov.

Na ZTM smo v letu 2018 začeli s postopkom **testiranja krvi nosečnic**, pri katerem se z molekularnimi metodami ugotavlja, ali nosečnice s krvno skupino RhD-negativno nosijo RhD-pozitiven plod. Posledično zgolj tem nosečnicam nudimo zaščito s posebnimi protitelesi, kar prepreči okvare ploda.

Depending on the diagnostic method, we perform **simpler, serological** or somewhat **more sophisticated, i.e. molecular biological**, tests.

We perform **red blood cell**, **platelet** and **granulocyte tests**, **histocompatibility testing**, and the **determination of infectious markers** in patients.

Red blood cells' and granulocyte antigen genotyping, serological and molecular biological tests for determining platelet antigens, as well as the determination of platelet and granulocyte antibodies and their specificity, are only performed at BTC in Ljubljana.

BTC has introduced a **national telemedicine system** in the Slovenian Transfusion Service which has been successfully in operation since 2005 and enables transfusion medicine specialist to work remotely. Assisted by telemedicine, every pre-transfusion diagnostic test is validate remotely by a transfusion medicine specialist 24/7, reducing the cost of providing urgent transfusion services and enabling the same transfusion treatment for patients throughout Slovenia.

The Transfusion Service also participates in **pregnancy management programme** through immunohaematological investigations (blood group typing, indirect antiglobulin testing, antibody titers and volume of fetomaternal hemorrhage determination) and counselling regarding the need for prophylaxis of RhD-negative pregnant women with immunoglobulin anti-D. These investigations and prophylaxis with immunoglobulin anti-D have significantly reduced foetal mortality during pregnancy and in newborns.

At BTC in Ljubljana, we started in 2018 with **national targeted prophylaxis programme** for RhD-negative pregnant women. Using molecular methods we determine whether RhD-negative woman is pregnant with RhD-negative or RhD-positive child. Only pregnant women bearing RhD-positive child are treated with immunoglobulin anti-D to prevent formation of anti-D antibodies.

V **nacionalnih programih presajanja organov in tkiv** sodelujemo z ugotavljanjem tkivne skladnosti. To po eni strani obsega kompleksne preiskave (tipizacijo humanih levkocitnih antigenov (HLA), presejalna testiranja na protitelesa anti-HLA, navzkrižne preizkuse med prejemniki in darovalci organov), ki omogočajo presaditev organov pri bolnikih na čakalnem seznamu **neprofitne organizacije za izmenjavo organov Eurotransplant**, katere članica je tudi Slovenija. Imunskemu statusu prejemnikov organov sledimo tudi po presaditvi, s čimer sodelujemo pri preprečevanju zavrnitvenih reakcij, ki lahko vodijo do izgube organa. Po drugi strani z najzahtevnejšo tipizacijo HLA na visoki stopnji ločljivosti, ki jo izvajamo s sekvencioniranjem DNA, pripravimo podlago, na osnovi katere lahko začnemo iskanje tkivno skladnih darovalcev krvotvornih matičnih celic (KMC) za bolnike z mnogimi malignimi in tudi drugimi boleznimi, ki se lahko zdravijo s presaditvijo KMC.

With histocompatibility testing we participate in **national organ and tissue transplant programmes**. This includes complex tests (human leukocyte antigen (HLA) typing, screening tests for anti-HLA antibodies, cross-testing between recipients and organ donors) that enable organ transplantation for patients on the waiting list. **Slovenia is a member of non-profit organ exchange organisation Eurotransplant**. The immune status of organ recipients is also monitored after transplantation, thus helping to prevent rejection reactions that can lead to organ loss. The most sophisticated high-resolution HLA typing performed by DNA sequencing provides a basis on which we can begin histocompatibility searching for compatible HSC donors for patients who are candidates for HSC transplantation.

Z ugotavljanjem prisotnosti določenih genskih različic HLA, ki predstavljajo dejavnike tveganja za nastanek nekaterih avtoimunskih in drugih bolezni, nudimo tudi podporo pri njihovem diagnosticiranju.

Močno povezano z ugotavljanjem tkivne skladnosti je delo, ki ga opravljamo v registru Slovenija Donor, saj sta samo tkivno skladna bolnik in darovalec KMC ustrezen par na poti do presaditve KMC. Slednjo za področje Slovenije v veliki večini primerov opravimo na ZTM v sklopu terapevtskih storitev.

Vodimo register **Slovenija Donor**, ki je **slovenski register nesorodnih darovalcev KMC**, ki so pripravljeni darovati celice za bolnike, za katere je presaditev KMC velikokrat edina možnost zdravljenja. Vključenost registra Slovenija Donor v svetovni register darovalcev KMC (*Bone Marrow Donors Worldwide*) omogoča iskanje med darovalci z vsega sveta.

Velik del naše dejavnosti so preiskave v zvezi z določanjem označevalcev okužb za bolnike. Za zagotovitev izjemne kakovosti naših preiskav imamo te tudi certificirane s strani pomembnih akreditacijskih ustanov. Naša velika prednost za naročnike je 24-urna dostopnost. Naše preiskave so del diagnostike okužb s hepatitisom A, B in C, s povzročiteljem AIDSA, sifilisa, CMV okužbe in toksoplazmoze.

Podpora naši dejavnosti so tudi tri raziskovalne skupine, ki z razvojem in raziskovalnimi projekti nenehno nadgrajujejo našo dejavnosti in razvijajo nove storitve, ki jih potem v rutini ponudimo naročnikom.

Cilj diagnostičnih preiskav je pravočasno zagotoviti varne in kakovostne storitve za vse paciente. Zato našo dejavnost na podlagi rezultatov raziskovalnih in razvojnih projektov nenehno nadgrajujemo in izboljšujemo.

V zadnjih letih smo to nadgradnjo usmerili predvsem v avtomatizacijo postopkov, ki omogočajo še večjo kakovost in sledljivost vseh preiskav. Izjemno pomembna pa sta tudi stalno izobraževanje zaposlenih in skrb za njihovo dobro počutje.

By identifying certain genetic HLA variants, which represent the risk factors for developing certain autoimmune and other diseases, we also offer support for their diagnostics.

Closely related to determining histocompatibility in tissue testing is our work at the Slovenia Donor Registry because only a tissue-compatible patient and the HSC donor are a matching pair on the way to HSC transplantation. In the vast majority of cases the latter is performed for the area of Slovenia at BTC in Ljubljana as a part of the therapeutic services.

We manage the **Slovenia Donor Registry, a Slovenian registry of unrelated HSC donors** motivated to donate HSC for patients where HSC transplantation is often the only treatment option. The Slovenia Donor Registry takes part in the *Bone Marrow Donors Worldwide*, which makes it possible to search among donors from all over the world.

A large part of our activity comprises diagnostic tests for detection of infection markers in patients. To ensure the exceptional quality of our testing, our processes are certified by important accreditation institutions. Our major advantage for customers is 24/7 availability. We perform hepatitis A, B and C, HIV, CMV, syphilis and toxoplasmosis laboratory testing.

Three research groups are constantly developing new services through development and research projects, which we then routinely offer to our clients. The groups also support our activities.

The aim of the diagnostic testing activities is to provide safe and high-quality services to all patients promptly. Therefore, we are constantly expanding and improving our activities based on the results of research and development projects.

In recent years, we have focused our upgrades primarily on automating procedures that allow for even higher quality and traceability of all tests performed. It is also extremely important to continuously educate employees and also look after their well-being.

TERAPEVTSKE STORITVE
THERAPEUTIC SERVICES

Marko Cukjati

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Head of the Department of Therapeutic Services

Terapevtske storitve se izvajajo že od samega začetka delovanja ZTM. Že v 80. letih so se, poleg odvzemov krvi za avtotransfuzijo pred načrtovanim operativnim posegom in terapevtskih odvzemov, uveljavili aferezni postopki odvzema posameznih sestavin krvi. Z omenjenimi postopki se lahko zbirajo posamezne komponente krvi pri krvodajalcih (plazma, trombociti, granulociti) ali bolnikih, pri katerih je potrebno za zdravljenje zbrati določeno vrsto celic iz polne krvi oziroma jih odstraniti iz telesa.

Leta 1994 smo na ZTM opravili **prvi odvzem krvotvornih matičnih celic (KMC)** iz periferne krvi s postopkom afereze. Lahko rečemo, da se od takrat dejavnost nenehno razvija, širijo se indikacije, vpeljujejo se novi postopki odvzema in obdelave celic.

Therapeutic services have been provided since the beginning of BTC operations. As early as the 1980s, apheresis procedures for obtaining individual blood components were established in addition to blood collection for autotransfusion prior to planned surgeries and therapeutic collections. With these procedures, individual blood components can be collected from blood donors (plasma, platelets, granulocytes) or from patients who require a specific type of blood cell to be added or removed from the body for treatment.

In 1994, **the first collection of haematopoietic stem cells (HSC)** from peripheral blood by apheresis was performed at the BTC. It can be said that since then, the activity has been constantly developing, indications are spreading, and new methods of cell collection and processing are introduced.

Skladno z globalnimi trendi regenerativne medicine, imunoterapije, personalizirane medicine in naprednih zdravljenj so v zadnjih letih terapevtske storitve doživele skokovit porast in dejavnost je prepoznana kot ena ključnih strateških usmeritev na ZTM.

In line with the global trends of regenerative medicine, immunotherapy, personalised medicine and advanced therapies, therapeutic services have greatly advanced in recent years, and the activity is recognised as one of the main strategic priorities at BTC.

Zato smo v maju 2014 ustanovili nov **Oddelek za terapevtske storitve**, ki je združil obstoječe dejavnosti preskrbe s celicami in tkivi, ki so bile pred tem razsejane med različnimi organizacijskimi enotami. V sklopu novega oddelka so se ustanovili **Center za afereze (CA)**, znotraj katerega deluje tudi Ambulanta za terapevtske storitve, **Center za kriobiologijo (CK)** in **Center za razvoj naprednih zdravljenj (CRNZ)**, s katerim so bolniki v Sloveniji dobili prvo javno institucijo, ki deluje kot nacionalni center za izdelavo visokokakovostnih zdravil za napredna zdravljenja (ZNZ).

Therefore, in May 2014, we established a new **Department of Therapeutic Services**, which consolidated the existing cell and tissue supply activities that were previously distributed among different organisational units. As part of the new department (DTS), the **Centre for Apheresis (CA)** was established, which also includes Ambulatory Care Unit, the **Centre for Cryobiology (CK)** and the **Centre for the Development of Advanced Therapies (DAT)**, which gave patients the first public facility in Slovenia to function as a national centre to produce high-quality Advanced Therapy Medicinal Products (ATMPs).

V **CENTRU ZA AFEREZE** (CA) vse aktivnosti potekajo neposredno ob bolnikih oz. darovalcih celic in tkiv. Izvajamo postopke **odvzema KMC za transplantacije in regenerativno medicino** in odvzem mononuklearnih celic za izdelavo zdravil za napredno zdravljenje nekaterih vrst raka (tumorske vakcine, CAR-T). V decembru 2014 smo izvedli prvi odvzem KMC pri otroku z nizko telesno težo in se s tem uvrstili ob bok najbolj razvitim afereznim centrom. Tovrstne odvzeme opravljamo redno v sodelovanju s Kliničnim oddelkom za otroško hematologijo in onkologijo Pediatrične klinike UKC Ljubljana, zato otrok ni potrebno več pošiljati na zdravljenje v tujino. Izvajamo tudi postopke **zunajtelesne fotofereze** (ECP, angl. *Extracorporeal photopheresis*) v sklopu zdravljenja določenih bolezni. Večinoma zdravimo bolnike po alogenski transplantaciji KMC, pri kateri pride do akutnega ali kroničnega zavrnitvenega odziva presadka proti gostitelju. Zdravimo tudi dermatološke bolnike z napredovalo obliko T-celičnega limfoma in bolnike z zavrnitvenim odzivom po presaditvi solidnih organov. Indikacije za ECP se nenehno širijo in ta oblika zdravljenja postaja aktualna tudi na drugih kliničnih področjih. Z afereznimi odvzemi **zagotavljamo tudi kakovostne celične pripravke za napredna zdravljenja**. Z uvajanjem novih indikacij, boljšim poznavanjem imunskega sistema in funkcij posameznih celic ter prilagajanjem terapije za vsakega bolnika posebej se je jasno pokazalo, da brez kakovostnega začetnega bioloških materiala ni mogoče razvijati specifičnih zdravil za napredno zdravljenje. Afereze so zato ključen korak v pripravi zdravil za napredno zdravljenje in vloga ustreznega afereznega odvzema bo tudi v prihodnje vse bolj pomembna in prepoznana in posledično tudi vse bolj zahtevna.

In the **CENTRE FOR APHERESIS** all activities take place directly next to patients or cell and tissue donors. We perform **HSC collection procedures for transplantation and regenerative medicine**, as well as the collection of mononuclear cells to produce drugs for the advanced treatment of certain cancers (tumour cell vaccines, CAR -T). In December 2014, we performed the first HSC collection from a child with low body weight, making us one of the most comprehensive apheresis centres. Such collections are regularly performed in cooperation with the Clinical Department of Paediatric Haematology and Oncology the Division of Paediatrics UMC Ljubljana, so that the child no longer has to be sent abroad for treatment. We also perform **extracorporeal photopheresis** (ECP) procedures as part of the treatment of certain diseases. We mainly treat patients after allogeneic HSC transplantation where there is acute or chronic rejection of the graft against the host. We also treat dermatological patients with advanced T cell lymphoma and patients with rejection after solid organ transplantation. The indications for ECP are constantly expanding, and this form of treatment is also becoming relevant in other clinical areas. **We also perform apheresis collections of high-quality cellular preparations for advanced treatments**. With the introduction of new indications, better knowledge of the immune system and the functions of individual cells, as well as the customisation of therapy for each patient individually, it has become clear that without high-quality biological starting material, specific drugs for advanced treatments cannot be developed. Apheresis is therefore an important step in the preparation of drugs for advanced treatment, and the role of appropriate apheresis will continue to become more important and recognised, and thus more challenging, in the future.

Z uvajanjem novih indikacij, boljšim poznavanjem imunskega sistema in funkcij posameznih celic ter prilagajanjem terapije za vsakega bolnika posebej se je jasno pokazalo, da brez kakovostnega začetnega bioloških materiala ni mogoče razvijati specifičnih zdravil za napredno zdravljenje.

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V postopkih zdravljenja bolnikov tesno sodelujemo s Kliničnim oddelkom (KO) za hematologijo Interne klinike UKC Ljubljana, KO za otroško hematologijo in onkologijo Pediatrične klinike UKC Ljubljana, KO za kardiologijo, KO za pljučne bolezni in alergologijo, Dermatovenerološko kliniko, Očesno kliniko UKC Ljubljana, Onkološkim inštitutom v Ljubljani, UKC Maribor in različnimi ustanovami doma in v tujini. Skupaj se trudimo postaviti in vzdrževati visoke standarde kakovosti v smislu varnosti in učinkovitosti ter zagotavljanja najsodobnejših oblik zdravljenja naših bolnikov. Zato smo v postopku pridobitve svetovno prepoznavne akreditacije JACIE za področje aferez.

When treating patients, we cooperate closely with the Clinical Departments such as Department of Haematology of the Division of Internal Medicine of the University Medical Centre Ljubljana, the Department of Paediatric Haematology and Oncology of the Division of Paediatrics, University Medical Centre Ljubljana, the Department of Cardiology, the Department of Pulmonary Diseases and Allergy, the Department of Dermatovenerology, Department of Ophthalmology, Institute of Oncology in Ljubljana, UMC Maribor and various other institutions at home and abroad. Together, we strive to set and maintain high standards of quality in terms of safety and efficacy, and to offer our patients state-of-the-art treatments. That is why we are in the process of achieving the globally recognised JACIE accreditation for the field of apheresis.

Ambulanta za terapevtske storitve deluje že od leta 1987 in poleg odvzemov avtologne krvi za predoperativno transfuzijo in terapevtskih odvzemov polne krvi v sklopu razvoja novih naprednih zdravljenj opravljamo odvzem avtologne oziroma alogenskega seruma za pripravo očesnih kapljic oziroma za gojenje mezenhimskih matičnih celic. V ambulanti potekajo tudi konziliarni pregledi bolnikov in zdravih darovalcev pred načrtovanim afereznim odvzemom celic (KMC, MNC), pred predvidenim zdravljenjem z zunajtelesno fotoferezo in pred načrtovanim zdravljenjem s celično terapijo (zdravljenje srčnega popuščanja, tumorske vakcine).

Z leti se struktura naših storitev spreminja. Z uvajanjem novih kirurških tehnik ni več potrebno zagotavljati avtologne krvi za operacijo kolka oziroma kolena, kar so bile najpogostejše indikacije za avtotransfuzijo, zato se je njihovo število v tem desetletju zmanjšalo skoraj za desetkrat. Po drugi strani pa se povečuje število odvzemov avtologni oziroma alogenskih KMC in afereznih odvzemov za celične terapije. Prav tako se zaradi novih indikacij povečuje število zunajtelesnih fotoferez od začetka leta 2013, ko smo začeli s tovrstno terapijo, za najmanj četrtino na leto. Opažamo tudi skokovit porast odvzemov za alogenski serum, kar sledi zdravljenju z mezenhimskimi matičnimi celicami.

The outpatient clinic for therapeutic services has been in operation since 1987. In addition to autologous blood collections for preoperative transfusions and therapeutic whole blood collections, we perform autologous or allogeneic serum for the preparation of eye drops or as medium for the mesenchymal stem cell cultures as part of the development of new advanced treatments. The outpatient clinic also performs consultative examinations of patients and healthy donors before the planned apheresis cell collection (HSC, MNC), before the planned treatment with extracorporeal photopheresis and other types of therapeutic apheresis.

The structure of our services has changed over the years. With the introduction of new surgical techniques, it is no longer necessary to provide autologous blood for hip or knee surgery, which were the most common indications for autotransfusion, so their number has decreased almost tenfold in this decade. On the other hand, the number of collections of autologous or allogeneic HSCs and apheresis collections for cell therapies is increasing. The number of extracorporeal photopheresis is also increasing by at least a quarter per year due to new indications since the beginning of 2013, when we started this form of therapy. We also observe a strong increase in allogeneic serum collections for mesenchymal stem cell therapy.

Zaradi epidemije covida-19 je bilo potrebno izvesti vrsto preventivnih ukrepov in reorganizirati nekatere procese dela z namenom, da zaščitimo bolnike, ki so zaradi oslabljenega imunskega sistema še posebno izpostavljeni tveganju bolezni. S predano ekipo zaposlenih in doslednim upoštevanjem ukrepov ter tudi vestnim sodelovanjem bolnikov in darovalcev smo uspeli zagotoviti, da v tem času ni prišlo do nobenega prenosa okužbe.

Due to the COVID 19 epidemic, several preventive measures had to be taken and some workflows reorganised to protect patients who are particularly at risk of disease due to a weakened immune system. With a dedicated team and consistent adherence to measures, as well as the conscientious cooperation of patients and donors, we were able to ensure that there was no transmission of the infection during this period.

V **CENTRU ZA KRIOBIOLOGIJO** opravljamo zamrzovanje in shranjevanje KMC za avtologno presaditev, zamrzovanje in shranjevanje popkovnične krvi za javno banko in usmerjene sorodne odvzeme, koncentriranje kostnega mozga in izolacijo celic CD34+. **Zamrzovanje in shranjevanje KMC ima na ZTM več kot 30-letno zgodovino** in se je razvijalo vzporedno s programom transplantacij KMC na UKC Ljubljana.

Indikacije za zamrzovanje in shranjevanje celic se širijo. Če so bile na začetku povezane s krvnimi boleznimi, gre zdaj za najrazličnejše bolezni, od solidnih tumorjev do avtoimunskih bolezni. Celice zamrzujemo in obdelujemo tudi za farmacevtsko industrijo (npr. mononuklearne celice za izdelavo celic CAR-T). V zadnjih letih se zaradi večjih zahtev glede odmerka celic in števila želenih transplantacij povečuje količina shranjenih celic za posameznega bolnika.

At the **CENTRE FOR CRYOBIOLOGY** we perform freezing and storage of HSC for autologous and allogeneic transplantation, freezing and storage of cord blood for a public bank and associated targeted collection, bone marrow concentration and CD34 + cell isolation. **HSC freezing and storage has a history of more than 30 years at the BTC** and has developed in parallel with the bone marrow transplantation programme at University Medical Centre Ljubljana.

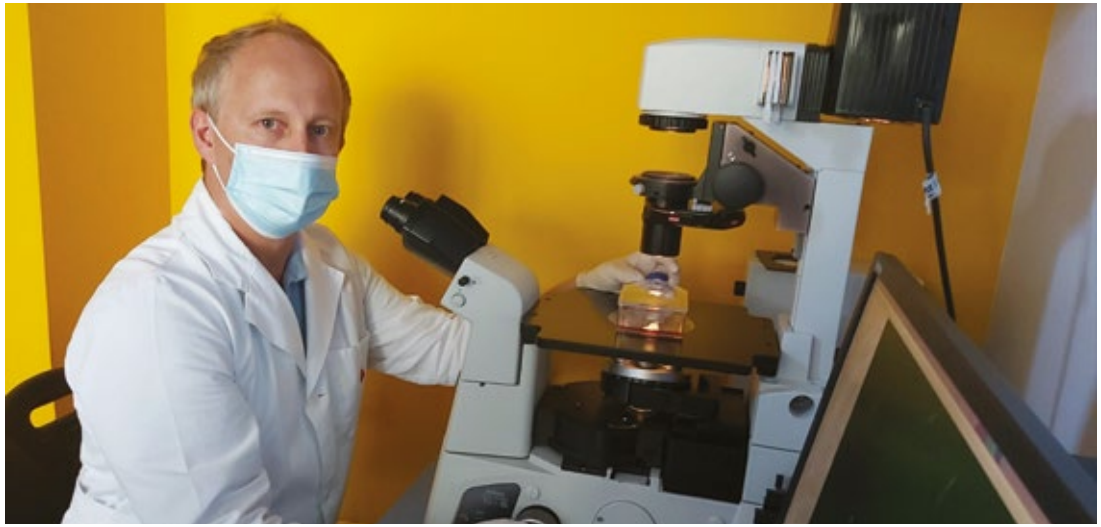
The indications for freezing and storing cells are spreading. Originally associated with blood diseases, they are now used for a wide range of diseases, from solid tumours to autoimmune diseases. Cells are also frozen and processed for the pharmaceutical industry (e.g. mononuclear cells for CAR -T cell production). Due to higher cell dose requirements and the number of desired transplants, the amount of stored cells per patient is increasing.

Center za kriobiologijo je v zadnjih nekaj letih vpeljal najsodobnejše postopke obdelave celic po zgledu naprednih centrov na zahodu. Leta 2020 je tudi pridobil **akreditacijo JACIE za procesiranje celic**, kar pomeni potrditev odličnosti na mednarodni ravni in zagotavlja najvišji nivo kakovosti in varnosti. Kontrole procesa, ki jih je uvedel JACIE, med drugim zahtevajo beleženje in poročanje časov regeneracije celic po avtologni transplantaciji KMC vsako četrtletje, fizično preverbo vrečk presadka v kriobanki pred začetkom mieloablativne kemoterapije v okviru transplantacije itd.

Osebje zaposleno v CK je visoko usposobljeno in predano izključno področju obdelav in shranjevanja celic in tkiv ter pripravi zdravil za napredna zdravljenja, kar je pogoj za zagotavljanje najvišje kakovosti zahtevnih postopkov dela. Že od leta 2000 obdelujemo in shranjujemo amnijsko membrano za zdravljenje roženičnih okvar. Trombocitni gel pripravljamo za pospeševanje in zdravljenje kostnih zlomov in kožnih razjed. **Imunoselekcija celic CD34+**, ki je pomemben postopek obdelave presadkov krvotvornih matičnih celic in za regenerativno medicino, je bila prvič opravljena že leta 2006, takrat na aparatu Isolex, pozneje pa se je izvajala na Clinimacsu in je med našimi storitvami tudi danes. Ena od storitev, ki so bile razvite v zadnjih letih, so **avtologne serumske kapljice**, ki jih uporabljajo bolniki s sindromom suhega očesa (Sjoegrenov sindrom, GVHD ...).

In recent years, the Centre for Cryobiology has introduced state-of-the-art cell treatment procedures, following the example of advanced centres in the West. In 2020, it also received **JACIE accreditation for cell processing**, which is a confirmation of excellence at an international level and ensures the highest level of quality and safety. The process controls put in place by JACIE require, among other things, quarterly recording and reporting of cell regeneration times after autologous HSC transplantation, physical verification of graft bags in a cryobank before the start of myeloablative chemotherapy as part of transplantation, and so on.

The staff in CC is highly qualified and dedicated exclusively to the field of processing and storage of cells and tissues, as well as the preparation of drugs for advanced treatments, which is a prerequisite for ensuring the highest quality of sophisticated workflows. Since 2000, **amniotic membrane** has been prepared and stored for the treatment of corneal defects. **Platelet gel** is prepared to accelerate the healing of bone fractures and skin ulcers. **Immunoselection of CD34 + cells**, which is an important process for the treatment of haematopoietic stem cell transplantation and for regenerative medicine, was first performed in 2006, then on the Isolex machine, later on CliniMACS, and is still one of our services today. One of the services developed in recent years is **autologous serum eye drops** used by patients with dry eye (Sjoegren's syndrome, GVHD ...).



Pri razvoju celičnih terapij in zdravil za napredno zdravljenje je ključno povezovanje CK z drugimi organizacijskimi enotami znotraj OTS in celotnega ZTM kot tudi z različnimi kliničnimi oddelki. Dober primer takšnega sodelovanja je gojenje mezenhimskih matičnih celic za zdravljenje bolezni presadka proti gostitelju (GVHD), poškodb hrbtenjače, zavrnitve presajenega organa, osteoartroze itd. Plod tega sodelovanja so tudi **virusno specifični limfociti (EBV in CMV)** in **limfocitno osiromašeni presadki KMC (alfa beta deplecija)**. Oba celična pripravka smo validirali na **platformi Prodigy**.

Med epidemijo covida-19 smo zaradi priporočil mednarodnih strokovnih združenj začeli tudi z **zamrzovanjem alogenskih celičnih proizvodov**, kar omogoča predvidljivejše in varnejše transplantacije KMC. Obseg dela se je zato v zadnjem času povečal, število bolnikov, katerih celične pripravke hranimo v kriobanki, pa stabilno raste kar terja tudi ustrezno širitev naših kapacitet. Storitve kriobanke so ključne za izvajanje transplantacijske dejavnosti, regenerativne medicine in imunoterapije v celotnem slovenskem prostoru. V prihodnje želimo z vzpostavitvijo proizvodnje celic **CAR-T na platformi Prodigy** prav tako povečati zmogljivost naših proizvodnih prostorov za gojenje celic in še naprej optimizirati obstoječe in razvijati nove postopke obdelav celic in tkiv.

In the development of cell therapies and advanced therapy medicines, the networking of CC with other organisational units within the DTS and across the BTC, as well as with various clinical departments, is crucial. A good example of such collaboration is the cultivation of mesenchymal stem cells for the treatment of graft-versus-host disease, spinal cord injury, organ transplant rejection, osteoarthritis and others such issues. The fruits of this collaboration are also **virus-specific lymphocytes (EBV and CMV)** and **lymphocyte-depleted HSC grafts (alpha-beta depletion)**. Both cell preparations were validated on the **Prodigy platform**.

During the COVID-19 epidemic, based on the recommendations of international professional societies, we also started **freezing allogeneic cell products**, which allows for more predictable and safer HSC transplantation. The scope of work has therefore increased recently, and the number of patients whose cell preparations are stored in a cryobank is constantly growing, which also requires a corresponding expansion of our capacities. The Cryobank services are crucial for the implementation of transplantation, regenerative medicine and immunotherapy throughout Slovenia. With the establishment of **CAR -T cell production on the Prodigy platform**, we also aim to increase the capacity of our cell culture production facilities in the future and further optimise existing and new cell and tissue treatment processes.

CENTER ZA RAZVOJ NAPREDNIH ZDRAVLJENJ je osredotočen na razvoj, proizvodnjo in izvajanje kliničnih študij na področju Zdravil za napredna zdravljenja. **Zdravila za napredna zdravljenja (ZNZ)** je prevod angleške skovanke *Advanced Therapy Medicinal Products* (ATMPs), s katero je to novo generacijo zdravil poimenovala Evropska agencija za zdravila (EMA). Mednje sodijo zdravila za gensko zdravljenje in celično zdravljenje, tkivno inženirski proizvodi in kombinirana ZNZ.

Razvoj dejavnosti v preteklih letih je omogočil, da izdelava ZNZ poleg diagnostičnih storitev in preskrbe s krvjo prehaja med osnovne dejavnosti ZTM. Zaradi pomembnosti te dejavnosti smo trenutno v postopku pridobitve dovoljenja za proizvodnjo zdravil za namen kliničnega preskušanja. Mejnikov, ki so transfuzijsko dejavnost vedno močneje postavljali v te tirnice, je več in težko izpostavimo najpomembnejšega. Že osnovna transfuzijska dejavnost je močno povezana s celično terapijo, torej terapijo z eritrociti. Temu je sledil izjemen premik pri zdravljenju hematoloških bolezni s transplantacijo in zdravljenjem s KMC. Lahko bi rekli, da so se glavni premiki v mišljenju na področju ZNZ začeli leta 2014 z uvedbo postopka zunajtelesne fotofereze.

Zunajtelesna fotofereza je odvzem pacientovih levkocitov in njihova obdelava *ex vivo*, česar prej nismo počeli. Limfociti, na katere v postopku najbolj vplivamo, po vrnitvi v bolnika izkazujejo imunosupresiven učinek. V tem smislu gre za prvo celično imunoterapijo, ki smo jo opravljali.

CENTER FOR DEVELOPMENT OF ATMPs is focused on development, manufacture and implementation of clinical studies in the field of Advanced Therapy Medicinal Products. With the term **Advanced Therapy Medicinal Products (ATMPs)**, the European Medicines Agency (EMA) has named a new generation of medicines which include gene therapy medicines, somatic-cell therapy medicines, tissue-engineered medicines and combined ATMPs.

The development of activities in recent years has led to the production of ATMPs becoming one of BTC's fundamental activities, alongside diagnostic services and blood supply. Due to importance of this activity we are currently in the process of obtaining a GMP manufacturing authorization for investigational ATMPs. There are several milestones that have increasingly placed the transfusion activity on this line, and it is difficult to highlight the most important ones. Already, the basic transfusion activity is strongly linked to cell therapy, i.e. red cell transfusion. There followed a remarkable shift in the treatment of haematological diseases, transplantation and treatment with HSC. One could say that the most important upheavals in the field of ATMPs began in 2014 with the introduction of extracorporeal photopheresis.

Extracorporeal photopheresis is taking leukocytes from a patient and processing them *ex vivo*, something we had not done before. The lymphocytes most affected in this process show an immunosuppressive effect after they are administered back to the patient. In this sense, this is the first cellular immunotherapy we have performed.

V letu 2018 smo stopili na področje regenerativne medicine z vpeljavo prvih proizvodov na osnovi **mezenhimskih matičnih celic (MMC)**. MMC izražajo številne koristne učinke. So kot majhne biološke tovarne, ki na mestu poškodbe izločajo biomolekule in pospešujejo regeneracijo. So tudi izrazito imunomodulatorne. V istem letu smo pripravili prvi odmerek za zdravljenje pacienta, ki je trpel zaradi bolezni presadka proti gostitelju. Kmalu smo se povezali s KO za travmatologijo in vse do danes proizvajamo MMC za zdravljenje poškodb hrbtenjače. Med pisanjem tega prispevka smo v klinično študijo vključili že desetega pacienta. Z MMC, ki smo jih pripravili na ZTM, so se do danes zdravili tudi pacienti v estetski kirurgiji in na KO za nefrologijo za zdravljenje humoralne zavrnitve ledvice. Potekajo tudi priprave za začetek kliničnih študij zdravljenja osteoartritisa kolena z MMC ter uporabe MMC za zdravljenje parodontalnih bolezni.

In 2018, we entered the field of regenerative medicine with the launch of the first **mesenchymal stem cell (MMC)-based products**. MMCs express a range of beneficial effects. They are like small biological factories that secrete biomolecules at the site of injury and accelerate regeneration. They are also strong immunomodulators. That same year, we prepared the first dose to treat a patient suffering from graft-versus-host disease. Soon, we joined forces with the Department of Traumatology and continue to produce MMC for the treatment of spinal cord injuries to this day. At the time of writing, we have enrolled a tenth patient in a clinical trial. Thus far, patients undergoing cosmetic surgery and in the Department of nephrology have also been treated with MMCs manufactured at BTC for the treatment of humoral renal rejection. Preparations are also underway to start clinical trials for the treatment of knee osteoarthritis and periodontal diseases with MMCs.

Konec leta 2019 je bil pomembna prelomnica za OTS. Pridobili smo platformo za avtomatizirano gojenje in obdelavo celic v zaprtem sistemu (CliniMACS Prodigy®). S tem so se za ZTM odprle številne možnosti in seveda izzivi za izdelavo novih in tehnološko zahtevnih ZNZ. V preteklem letu smo v tem smislu vzpostavili proizvodnjo za izdelavo ZNZ na osnovi **virusno specifičnih limfocitov T** za zdravljenje nenadzorovanih okužb različnih patogenov (citomegalo virus, Epstein-Barr in adenovirus). Zelo pomemben projekt za v prihodnje je sodelovanje s KO za hematologijo za vpeljavo proizvodnje **zdravila za gensko zdravljenje CD19 CAR-T**. Gre za ZNZ, pri katerem limfocite oborožimo s himernim antigenskim receptorjem, ki specifično prepozna tumorske celice določenih hematoloških rakov. Terapija je zelo pomembna, saj kaže izjemno klinično odzivnost in visok odstotek pacientov, drugače »obsojenih« na smrt, doseže popolno remisijo. Z vpeljavo lokalne proizvodnje CD19 CAR-T bi se dostopnost zdravila za slovenske paciente povečala, kakor tudi nabor potencialnih indikacij.

Razvoj in izdelava visokokakovostnih ZNZ na ZTM predstavljata velike obete za prihodnost zdravljenja slovenskih pacientov. S to dejavnostjo se namreč pridružujemo najrazvitejšim transfuzijskim in hematološkim centrom ter postavljamo temelje na področju, ki kaže nedvoumno rast v vseh državah razvitega sveta.

The end of 2019 was an important turning point for OTS. We acquired a platform for automated cell culture and processing in a closed system (CliniMACS Prodigy®). This opened many opportunities and, of course, challenges for the BTC to develop new and technologically sophisticated ATMPs. Last year, we established production for the manufacture of ATMPs based on **virus-specific T lymphocytes** for the treatment of uncontrolled infections of various pathogens (cytomegalovirus, Epstein-Barr virus, and adenovirus). A very important project for the future is the collaboration with the Department for haematology to introduce the production of the **gene therapy CD19 CAR-T**. This is an ATMP that can be used for the treatment of cancer. It consists of lymphocytes that are equipped with a chimeric antigen receptor that specifically recognises tumour cells of certain haematological cancers. The therapy is very important, as it shows exceptional clinical response and a high percentage of patients otherwise "sentenced" to death achieve complete responses. The introduction of local production of CD19 CAR -T would increase the availability of the drug to Slovenian patients, as well as the number of possible indications.

The development and production of high-quality ATMPs at the BTC represents a great perspective for the future of treatment of Slovenian patients. With this activity we join the most developed transfusion and haematology centers and lay the foundation in a field that is clearly growing in all countries of the developed world.

Razvoj in izdelava visokokakovostnih zdravil za napredna zdravljenja na ZTM predstavljata velike obete za prihodnost zdravljenja slovenskih pacientov. S to dejavnostjo se namreč pridružujemo najrazvitejšim transfuzijskim in hematološkim centrom ter postavljamo temelje na področju, ki kaže nedvoumno rast v vseh državah razvitega sveta.

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PRESKRBA Z ZDRAVILI IZ KRVI

SUPPLY OF PLASMA-DERIVED MEDICINAL PRODUCTS

Marjana Rus Iskra

Začetki Farmacevtskega oddelka, ki je bil ustanovljen za pripravo ohranitvenih raztopin za kri in krvne pripravke ter medicinskih pripomočkov za potrebe ZTM, segajo od ustanovitve Zavoda za transfuzijo krvi. Z razvojem farmacije ter dvigom zahtev glede kakovosti in večje dosegljivosti komercialnih izdelkov se je Farmacevtski oddelek leta 2004 reorganiziral in preimenoval v **Center za oskrbo in promet z zdravili in medicinskimi pripomočki (COPZMP)**. Skladno z zakonodajo je istega leta opravil verifikacijo s strani Javne agencije RS za zdravila in medicinske pripomočke ter pridobil dovoljenje za opravljanje prometa z zdravili na debelo. Od takrat uspešno oskrbujemo slovenske bolnišnice in javno lekarniško mrežo v RS skladno z:

- Zakonom o zdravilih in podzakonskimi predpisi,
- Direktivo 2001/83/ES,
- Smernicami dobre distribucijske prakse (DDP),
- Pravilnikom o farmakovigilanci zdravil za uporabo v humani medicini,
- Uredbo EU 2016/161 o uporabi zaščitnih elementov na ovojnini zdravil za uporabo v humani medicini.

MARJANA RUS ISKRA

mag. farm., spec. za oblikovanje zdravil /
MS in Pharm., Spec. for forming medicinal products

Predstojnica Centra za oskrbo in promet z zdravili in medicinskimi pripomočki
Head of the Centre for the Supply and Trade of Medicinal Products and Medical Devices

The Pharmaceutical Department was originally set up to produce anticoagulant solutions for blood, blood-derived products and medical devices for the needs of Blood Transfusion Centre of Slovenia (BTC). It was established at the very beginning of the BTC. With developing pharmacy, the increase of requirements for quality and the greater availability of commercial products, the Pharmaceutical Department was reorganised in the year 2004 and renamed as the **Centre for the Supply and marketing of medicinal product and medical devices (COPZMP)**. Under legislation, in the same year, it was reviewed by the Agency for Medicinal Products and Medical Devices of the Republic of Slovenia and obtained a licence for wholesale distribution of medicinal products. Since then, we have been successfully supplying Slovenian hospitals and the public pharmacy network in the Republic of Slovenia under:

- Medicinal Products Act and other Regulations,
- Directive 2001/83/EC,
- Guidelines for Good Distribution Practise (GDP),
- Rules on Pharmacovigilance of Medicinal Products for Human Use,
- EU Regulation 2016/161 on detailed rules for the safety features appearing on the packaging of medicinal products for human use.

Slovenski trg oskrbujemo z zdravili iz krvi in rekombinantnimi koagulacijskimi faktorji, kot so **albumini, polispecifični in specifični imunoglobulini ter krvni koagulacijski faktorji**, ki kot biološka zdravila zahtevajo poseben režim shranjevanja in transporta. Vsako pošiljko zdravil natančno pregledamo, preverimo njeno avtentičnost skladno s preprečevanjem vstopa ponaredkov na trg, pridobimo evropski sprostitveni certifikat (OCABR), opravimo posebno kontrolo kakovosti in ob izpolnjevanju vseh zahtev odgovorna oseba sprosti zdravilo na trg. Za vsa zdravila, ki jih distribuiramo, imamo vzpostavljen sistem farmakovigilance.

COPZMP že vrsto let izvaja organiziran sistem oskrbe z zdravili iz krvi, ki sloni na nacionalnem programu preskrbe s krvjo. **Bolnikom zagotavlja kakovostna, varna in učinkovita zdravila iz krvi, izdelana iz humane plazme, zbrane od prostovoljnih neplačanih krvodajalcev v RS.** Namenjena so zdravljenju redkih bolezni, katerih vzrok je večinoma v genskih pomanjkljivostih, ki se pojavijo v otroštvu in so pogosto doživljenjske. Glede na stalne izboljšave v diagnostiki in daljši pričakovani življenjski dobi bo tudi v prihodnje potrebnih vedno več zdravil proizvedenih iz plazme, s čimer bo potreba po plazmi za frakcioniranje vse večja. ZTM letno zbere v povprečju 18.500 l humane plazme za frakcioniranje, kar je premalo za pokritje vseh potreb po zdravilih, ki vsebujejo humani polispecifični imunoglobulin za intravensko aplikacijo in albumin.

We supply the Slovenian market with medicinal products derived from plasma and recombinant coagulation factors, such as **albumins, polyspecific and specific immunoglobulins and blood coagulation factors**. As biological medicinal products, these require a special storage and transport regime. We carefully check each shipment of medicinal products, verify their authenticity in terms of counterfeit protection, obtain a European Certificate of Official Control Authority Batch Release (OCABR), carry out a special quality control process and release the medicinal product to the market if all requirements are met. We have established a pharmacovigilance system for all the medicinal products we distribute.

COPZMP has been for many years implementing an organised supply plasma- derived medicinal products system based on the National Blood Supply Programme. **It provides patients with high-quality, safe and effective medicinal products produced from human plasma that is collected from voluntary, unpaid blood donors in the Republic of Slovenia.** They are intended to treat rare diseases, most of which are caused by genetic defects that occur in childhood and are often lifelong. Because of the constant improvements in diagnostics and the extension of life expectancy, many patients will need more therapies, which will require more plasma-derived medicinal products and therefore an increasing need for human plasma for fractionation. BTC collects an average of 18,500 litres of human plasma for fractionation each year, which is insufficient to meet all the demand for medicinal products containing human polyspecific immunoglobulin for intravenous administration and albumin.

Glede na stalne izboljšave v diagnostiki in daljši pričakovani življenjski dobi bo tudi v prihodnje potrebnih vedno več zdravil proizvedenih iz plazme, s čimer bo potreba po plazmi za frakcioniranje vse večja.

Because of the constant improvements in diagnostics and the extension of life expectancy, many patients will need more therapies, which will require more plasma-derived medicinal products and therefore an increasing need for human plasma for fractionation.

V okviru **javne službe** ter skladno z navodili Ministrstva za zdravje RS (MZ) in določili Splošnega dogovora z Zavodom za zdravstveno zavarovanje Slovenije oskrbujemo skladno z razdelilnikom, ki ga pripravi MZ, bolnišnice z zdravili (albumini, polispecifičnim imunoglobulinom in protrombinskim kompleksom), izdelanimi le iz plazme, zbrane v RS, ki ustrezajo zahtevam Evropske farmakopeje. Obenem smo zadolženi za **zbiranje podatkov o porabi in zalogah teh zdravil po slovenskih bolnišnicah**, ki jih mesečno posredujemo MZ.

Z zdravili izdelanimi iz plazme, zbrane v RS, pokrijemo približno 55–60 % potreb bolnišnic po teh zdravilih. Globalno se pojavljajo težave pri preskrbi s polispecifičnim imunoglobulinom za intravensko aplikacijo, ki je vodilna učinkovina v EU in tudi v RS, saj njegova poraba ves čas narašča, vendar je njena dobavljivost mnogokrat nepredvidljiva. Zato sistem razdeljevanja zdravil izdelanimi iz plazme, zbrane v RS, zagotavlja enakovreden in dokaj stabilen dostop vseh slovenskih bolnišnic do navedenih zdravil iz krvi.

Posamezne evropske države imajo v svoji strategiji cilj doseči čim večjo strateško neodvisnost.

Within the **public service** and under the instructions of the Ministry of Health (MH) and the General Agreement with the Health Insurance Institute of Slovenia, we supply hospitals with medicinal products (albumins, polyspecific immunoglobulins and prothrombin complex) produced only from plasma collected in the Republic of Slovenia which meets requirements of the European Pharmacopoeia. We collect **consumption and stocks data of these medicinal products in Slovenian hospitals**, which we report each month to the MH.

Approximately 55–60% of the hospitals' need for these medicinal products is covered by plasma collected in the Republic of Slovenia. Globally, there are problems with the supply of polyspecific immunoglobulin for intravenous administration, the leading active ingredient from plasma, in both the EU and the Republic of Slovenia. Its consumption and demand is constantly increasing, but its availability is often unpredictable. Therefore, the distribution system for medicinal products from human plasma collected in the Republic of Slovenia provides all Slovenian hospitals with equal and stable access to these medicines.

In their strategy, individual European countries strive for the greatest possible strategic independence.

Tudi ZTM se bo ravno zaradi nepredvidljivosti in morebitnega pomanjkanja polispecifičnega imunoglobulina za intravensko aplikacijo v sodelovanju z MZ trudil pridobiti čim večjo samozadostnost na področju zdravil iz krvi.

Due to the unpredictability and possible shortage of polyspecific immunoglobulin for intravenous administration, the BTC, in cooperation with the MH, will also strive for maximum self-sufficiency in plasma-derived medicinal products.

COPZMP oskrbuje ZTM in pridružene Centre za transfuzijsko dejavnost (CTD) z **medicinskimi pripomočki oziroma diagnostičnimi reagenti** ter **pripravlja laboratorijske raztopine, demineralizirano vodo in opravlja storitve sterilizacije za potrebe ZTM.** Oskrba ZTM in CTD poteka skladno z zahtevami Zakona o medicinskih pripomočkih in DDP, kar je večkrat letno preverjeno z notranjimi in zunanjimi presojami (JAZMP, ISO, JACIE).

Za potrebe celotnega ZTM pripravimo letno več kot 40.000 l demineralizirane vode, ki jo analiziramo skladno z zahtevami Evropske farmakopeje. Izvajamo tudi postopek parne sterilizacije za potrebe ZTM in CTD.

Za Zavod RS za blagovne rezerve (ZRSBR) COPZMP skladišči in obnavlja **državne blagovne rezerve zdravil iz krvi in vrečk za zbiranje krvi**, kar letno preverja ZRSBR.

COPZMP supplies **medical devices or diagnostic reagents** to BTC and associated Blood Transfusion Units (BTU) and **prepares laboratory solutions, demineralised water and provides sterilisation services for the needs of the BTC.** The BTC and PTCs are supplied according to the Medical Devices Act and the GDP, which are verified several times a year through internal and external audits (JAZMP, ISO, JACIE).

Each year we prepare over 40,000 l of demineralised water for the needs of the entire BTC, which is analysed according to the European Pharmacopoeia. We also carry out the process of steam sterilisation for the needs of the BTC and BTUs.

For the Agency of the Republic of Slovenia for Commodity Reserves (ZRSBR), COPZMP stores and replenishes the **state commodity reserves of plasma derived medicinal products and blood collection bags**, which are checked annually by ZRSBR.

3.

TRANSFUZIJSKA DEJAVNOST MED EPIDEMIJO COVIDA-19

TRANSFUSION ACTIVITY DURING THE COVID-19 EPIDEMIC

Polonca Mali
Natalija Lampreht
Ana Milojković
Irena Razboršek

V Sloveniji je bila epidemija covida-19 razglašena 12. marca 2020, s tem pa tudi uvedba številnih ukrepov za zajezitev širjenja okužbe na vseh področjih javnega življenja. Kljub izrednim razmeram in okrnjenim zdravstvenim programom so bolniki potrebovali nujna in neodložljiva zdravljenja in storitve; tako so še vedno potrebovali zdravljenje s krvjo, celicami in tkivi pa tudi diagnostične storitve. Zaradi zagotavljanja oskrbe in storitev je transfuzijska služba morala nemudoma uvesti postopke, s katerimi smo lahko zagotovili varno okolje za zaposlene, paciente in krvodajalce. Takoj ob pojavu novega koronavirusa je bilo ugotovljeno, da se **s transfuzijo krvi bolezen covid-19 ne prenaša, kar je omogočilo preskrbo s krvjo brez uvedbe dodatnih testov.**

Ukrepe, navodila in prilagoditve je sprejemal krizni tim na ZTM v sodelovanju s Komisijo za obvladovanje bolnišničnih okužb in skladno z navodili Ministrstva za zdravje RS in ukrepi Vlade RS. Krizni tim na ZTM sta imenovala v. d. direktorja Stevo Lekič in v. d. strokovne direktorice prim. Snežna Levičnik Stezinar (10. marca 2020). V krizni tim so bili imenovani naslednji sodelavci: vodja Polonca Mali in drugi člani: Irena Razboršek, Urška Rahne Potokar, Nataša Lovšin, Natalija Lampreht in Iztok Krumpak. Njegovi nalogi sta bili izvajanje in koordinacija delovanja ZTM in tudi transfuzijske službe v Sloveniji, zlasti na področju zagotavljanja nemotene preskrbe s krvjo.

In Slovenia, the COVID-19 epidemic was declared on 12 March 2020, initiating a series of measures to contain the spread of the infection in all areas of public life. Despite the state of emergency and the restricted medical programme, patients needed urgent and emergency treatment and services. For example, patients continued to require blood, cell and tissue therapies as well as diagnostic services. To provide care and services, the Transfusion Service had to implement procedures virtually overnight that allowed us to create a safe environment for staff, patients and blood donors. Immediately after the coronavirus outbreak, it was established that **COVID-19 was not transmitted by blood transfusion, which allowed us to continue blood supply without the introduction of additional tests.**

The Crisis Team took measures, instructions and adjustments at the BTC in cooperation with the Commission for prevention and control of hospital infections and in accordance with the instructions of the Ministry of Health and measures of the Government of the Republic of Slovenia. The Crisis Team was appointed by the Acting Director Stevo Lekič and the Acting Medical Director Snežna Levičnik Stezinar (10 March 2020). The following were appointed to the crisis team: the head Polonca Mali, other members: Irena Razboršek, Urška Rahne Potokar, Nataša Lovšin, Natalija Lampreht and Iztok Krumpak. The team's tasks were to implement and coordinate the all activities of the BTC and the Transfusion Service in Slovenia, especially in ensuring an uninterrupted blood supply.

Zaradi zagotavljanja oskrbe in storitev je transfuzijska služba morala skoraj čez noč uvesti postopke, s katerimi smo lahko zagotovili varno okolje za zaposlene, paciente in krvodajalce.

To provide care and services, the Transfusion Service had to implement procedures virtually overnight that allowed us to create a safe environment for staff, patients and blood donors.

MATINA

Na vseh področjih delovanja ZTM smo prilagodili procese in organizacijo dela tako, da smo v največji možni meri zadostili pogojem za preprečevanje širjenja okužb, kot so: zmanjšanje števila prisotnih oseb, vzpostavitev dela na domu, zagotovitev rezervnega osebja, ki lahko nadomesti delujočo ekipo ob okužbi, preprečevanje križanj poti bolnikov, krvodajalcev in osebja, zagotavljanje varnih stikov in razdalje med osebjem, dosledno izvajanje higienskih standardov v zdravstvu, uvedba uporabe osebne varovalne opreme za zaposlene in krvodajalce ter preverjanje in spremljanje zdravstvenega statusa zaposlenih, krvodajalcev in uporabnikov naših storitev (vzpostavitev triažne vstopne točke), in vpeljali redno tedensko testiranje osebja s hitrimi antigenskimi testi. Ves čas smo vzpodbujali odgovorno vedenje vsakega posameznika.

Kot del zdravstvenega sistema smo na ZTM ves čas epidemije delovali neprekinjeno ter se prilagajali naročilom naših storitev in zdravljenju pacientov. Tako smo opravljali večino diagnostičnih pa tudi terapevtskih storitev.

Zagotavljali smo vse predtransfuzijske in druge imunohematološke preiskave, preiskave v okviru programa vodenja nosečnosti, vse storitve za zagotavljanje nemotene transplantacijske dejavnosti in preiskave v zvezi z določanjem označevalcev okužb. Zaradi pojava covida-19 smo v okviru diagnostičnih storitev uvedli nove laboratorijske preiskave, npr. kvantitativno določitev protiteles proti virusu SARS-CoV-2 tako pri krvodajalcih kot samoplačnikih, in vzpostavili izvedbo hitrih antigenskih testov za ugotavljanje prisotnosti okužbe s covidom-19 pri vseh, ki so vključeni v nacionalno podatkovno bazo (z-VEM).

Med epidemijo smo posebno skrb namenili obravnavi bolnikov na Oddelku za terapevtske storitve. Zaradi oblike bolezni teh bolnikov je zdravljenje potekalo neprekinjeno pod dodatnimi zaščitnimi pogoji in ukrepi pri zaposlenih in bolnikih. Zaradi preventivne izolacije bolnikov smo vpeljali tudi nekaj organizacijskih sprememb za dodatno ločevanje bolnikov od krvodajalcev, uvedli pa smo tudi redno testiranje bolnikov na SARS-CoV-2 s testom PCR pred prihodom. Kot dodatni varovalni ukrep smo uvedli zaščitna oblačila (predpasnik) za daljše intervencije in tudi zaščitna očala pri zaposlenih.

In all areas of BTC activities, we have adapted procedures and work organisation to create the conditions for preventing the spread of infection as much as possible: reducing the number of people present, encouraging work from home, providing back-up substitute staff in case of staff morbidity, providing a separate pathways for patients, blood donors, and staff, ensuring safe distances and contacts between staff, consistently implementing healthcare hygiene standards, introducing personal protective equipment for staff and blood donors, checking and monitoring the health status of staff, blood donors, and customers (COVID-19 screening check point) and introducing regular weekly testing of staff with rapid antigen tests. We have constantly promoted the responsible behaviour of each individual.

As part of the health system, we at BTC were in continuous operation throughout the epidemic, adapting our services to patients needs and customers. Thus, we performed most of the diagnostic as well as therapeutic services.

We provided all pre-transfusion and other immunohaematological testing, prenatal testing as part of pregnancy management programme, all services to support transplantation programmes, as well as tests for infectious markers detection. Due to the emergence of COVID-19, we introduced new laboratory tests in the area of diagnostic services, such as the quantitative determination of antibodies against SARS-CoV-2 for blood donors and customers. We have introduced rapid antigen tests to detect COVID-19 infection for staff and patients, the results of which are included in the national database (z-VEM).

During the epidemic, patients in the Department of Therapeutic Services were given a special attention and care. Because of the patients' conditions, treatment was continuously carried out under additional protective conditions and measures among staff and patients. To provide the preventive isolation of patients, we also performed some reorganisation to further separate patients from the blood donor population, as well as introducing the regular testing of patients for SARS-CoV-2 with a real-time polymerase chain reaction (PCR) swab test before arrival. Protective clothing (apron) in case of prolonged care for patients and protective glasses for staff were additionally introduced as protective measures.

Že prvi tedni epidemije so pokazali, da bo ta bistveno vplivala tudi na področje transplantacij krvotvornih matičnih celic (KMC). Zato je združenje EBMT (ang. *The European Society for Blood and Marrow Transplantation*) začelo izdajati redna priporočila za transplantacijske centre, odvzemne centre in registre darovalcev kostnega mozga (v sodelovanju z WMDA, ang. *World Marrow Donor Association*). Med prvimi priporočili sta bila zamrzovanje vseh pripravkov KMC za alogensko transplantacijo in začetek kondicioniranja bolnika šele, ko je zagotovljen varen pripravek. Skladno s tem smo za bolnike z načrtovano transplantacijo KMC krvodajalčeve odvzete celice za določen čas zamrznili. Kljub posameznim poročilom o določenem številu neuporabljenih pripravkov je večina centrov ugotavljala, da ni razlike v kliničnem poteku stanja bolnikov po presaditvi z zamrznjenimi pripravki v primerjavi s svežimi, kar je bila praksa do sedaj. **Ta ugotovitev bi lahko bila pomembna in uporabna z vidika povečanja varnosti in dostopnosti pripravkov tudi po epidemiji.**

In the first weeks of the epidemic, it had already become apparent that it would also have a significant impact in haematopoietic stem cell transplant programmes (HSC). So the EBMT (The European Society for Blood and Marrow Transplantation) has started to issue regular recommendations for transplant centres, collection centres and bone marrow donor registries (in collaboration with the WMDA – *World Marrow Donor Association*). One of the first recommendations was to freeze all HSC units for allogeneic transplantation and not to start conditioning the patient until a safe unit is available. In accordance with the recommendations, in patients with planned HSC transplantation, donors' harvested cells were frozen for a certain period of time. Despite individual reports of a certain number of unused units, most centres found that there was no difference in the clinical outcome of patients after transplantation with frozen units compared to fresh units, as had previously been the practice. **This finding could also be important and useful for increasing safety and availability of units after the epidemic.**

Največje prilagoditve, spremembe in izzive pa je epidemija prinesla pri preskrbi s krvjo v procesu zbiranja krvi, ki je moral potekati brez prekinitve.

The epidemic has created the greatest adjustments, changes and challenges in blood supply within the process of blood collection, which had to continue without interruption.

Hayco

Že konec februarja 2020 smo prilagodili merila za izbor krvodajalcev, ki smo jih ažurno dopolnjevali in prilagajali glede na epidemiološko stanje v državi in regiji. Uvajali in povečevali smo varnostne ukrepe v prostorih, kjer se izvaja darovanje krvi, tako na terenskih krvodajalskih akcijah kot v transfuzijskih centrih. Uradna razglasitev epidemije je korenito zarezala v naše procese, organizacijo in delovanje. Čez noč smo prešli s klasičnega vabljenja krvodajalcev na SMS-pozive in dogovore o mestu in uri odvzema. Dodatna vprašanja krvodajalcem in osebju o zdravstvenem stanju so postala stalnica v našem vsakdanu. Osebna varovalna oprema, ki je žal prihajala postopoma in v nezadostnih količinah, je sicer omogočila izvajanje vseh procesov. Usmerjeni smo bili predvsem v zagotavljanje varnega okolja za krvodajalce, da jih strah pred možnostjo okužbe ne bi odvrnil od prihoda. Tudi zato smo uvedli uporabo zaščitnih mask pri krvodajalcih, ki smo jih v prvem valu zaradi težav pri nabavi izdelovali kar sami.

Na datum razglasitve epidemije smo imeli zadovoljive zaloge krvi, ki pa so se že v naslednjem tednu prepolovile, saj se je močno zmanjšalo število odvzemov zaradi uvajanja ukrepov in prilagoditev.

Potrebe po krvi se niso toliko zmanjšale, kot smo glede na zaustavitev programov v zdravstvu sprva predvideli, zato je bilo treba zagotoviti stalen prihod krvodajalcev in ustrezno količino krvi. Krvodajalske akcije smo izvajali po letnem načrtu, prilagojeno in skladno z vsemi zahtevanimi zaščitnimi ukrepi za preprečevanje širjenja okužbe.

At the end of February 2020, we had already updated the donor eligibility criteria according to the epidemiological situation in the country and the region. All needed prevention and protection safety measures in fixed and mobile collection sites were introduced. The official announcement of the epidemic has radically interfered with our processes, organisation and way of working. Overnight, we changed from the "classic" invitation of blood donors to SMS invitations and appointment scheduling. Additional questions about health to blood donors and staff have become a daily routine for us. The personal protective equipment, which unfortunately only arrived gradually and in insufficient quantities, otherwise enabled all processes to be carried out. Our primarily focus was creating a safe environment for blood donors to eliminate their fear of possible infection and to encourage them to come. Face masks for blood donors were immediately introduced at the beginning. Due to interrupted face mask supply, masks were made onsite in BTC in Ljubljana.

When the epidemic was declared, blood stocks were sufficient, but had already halved the following week, as the number of collections was drastically reduced due to the measures and adjustments put in place.

The demand for blood did not decrease as much as we had initially expected, given the suspension of other health programmes. Therefore, it was necessary to ensure the constant arrival of blood donors and a sufficient blood supply. The blood donation sessions were carried out according to the annual plan, adapted and in compliance with all necessary protective measures to prevent the spread of infection.

Usmerjeni smo bili predvsem v zagotavljanje varnega okolja za krvodajalce, da jih strah pred možnostjo okužbe ne bi odvrnil od prihoda.

Our primarily focus was creating a safe environment for blood donors to eliminate their fear of possible infection and to encourage them to come.


051 389 325
POMEMBNO OBVESTILO,
OBVEZNO JE NAROČILO!
#darujkri
#darujvarno

Prva terenska krvodajalska akcija, ki smo jo uspešno organizirali pod spremenjenimi pogoji med epidemijo, je bila na Vrhniki (18. marca 2020). Način organiziranja krvodajalske akcije in prve izkušnje so prevzeli v centrih za transfuzijsko dejavnost ZTM pa tudi v Centru za transfuzijsko medicino UKC Maribor in Transfuzijskem centru SB Celje. V nekaj dneh smo prešli na popolnoma drugačno organizacijo krvodajalcev in kljub epidemiji pri tem prestopili na višjo raven – prihod na odvzem krvi ob dogovorjeni uri. Vzpostavili smo kontaktni telefon, ki je deloval 24 ur na dan vse dni v tednu, in priročen program za vodenje seznama in beleženje prihodov krvodajalcev.

Za osrednjo točko komuniciranja s krvodajalci, organizatorji, mediji in javnostjo smo določili spletno stran ztm.si. Ker smo krvodajalske akcije načrtovali dnevno glede na potrebe, epidemiološko stanje, primernost prostorov, razpoložljivost ekip in krvodajalcev ipd., smo sproti posredovali informacije o datumu, kraju in času krvodajalskih akcij, pogojih za darovanje krvi, zalogah krvi, organizaciji vabljenja, telefonske številke za prijavo ipd., ki so bile na voljo za celotno Slovenijo. Seveda smo izkoristili vse medije, da smo javnost obvestili o spletnem mestu, na katerem so na voljo najnovejše informacije. Tudi za organizatorja krvodajalskih akcij – Rdeči križ Slovenije – je bil to glavni vir informacij.

Že v začetku aprila 2020 so se začeli krvodajalci sami prijavljati na odvzeme krvi. Vabljenje krvodajalcev je potekalo prek SMS-sporočil s posredovanjem telefonskih številk, na katere so krvodajalci poklicali. Ob telefonskem naročilu in vpisu v razpoložljiv termin smo preverjali zdravstveno stanje, primernost za darovanje krvi in epidemiološko anamnezo krvodajalca že pred njegovim prihodom. Zato so se odkloni od uvedbe telefonske triaže v primerjavi z enakimi obdobji iz preteklih let z okoli 13 % znižali na okoli 8 %. Z načinom naročanja na termin so bili izjemno zadovoljni tudi sami krvodajalci, zato ga bomo ohranili in nadgradili. Hkrati ta način omogoča transfuzijski službi boljše vodenje zalog in usmerjeno vabljenje krvodajalcev s tisto krvno skupino, ki je primanjkuje.

The first mobile blood collection session was successfully organised under changed conditions during the epidemic in Vrhnika (18 March 2020). The practice of organising the blood donation sessions and the first experiences were adopted by the units of the BTC as well as the Transfusion Medicine Centre Maribor and the Transfusion Centre Celje. In a few days, a completely different organisation of blood donation was implemented to achieve a higher level of organisation of blood donors – appointment system for blood donation. We set up a 24/7 contact phone and a handy programme to manage a schedule.

We established the website ztm.si as the central point of communication with blood donors, organisers, the media, and the public. As blood donation sessions were planned on a daily basis, depending on the need, epidemiological situation, suitability of collection environment, availability of teams and blood donors, etc., we provided up to date information about the date, place and time of blood donation sessions, blood donation eligibility criteria, blood stocks, invitation organisation, contact phone numbers for registration. The information was available for the whole of Slovenia. We used all media to inform the public about the website where the latest information was available. This was also the main source of information for the Slovenian Red Cross as organisers of blood donation sessions.

At the beginning of April, blood donors already started to apply for a donation of blood themselves. SMS text messages invitations to blood donors included telephone numbers to appoint the donation. At the time of telephone appointment, the health status eligibility for blood donation, and epidemiological history were checked first. As a result, the deferral rate decreased from approximately 13 % to 8 % compared to the previous years of the same period due to the introduction of this so-called telephone triage. The new appointment system was extremely well accepted by blood donors. Therefore, we will keep it and develop it further. At the same time, this system enables the Transfusion Service to better manage stocks of blood units per blood group type and target proper blood donors when needed.

Z načinom naročanja na termin so bili izjemno zadovoljni tudi sami krvodajalci, zato ga bomo ohranili in nadgradili. Hkrati ta način omogoča transfuzijski službi boljše vodenje zalog in usmerjeno vabljenje krvodajalcev s tisto krvno skupino, ki je primanjkuje.

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Zaradi ukrepov za preprečevanje širjenja okužb in zagotavljanja varnega okolja za krvodajalce in zaposlene (posamični sprejemi, omejitve glede števila oseb v določenem prostoru ipd.) smo od uvedbe ukrepov (od aprila do decembra 2020) zabeležili okoli 20 % manj sprejemov krvodajalcev na krvodajalskih akcijah v primerjavi z lanskim letom, v **celoletnem povprečju pa slabih 10 %** manj tudi zaradi telefonske triaže ob naročilu. Zato smo se morali prilagoditi na preskrbo z nižjimi zalogami enot krvi, tako da smo skoraj celo »koronsko« leto zagotavljali preskrbo s krvjo s 3- do 4-dnevnimi zalogami. Pred epidemijo so bile naše zaloge v povprečju 7-dnevne.

Potrebe po krvi pa so bile kljub epidemiji **le nekoliko znižane (okoli 5 %)**, saj so bolnišnicah skoraj v enaki meri kot pred epidemijo potekala zdravljenja hematoloških in onkoloških bolnikov, izvajale so se kardiološke operacije, transplantacije in vsa nujna zdravljenja itd. Kri za zdravljenje so potrebovali tudi covidni bolniki zaradi intenzivnega zdravljenja.

Due to measures to prevent the spread of infections and to ensure a safe environment for blood donors and staff (individual admissions, limiting the number of people in a given area, etc.), we recorded about 20 % fewer registrations of blood donors at blood sessions compared to last year (April to December 2020), **an annual average of almost 10 %**, also due to pre-donation telephone triage. Therefore, we had to adjust to lower stocks of blood units as the supply of blood units dropped to three to four-day stocks for almost the entire "corona year". Before the epidemic, our supplies lasted an average of seven days.

Despite the epidemic, **the need for blood was only slightly reduced (about 5%)** because haematological and oncology patients were treated at the same rate as before the epidemic, also cardiovascular surgery, transplantations and all emergency treatments were performed. Blood for treatment was also needed for COVID-19 patients.

Podoben vpliv epidemije na krvodajalstvo in preskrbo s krvjo beležijo tudi ostale evropske transfuzijske službe, s katerimi smo redno izmenjevali izkušnje in dobre prakse. Redna srečanja so potekala v organizaciji združenja transfuzijskih ustanov na ravni Evrope EBA (ang. *European Blood Alliance*) prek telekonferenc.

Uspelo nam je, da smo tudi med epidemijo zagotavljali potrebne količine krvi in da so jo vsi bolniki, ki so jo potrebovali, tudi dobili. Pri tem pa ne smemo pozabiti na sodelovanje naročnikov in uporabnikov naših storitev, ki so upoštevali poziv za racionalno naročanje krvnih in skrbno porabo.

A similar impact of the epidemic on blood donation and supply is also recorded by other European transfusion services with whome we regularly share experiences and good practices. Regular meetings were organised by the European Blood Alliance (EBA) in the form of video conferences.

We managed to provide the necessary quantities of blood, even during the epidemic, and for all patients who needed it. We must not forget the cooperation of the all customers who responded to the call for rational ordering of blood components and careful consumption.

Ocenjujemo, da nam je hitra prilagoditev uspela zaradi odzivnosti, razumevanja in zaupanja krvodajalcev, kar je vsekakor tudi doprinos uspešne 10-letne krvodajalske pobude Daruj energijo za življenje, v kateri sodelujejo ZTM, Rdeči križ Slovenije in družba Petrol. V teh letih smo izboljšali in posodobili komunikacijo s krvodajalci, izboljšali sistem obveščanja, informiranost in dosegli višjo raven medsebojnega razumevanja in sodelovanja. Krvodajalci so sprejeli in razumejo pomen trditve »pravi krvodajalec ob pravem času« in tako aktivno sodelujejo pri uravnavanju zalog krvi.

We believe that our rapid adaptation has been successful because of the responsiveness, understanding and trust of blood donors, which is certainly the contribution of the 10-year blood donation initiative "Donate Energy for Life",in which BTC, SRC and Petrol participate. In these years of successful blood donation initiatives we have upgraded and modernised communication with blood donors, improved information and achieved a higher level of mutual understanding and cooperation. The blood donors have accepted and understood the meaning of "the right blood donation at the right time" and thus actively participate in regulating the blood stock.

Krvodajalstvo smo uspeli predstaviti kot pomemben del zdravstvenega sistema, zato je bila udeležba na krvodajalski akciji opredeljena kot izjema v odredbi o prepovedi gibanja zunaj občine stalnega ali začasnega bivanja (28. marca 2020). Prav tako je Rdeči križ Slovenije skupaj s Civilno zaščito uspel ohraniti in organizirati krvodajalske akcije v prostorih vzgojno-izobraževalnih in drugih ustanov kljub odredbi o zaprtju (12. marca 2020).

Dobili smo tudi izredno priložnost, da smo sodelovali na vladni novinarski konferenci o aktualnem stanju glede bolezni covid-19 (1. decembra 2020). Zastopala nas je vodja kriznega tima Polonca Mali, ki je javnosti predstavila delovanje transfuzijske službe, preskrbe s krvjo in krvodajalstva med širjenjem covida-19 ter program zbiranja prebolevniške plazme, povabila k sodelovanju prebolevnike ter izrekla zahvalo krvodajalkam in krvodajalcem.

Ob dnevu slovenskega krvodajalstva 4. junija 2021 se je zaradi pomembne vloge krvodajalcev med epidemijo v videoposlanici tem zahvalil tudi predsednik Republike Slovenije Borut Pahor: »Krvodajalci ste naš vzor in navdih. Ob vašem prazniku vam želim sporočiti, da se vašega plemenitega poslanstva zavedamo, vas občudujemo in se vam zahvaljujemo.«

Tudi minister za zdravje Janez Poklukar, ki je na ta dan obiskal ZTM in daroval kri, se je na novinarski konferenci zahvalil krvodajalcem, transfuzijski službi in Rdečemu križu Slovenije, ki skrbijo, da imamo vedno na voljo dovolj krvi.

Blood donation as an important part of the health care system was successfully presented, so blood donation was defined as an exception in the regulation prohibiting movement outside the municipality of permanent or temporary residence (28 March 2020). Blood donors were allowed to travel to the blood sessions without restriction. The Slovenian Red Cross, together with the Civil Protection, also managed to maintain and organise mobile blood donation sessions on the premises of educational and other institutions, despite the closure order (12 March 2020).

We also had the extraordinary opportunity to attend a government press conference on the current situation regarding COVID-19 (1 December 2020). The head of the BTC crisis team Polonca Mali presented to the public the activities of the Transfusion Service, blood supply and blood donation during the spread of COVID-19, the convalescent plasma collection programme and thanked blood donors.

On the occasion of national Blood Donation Day on 4 June 2021, the President of the Republic of Slovenia Borut Pahor, in his video, sincerely thanked blood donors. "Blood donors are our role models and inspiration. On the occasion of your day, I wish to inform you that we are aware of your noble mission, admire you, and thank you."

The Minister of Health, Janez Poklukar, who also visited the BTC in Ljubljana that day and donated blood, at the press conference thanked the blood donors, the Transfusion Service and the Slovenian Red Cross for ensuring sufficient blood supply.

Darovanje krvi je humanitarna gesta brez primere, zato si želim, da bi se za krvodajalstvo odločalo še več ljudi. Krvodajalci ste naš vzor in navdih.

Blood donors are our role models and inspiration. On the occasion of your day, I wish to inform you that we are aware of your noble mission, admire you, and thank you.

— **Borut Pahor**

To je nekaj najbolj plemenitega, kar človek lahko naredi za sočloveka. V imenu slovenskega zdravstva, pacientov, se zahvaljujem krvodajalcem za pripadnost in darovanje krvi.

This is one of the most noble things a man can do for a fellow human being. On behalf of Slovenian healthcare, patients, I would like to thank blood donors for their affiliation and blood donation.

— **Janez Poklukar**

Pri zagotavljanju nemotene preskrbe s krvjo so nam bili v izredno pomoč mediji, ki so s prispevki in posredovanimi informacijami sledili našim želenim sporočilom in potrebam. Mediji so bili pomemben partner pri obveščanju, vabljenju in opozarjanju krvodajalcev o pomembnosti darovanja krvi tudi med epidemijo. Hkrati pa so krvodajalci sami promovirali krvodajalstvo prek družbenih medijev.

Naši ukrepi in pristopi so bili uspešni, saj nismo zabeležili nobenega prenosa bolezni med krvodajalci in osebjem pri odvzemu krvi.

Epidemija nam je prinesla nove izzive na strokovnem področju, na primer pri iskanju zdravila za zdravljenje bolnikov s covidom-19. Ena od možnosti zdravljenja je bila tudi prebolevniška plazma, zato so se na podlagi prvih izkušenj v svetu in Evropi začele dejavnosti za zbiranje plazme prebolevnikov po covidu-19 tudi v Sloveniji.

Following our messages and needs with their contributions and information, the media were a great help to us in ensuring necessary blood supply. The media were important partners in informing, inviting blood donors and drawing attention to the importance of blood donations even during the epidemic. The blood donors themselves also promoted blood donation via social media.

Our measures and approaches were successful, as we did not record any disease transmission between blood donors and staff during blood collection.

The epidemic brought us new challenges in the transfusion medicine activities, such as finding a specific therapeutics for patients with COVID-19. The use of convalescent plasma was also one of the treatment options, so based on the initial experience in the world and Europe, activities to collect convalescent plasma also started in Slovenia.

Janez Poklukar,
minister za zdravje
Minister of Health

4.

ZBIRANJE PLAZME PREBOLEVNIKOV PO COVIDU-19 IN POMOČ EVROPSKE KOMISIJE PRI IZVEDBI PROGRAMA

PLASMA DONATIONS FROM RECOVERED COVID-19 PATIENTS (DONORS) AND SUPPORT OF THE EUROPEAN COMMISSION IN THE IMPLEMENTATION OF THE PROGRAMME

Polonca Mali
Natalija Lampreht
Urška Rahne Potokar
Mojca Jež
Slavica Stanišić

Konec decembra 2020 so iz Kitajske poročali o novi bolezni, povzročeni z novim koronavirusom SARS-CoV-2, za katero sta značilna hitro širjenje med ljudmi in zbolevanje s hujšimi kliničnimi stanji in umrljivostjo, še posebno med starejšimi.

Zaradi posebne klinične slike bolezni so raziskovalci že kmalu začeli z ugotavljanjem podobnosti z znanimi koronavirusnimi boleznimi in iskanjem specifično usmerjenega zdravila za zdravljenje te bolezni.

Prebolevniško plazmo, ki vsebuje specifična proti povzročitelju usmerjena protitelesa so že uporabili pri zdravljenju drugih koronavirusnih okužb (SARS, MERS). Izsledki teh študij so pokazali, da uporaba prebolevniške plazme krajša čas hospitalizacije in zmanjšuje umrljivost. Takšna oblika zdravljenja se je zato prenesla na covidne bolnike, saj specifičnih protivirusnih zdravil za preventivo in zdravljenje covidnih bolnikov ni bilo na voljo.

Zaradi pandemije na svetovni ravni v začetku leta 2020 so transfuzijske službe začele z vzpostavljanjem programov za zbiranje plazme prebolevnikov po covidu-19. Programi zbiranja so tako upoštevali dejstvo, da je zbiranje plazme za transfuzijsko službo ustaljen postopek, še posebej tam, kjer že poteka zbiranje plazme za izdelavo zdravil iz krvi. Hkrati pa so s širjenjem okužb na voljo številni prebolevniki, ki lahko po preboleli bolezni darujejo kri ali plazmo. V plazmi prebolevnikov so namreč **specifična protitelesa, usmerjena proti različicam virusa**. Njihova vsebnost je odvisna od posameznikovega imunskega odziva in intenzivnosti bolezni. Z večanjem števila hospitaliziranih bolnikov so predvsem v Ameriki in Evropi začeli z načrtovanjem različnih kliničnih študij za zdravljenje s prebolevniško plazmo. Namen študij zdravljenja covidnih bolnikov je ugotavljanje terapevtske učinkovitosti različnih protokolov zdravljenja s plazmo, zagotavljanje kakovosti in dostopnosti ter standardizacija krvne komponente.

At the end of December 2019, a new disease caused by the new coronavirus SARS-CoV-2 was reported from China, characterised by rapid spread among people, severe clinical conditions and mortality, especially in the elderly.

Due to the specificity of COVID-19, researchers soon recognised similarities with known coronavirus diseases and started investigation to find a specifically targeted drug to treat this disease.

Studies based on the experience of treating other coronavirus infections (SARS, MERS) with **convalescent plasma** containing specific antipathogen antibodies showed a shortening of hospital stays and a reduction in mortality. This form of treatment was transferred to patients suffering from COVID-19 as specific antivirus medicines for prevention and treatment were not yet available.

Due to the global pandemic in early 2020, transfusion services set up plasma collection donor programmes for reconvalescent COVID-19 patients (donors). The collection programmes thus considered the fact that plasma collection is a standard procedure for the transfusion service, especially if plasma collection is already being carried out to produce plasma-derived medicinal products. With the spread of infections, many reconvalescent COVID-19 patients were available to donate blood or plasma after recovery from the disease. **Specific antibodies directed against variants of the virus** were found in convalescent COVID-19 plasma. The level of antibodies depends on the individual immune response and the intensity of the disease. With the increase in the number of hospitalised patients, the design of various clinical trials for the treatment with convalescent COVID-19 plasma has begun, especially in America and Europe. The purpose of the studies in the treatment of patients suffering from COVID-19 is to determine the therapeutic efficacy of different plasma treatment protocols, the quality, availability and standardisation of the blood component.

Zaradi omogočanja takšnega zdravljenja smo na nacionalni ravni tudi v Sloveniji pripravili opazovalno študijo **Zbiranje in uporaba hiperimunske prebolevniške plazme COVID-19 v Sloveniji** (ang. *Collection and use of hiperimmune reconvalescent COVID-19 plasma in Slovenia*), ki jo koordinirata Zavod RS za transfuzijsko medicino in Klinika za infekcijske bolezni in vročinska stanja UKC LJ, pri čemer so sodelovale tudi ostale transfuzijske službe (TC SB Celje in CTM UKC Maribor) in klinični oddelki, na katerih se zdravijo bolniki s covidom-19 (Klinika za infekcijske bolezni in vročinska stanja UKC LJ, Univerzitetna klinika Golnik, Oddelka za infekcijske bolezni in vročinska stanja UKC Maribor in SB Celje).

Slovenska transfuzijska služba je v študiji prevzela uvedbo programa zbiranja hiperimunske prebolevniške plazme (HCP). Zbiranje plazme ali krvi je za transfuzijsko službo reden in utečen postopek, priprava krvnega pripravka pa standardna storitev. Program zbiranja HCP se je tako izvajal skladno z vsemi načeli in postopki, ki veljajo pri krvodajalcih, pri katerih je v ospredju skrb za varnost darovalca in varen odvzem krvi pa tudi zagotavljanje varne in kakovostne komponente krvi za prejemnika.

Za izvedbo programa zbiranja in uporabe HCP je bilo treba vzpostaviti celovito koordinacijo vseh sodelujočih, pridobiti soglasja in dovoljenja za nove programe in postopke (Strokovni svet ZTM, Komisija Republike Slovenije za medicinsko etiko, vloga za dovoljenje Javne agencije RS za zdravila in medicinske pripomočke ...) in tudi poiskati sredstva za izvedbo programa.

Konec leta 2020 smo pridobili pozitiven odziv na vlogo na EC-ESI (ang. E*vropean Commision Emergency Support Instrument*) **za dodelitev finančnih sredstev Evropske komisije (EK)**. Glavni namen EK je podpora državam članicam EU pri širjenju odvzemov plazme za doseganje strateške neodvisnosti v regiji, torej za povečanje zmogljivosti na področju pridobivanja prebolevniške plazme pa tudi plazme za izdelavo zdravil iz krvi. Pri projektu ZTM, ki ga je vodila Polonca Mali in smo ga interno poimenovali ESI projekt, je za širjenje programa plazmaferez namenjenih 1,4 milijona EUR.

To enable such treatment, we prepared an observational study, "**Collection and use of hyperimmune convalescent COVID-19 plasma in Slovenia**", at the national level in Slovenia, coordinated by the Blood Transfusion Centre and the Clinic for Infectious Diseases of the University Medical Centre Ljubljana, with the participation of other transfusion services (TC Celje and CTM Maribor) and clinical departments where patients with COVID-19 are treated (Clinic for Infectious Diseases Ljubljana, University Clinic Golnik, Maribor University Medical Centre and Celje General Hospital).

In the study, the Slovenian Transfusion Service undertook the implementation of a hyperimmune convalescent COVID-19 plasma (HCP) collection programme. Plasma/blood collection is a regular and routine procedure for the transfusion service, and blood processing is a standard service. Therefore, the HCP collection programme was implemented under all policies and procedures applicable to blood donors, focusing on donor safety, safe blood collection, and ensuring a safe and high-quality blood component for the recipient.

To implement the HCP collection and treatment programme, it was necessary to establish comprehensive coordination of all participants, obtain licences and approvals for implementing new programmes and procedures (BTC Expert Council, Medical Ethics Commission of the Republic of Slovenia, Agency for Medicinal Products and Medical Devices of the Republic of Slovenia) and to find funds for implementing the programme.

At the end of 2020, we received a positive response to the application letter of the European Commission Emergency Support Instrument (EC-ESI) for the allocation of funds from the European Commission (EC). The EC mainly supports Member States in expanding plasma collection to achieve strategic independence in the region, i.e. to increase the capacity to collect convalescent COVID-19 plasma and plasma to produce plasma-derived medicinal products. The BTC project, coordinated by Polonca Mali and referred internally as the ESI project, was allocated €1.4 million to expand the plasmapheresis programme.

Uvedba programa HCP ali plazmaferez je vključevala naslednje ureditve in prilagoditve:

1. **PRIDOBIVANJE PREBOLEVNIKOV - DAROVALCEV, KI SMO JIH K SODELOVANJU/DAROVANJU VABILI PREK MEDIJEV IN POZIVOV.**

Promocijo in pridobivanje prebolevnikov smo izvedli sami, prek lastnih komunikacijskih kanalov (spletne strani ztm.si in Daruj kri profila na Facebooku) in z veliko podporo medijev, ki so brezplačno promovirali program HCP. Veliko pa so pripomogli tudi sami darovalci, ki so predstavljali lastno izkušnjo z darovanjem in promovirali to vrsto pomoči covidnim bolnikom.

Najprej smo vabili tiste prebolevnike, ki so imeli potrjeno okužbo z verižno reakcijo s polimerazo v realnem času (PCR) – pozitiven bris nosno-žrelnega predela in klinično sliko covida–19, in tudi tiste, ki so jih opredelili kot možno okužene s covidom-19 na podlagi klinične slike in epidemiološke anamneze (brez potrjevanja okužbe z brisom). V program smo jih vključevali 4–6 tednov po preboleli bolezni, seveda ob upoštevanju vseh meril za darovanje krvi.

2. **VZPOSTAVITEV STIČNE TOČKE ZA PRIJAVE MOŽNIH DAROVALCEV HCP IN NUDENJE STROKOVNO-MEDICINSKIH INFORMACIJ.**

Stično točko smo vzpostavili na spletni strani ZTM, kjer so bile potencialnim darovalcem na voljo osnovne informacije o programu HCP in načinu vključitve vanj (objava telefonske številke in e-poštni naslov). Zagotovili smo zdravstveno osebje za nudenje dodatnih informacij in izvajanje triaže ter vključevanje darovalcev v program prek telefona in e-pošte. Odgovorili smo na več kot 1600 e-poštnih sporočil in sprejeli več kot 5500 klicev.

Introducing the plasmapheresis/HCP programme included these approaches and adjustments:

1. **RECRUITMENT OF DONORS/CONVALESCENT PATIENTS INVITED TO PARTICIPATE/DONATE THROUGH THE MEDIA AND APPEALS.**

The motivation and recruitment of reconvalescent donors were undertaken by ourselves through our own communication channels (website ztm.si and Facebook profile Daruj kri) and with great support from the media, which promoted the HCP programme for free. We also received great of publicity from the donors themselves, who presented their own experiences of donation and promoted this way of helping patients suffering from COVID-19.

We first invited those reconvalescent patients with a confirmed real-time polymerase chain reaction (PCR) infection – a positive nasopharyngeal swab and a clinical presentation of COVID-19, and those identified as possible COVID-19 based on their clinical picture and epidemiological history (without confirmation of infection with a swab). Taking into account all the eligibility criteria for blood donation, we recruited them four to six weeks after recovering from the disease.

2. **ESTABLISHED A CONTACT CALL CENTRE FOR REGISTRATION OF POTENTIAL HCP DONORS AND PROVIDING MEDICAL INFORMATION.**

A contact point was set up on the BTC website to provide potential donors with basic information about the HCP programme and how to participate (publication of telephone number and email address). We provided medical staff with additional information and triage and enrolment of donors into the programme via phone and email. We answered more than 1600 e-mails and received more than 5500 phone calls.


AB
Pejt z mano :)

3. PRILAGODITEV POSTOPKOV PRIPRAVE NOVE KOMPONENTE KRVI ZA KLINIČNO UPORABO – HIPERIMUNSKA COVID-19 SVEŽA ZMRZNJENA PLAZMA (HCP SZP)

in s tem zagotovitev popolne sledljivosti komponente od odvzema do izdaje bolnikom.

4. UVEDBA DODATNIH TESTIRANJ ODVZETE KRVI

za dokazovanje vsebnosti protiteles proti virusu SARS-CoV-2 in za zagotovitev dodatnih pogojev kakovosti in varnosti krvne komponente za klinično uporabo.

Za vsako odvzeto enoto prebolevniške plazme smo najprej naredili presejalni test na prisotnost protiteles proti SARS-CoV-2, da bi ugotovili vrednost vsebnosti teh specifično usmerjenih protiteles. Glede na to smo na podlagi določitve mejnih vrednosti na dodatna testiranja pošiljali le tiste odvzete enote, ki so dosegale postavljene vrednosti. Te smo določili na podlagi korelacije začetnih vrednosti presejalnih testiranj z rezultati nevtralizacijskega testa.

Po okužbi s SARS-CoV-2 namreč nastanejo protitelesa proti različnim delom virusa (proti lipidni ovojnici, membranskim proteinom, nukleokapsidi, koničastemu glikoproteinu), niso pa vsa enako učinkovita pri odstranjevanju virusa. Za to so najpomembnejša t. i. nevtralizirajoča protitelesa. Trenutno namreč za standardni in referenčni test velja le nevtralizacija virusa. Več kot naj bi bilo protiteles v plazmi glede na rezultat na presejalnem testu, večja je verjetnost, da ima tak krvodajalec tudi veliko količino nevtralizirajočih protiteles.

3. ADAPTATION OF PROCEDURES FOR PRODUCING A NEW BLOOD COMPONENT FOR CLINICAL USE – HYPERIMMUNE COVID-19 FRESH FROZEN PLASMA (HCP FFP),

thus ensuring full traceability of the component from collection to transfusion to the patient.

4. INTRODUCING ADDITIONAL LABORATORY TESTS

to detect the level of antibodies to SARS-CoV-2 and to ensure additional quality and safety of blood component for clinical use.

Each convalescent COVID-19 plasma collection was first tested with a SARS-CoV-2 antibody screening test to determine the value of the level of these specifically targeted antibodies. Depending on the content value of the antibodies in the screening test, only the units collected that reached the specified levels were sent for further testing based on determining cut-off values. These were determined by correlating the baseline screening test values with the neutralisation test results.

After infection with SARS-CoV-2, antibodies are formed against different parts of the virus (against the lipid envelope, membrane proteins, nucleocapsids, spike glycoprotein). However, not all these antibodies are equally effective in eliminating the virus. So-called neutralising antibodies are most important for virus removal. Only neutralising the virus applies to the standard and reference test. The more antibodies that can be expected in the plasma according to the screening test result, the more likely it is that such a blood donor will also have many neutralising antibodies.

Po okužbi s SARS-CoV-2 namreč nastanejo protitelesa proti različnim delom virusa, niso pa vsa enako učinkovita pri odstranjevanju virusa. Za to so najpomembnejša t. i. nevtralizirajoča protitelesa.

After infection with SARS-CoV-2, antibodies are formed against different parts of the virus. However, not all these antibodies are equally effective in eliminating the virus. So-called neutralising antibodies are most important for virus removal.


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Aurora
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1981
LIMITED EDITION

Najprej (od julija do decembra 2020) smo prisotnost protiteles proti SARS-CoV-2 presejalno določali s kvalitativnimi serološkimi testi, ki so bili v začetnih mesecih pandemije na voljo. Za klinično uporabne enote smo določili tiste, pri katerih smo z nadaljnim testiranjem ugotovili **titer nevtralizirajočih protiteles večji ali enak 1 : 80**. Pri nas so to preiskavo, zaradi testiranja z živim virusom, opravljali na Inštitutu za mikrobiologijo in imunologijo Medicinske fakultete v Ljubljani. Primerne titre nevtralizirajočih protiteles za klinično uporabo smo ugotovili v samo 30 % odvzetih enot.

V začetku leta 2021 smo določanje prisotnosti protiteles proti SARS-CoV-2 nadgradili in prešli na kvantitativno določanje, kar pomeni, da poleg prisotnosti določamo tudi količino specifičnih protiteles IgG v serumu ali plazmi prebolevnikov. V testu določamo protitelesa proti domeni virusa RBD, ki je del podenote S1 bodičaste beljakovine, ki je ključna za vezavo virusa na celico in njegov vstop vanjo. Določanje protiteles je avtomatizirano in temelji na uporabi paramagnetnih kroglic, prevlečenih z antigeni virusa SARS-CoV-2, na katere se vežejo protitelesa iz seruma ali plazme prebolevnikov. Vezavo protiteles zaznamo z dodatkom konjugata in kemiluminiscentno reakcijo. Z uvedbo nove kvantitativne metode določanja vsebnosti protiteles so rezultati presejalnega testa boljši oz. dobro korelirajo z nevtralizacijskim testom.

Glede na podatke iz literature je titer nevtralizirajočih protiteles prvih 7–10 dni po nastanku simptomov bolezni covid-19 nizek, nato se 2–3 tedne povečuje. Analize kažejo, da je pri prebolevnikih po covidu-19 s protitelesi posredovana imunost precej kratka, saj začne titer protiteles večinoma upadati že po 3–4 mesecih po koncu bolezni. Podobno ugotavljamo tudi pri darovalcih HCP.

Initially (July–December 2020), the determination of the presence of SARS-CoV-2 antibodies was performed using screening qualitative serological tests available during the first months of the pandemic. Those with a **neutralising antibody titre greater than or equal to 1:80** were determined as clinically useful units. In Slovenia, this test was performed at the Institute of Microbiology and Immunology at the Medical Faculty in Ljubljana for tests on live virus. Suitable titres of neutralising antibodies for clinical use were found in only 30 % of the units sampled.

At the beginning of 2021, we upgraded the screening test for the presence of SARS-CoV-2 antibodies and switched to a quantitative determination, i.e. we determined not only the presence but also specific IgG antibodies in the serum or convalescent COVID-19 plasma. In the test, we determine antibodies against the domain of the RBD virus part of the S1 subunit of the spike protein, which is crucial for the binding of the virus to the cell and its entry into it. Determining antibodies is automated and based on paramagnetic beads coated with SARS-CoV-2 antigens against the antibodies from serum or convalescent COVID-19 plasma. Antibody binding is detected by adding a conjugate and a chemiluminescence reaction. Introducing a new quantitative method for determining the content of antibodies meant the screening test results were better or correlated well with the neutralisation test.

According to the literature, the titre of neutralising antibodies is low in the first 7–10 days after the onset of symptoms of COVID-19 and then increases for 2–3 weeks. Analysis shows that in reconvalescent COVID-19 patients, antibody-mediated immunity is quite short, as the antibody titre usually decreases three to four months after the end of the disease. The same is true for HCP donors.

Istočasno smo izvajali presejalno testiranje krvi ali plazme na označevalce okužb, ki se prenašajo s krvjo (HIV, virus hepatitisa B in C ter sifilis), kar je del rednega testiranja odvzetih enot krvi za zagotavljanje varne krvi.

Za zagotavljanje zadostnih, kakovostnih in varnih enot prebolevniške plazme smo opravljali še nekatera dodatna testiranja, npr. prisotnost protiteles anti-HLA in anti-HNA. V enotah prebolevniške plazme smo določali tudi celokupno koncentracijo imunoglobulinov IgG, kar je bilo pomembno predvsem za krvodajalce, ki so na odvzem prebolevniške plazme prišli večkrat, in s tem zagotavljali tudi varen odvzem darovalcem.

Enote, ki niso dosegale minimalnih kriterijev vsebnosti protiteles, smo namenili za izdelavo zdravil iz krvi.

As part of regular blood collection to ensure safe blood, we also conducted blood/plasma screening for markers of transfusion transmitted infections (HIV, hepatitis B and C virus and T. Pallidum/syphilis).

To ensure sufficient, high-quality and safe units of convalescent COVID-19 plasma, we additionally performed other tests, e.g. the presence of anti-HLA and anti-HNA antibodies. We also determined the total concentration of IgG immunoglobulins in the units of convalescent COVID-19 plasma, which was particularly important for blood donors who came several times for convalescent COVID-19 plasma collection, thus ensuring the safe donation for donors.

Units that did not meet the minimum criteria for antibody content were then intended to produce other plasma-derived medicinal products.

Diagram procesa testiranja za izbor HCP SZP

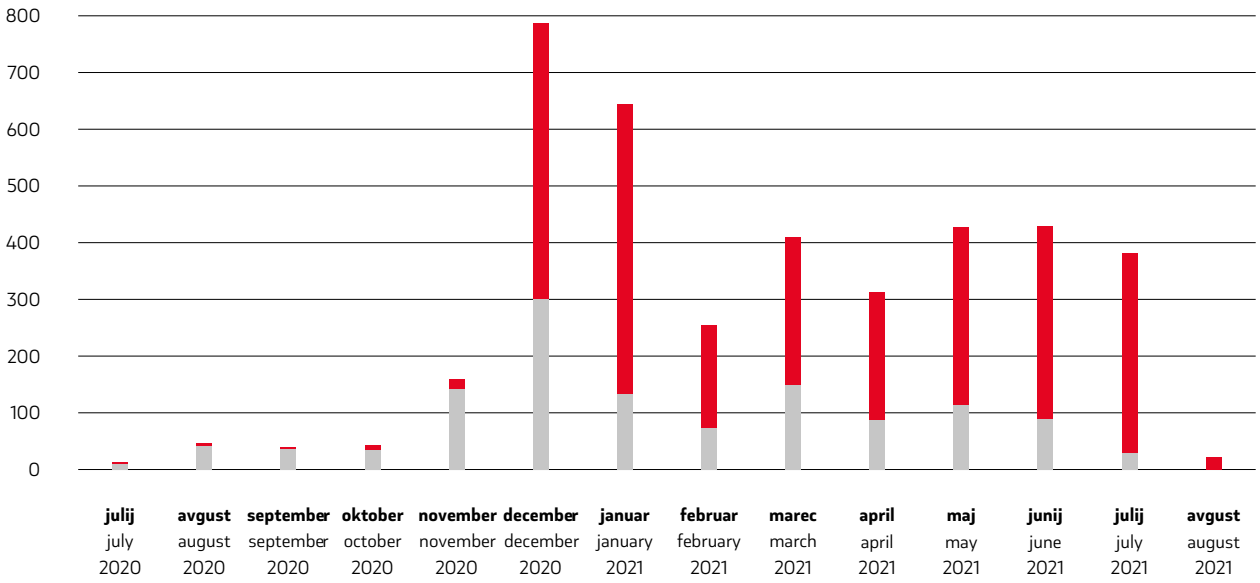
Display of the tests algorithm

5. UREDITEV DODATNIH KADROVSKIH, PROSTORSKIH IN TEHNIČNIH POGOJEV ZA DAROVANJE, SHRANJEVANJE IN TESTIRANJE ODVZETIH ENOT HCP

Številčnost in pripravljenost prebolevnikov za vključitev v program nas je vse presenetila. Kljub velikemu uspehu pri pridobivanju darovalcev pa je obravnava prebolevnikov občasno presegala naše razpoložljive kadrovske vire, kar je povzročalo dodatne obremenitve zaposlenih.

5. ADAPTING ADDITIONAL STAFF, WORK STATIONS AND TECHNICAL REQUIREMENTS FOR THE DONATION, STORAGE AND TESTING OF COLLECTED HCP UNITS

The number and preparedness of reconvalescent patients to be participated into the programme surprised us all. Despite the great success in recruiting donors, the demands of reconvalescent donor management exceeded our human resources, resulting in an additional burden on staff.



Plazmafereza Plasmapheresis

Polna kri Whole blood

Prikaz števila odvzemov plazme s plazmaferezo in število odvzemov polne krvi po mesecih (avgusta 2021 so odvzemi potekali le do 10. 8.)

Presentation of the number of plasma collections by plasmapheresis and the number of whole blood collections by month (August 2021, collections took place only until 10 August)

Plazmo zbiramo s postopkom, imenovanim **plazmafereza**, pri katerem krvodajalcu z aparatom odvzamemo polno kri, iz nje izločimo plazmo in vrnemo krvne celice nazaj v krvni obtok. Plazmo HCP pa lahko pridobimo tudi iz polne krvi prebolevnika. To predelamo v komponente krvi – plazmo namenimo za zdravljenje covidnih bolnikov, medtem ko z eritrociti in trombociti oskrbimo ostale bolnike.

Prebolevniki, ki so imeli visoko vsebnost protiteles proti SARS-CoV-2 v plazmi, odvzeti s postopkom plazmafereze ali darovanjem polne krvi, smo ponovno, tudi večkrat, povabili na dodaten odvzem samo plazme s plazmaferezo.

Vsem, ki so sodelovali v programu, smo izdali in na dom poslali rezultate preiskav, določitve vsebnosti protiteles proti SARS- CoV-2. Posebno usmerjeno smo v program odvzema polne krvi in plazmafereze vključevali darovalce redkih krvnih skupin (KS) B in AB, da bi lahko oskrbeli vse bolnike.

Plasma is collected through a process called **plasmapheresis**, in which whole blood is drawn from the blood donor, the plasma is removed, and the blood cells are returned to the bloodstream. HCP plasma can also be obtained from whole blood of the reconvalescent donor. Whole blood is processed into blood components – plasma is used to treat patients suffering from COVID-19, while erythrocytes and platelets are given to other patients.

Patients with high levels of antibodies to SARS-CoV-2 in plasma collected by plasmapheresis or whole blood donation were invited again, even several times, to collect additional plasma by plasmapheresis only.

To all those who participated in the programme, we issued and sent to their homes the results of the tests for determination of the level against SARS-CoV-2 antibodies. Donors of the rare blood group types B and AB were specially included in the whole blood collection and plasmapheresis programme to supply patients of all blood group types.

Prebolevnike, ki so imeli visoko vsebnost protiteles proti SARS-CoV-2 v plazmi, smo ponovno, tudi večkrat, povabili na dodaten odvzem samo plazme s plazmaferezo.

Patients with high levels of antibodies to SARS-CoV-2 in plasma collected were invited again, even several times, to collect additional plasma by plasmapheresis only.

Nov izziv pri zbiranju krvi pa sta prinesli dostopnost in uvedba cepljenja v Sloveniji. Cepljenje proti bolezni covid-19 ni ovira za darovanje krvi in HCP. Pri cepljenih prebolevnikih smo pri večini (nad 80 %) določili visoke titre nevtralizirajočih protiteles (1 : 1280).

A new challenge in blood collection was brought by the availability and introduction of vaccination in Slovenia. Vaccination against COVID-19 is not a reason not to donate blood and HCP. High titres (1:1280) of neutralising antibodies were observed in vaccinated reconvalescent donors in most samples (greater than 80%).

V Sloveniji smo prvi primer okužbe s covidom-19 potrdili 4. marca 2020. Od začetka julija 2020, ko smo opravili prvi odvzem HCP in tako začeli s programom zbiranja HCP, se je do 15. avgusta 2021 v program vključilo **3211 prebolevnikov** po covidu-19. Opravili smo **2711 odvzemov polne krvi** in **1203 plazmaferez**. Nekaj več kot 500 darovalcev še nikoli prej ni darovalo krvi.

Naš cilj je bil zbrati vsaj 1000 enot HCP, ki bodo primerne za klinično uporabo, torej ustrezale vsem zahtevam glede varnosti in kakovosti – to je za zdravljenje bolnikov s covidom-19 v prihodnje. Tako smo na ZTM v okviru projekta zbrali **1500 klinično uporabnih enot HCP** z visokimi titri.

V Sloveniji se prebolevniška plazma uporablja za zdravljenje covidnih bolnikov v okviru uradne prospektivne klinične raziskave. Koordinator zdravljenja je Klinika za infekcijske bolezni in vročinska stanja UKC Ljubljana v sodelovanju z ZTM.

Za različne covidne bolnike (predvsem za bolnike z oslabelim imunskim sistemom, kot so onkološki bolniki, bolniki po transplantacijah, bolniki s prirojenimi motnjami imunskega sistema ...), smo izdali **288 enot HCP** (31. avgusta 2021).

In Slovenia, the first case of COVID-19 infection was confirmed on 4 March 2020. From the beginning of July 2020, when we performed the first HCP collection and thus started the HCP collection programme, **3211 reconvalescent** COVID-19 donors were enrolled in the programme until 15 August 2021. We collected **2711 whole blood collections** and **1203 by plasmapheresis**. Up to 500 new donors had never given blood before.

Our goal was to collect at least 1000 units of HCP suitable for clinical use and thus meeting all safety and quality requirements, i.e. for future treatment of patients with COVID-19. Using the above approach, we collected **1500 clinically usable HCP units** with high titres at BTC in Ljubljana during the project.

In Slovenia, plasma from the reconvalescent donors will treat patients suffering from COVID-19 as part of an official, prospective clinical trial. The treatment coordinator is the Clinic for Infectious Diseases, University Medical Centre Ljubljana, in collaboration with the BTC.

We issued **288 units of HCP** (31 August 2021) for various patients suffering from COVID-19 (especially immunocompromised patients such as oncology patients and post-transplant patients to those with congenital disorders of the immune system and others).

Nekaj več kot 500 darovalcev še nikoli prej ni darovalo krvi.

Up to 500 new donors had never given blood before.


A BO moja prava?
HCP

Na ZTM smo tudi arhivirali vzorce krvodajalcev za dodatne raziskave v povezavi s covidom-19, kar bo obogatilo zakladnico znanja o tej koronavirusni bolezni.

At BTC, we have also archived donor samples for further research related to COVID-19, which will add to the knowledge on coronavirus diseases.

Vsa nova odkritja glede bioloških značilnosti in poteka covida-19 se analizirajo skladno z raziskovalnimi metodami, ki temeljijo na zbiranju in obdelavi zbranih podatkov, ki se zbirajo v enotni podatkovni bazi. Naše izkušnje in podatki o krvodajalcih in bolnikih bodo tako vključeni v veliko podatkovno bazo EU CCP database (euccp.dataplatform.tech.ec.europa.eu), ki jo je v sodelovanju z združenjem *European Blood Alliance* (EBA) podprl generalni direktorat (DG SANTE) za Zdravje in varnost hrane, Služba Komisije EU, ki je odgovorna za politiko EU na področju varnosti hrane in zdravja ter za spremljanje izvajanja s tem povezanih predpisov.

Pridružili smo se tudi projektu EU SUPPORT-E (ang. *SUPPORTing high--quality evaluation of COVID-19 convalescent plasma throughout Europe*), v katerem bodo podatki o zdravljenju s hiperimunsko plazmo dali odgovore o njeni učinkovitosti, odmerjanju in časovni uporabi med boleznijo ter omogočili standardizacijo in kakovostne pogoje za to novo krvno komponento. V tej evropski bazi podatkov z odprtim dostopom so na voljo podatki o darovanjih plazme in kliničnem zdravljenju.

Any new knowledge about the biological characteristics and progression of COVID-19 will be analysed according to research methods based on the collection and processing of the collected data in a single database. Our experience and donor and patient data will thus feed into the broad EU CCP database (euccp.dataplatform.tech.ec.europa.eu), which is supported by the European Blood Alliance (EBA) Directorate (DG SANTE) for Health and Food Safety, the EU Commission service responsible for EU food and health policy and for monitoring the implementation of related legislation.

We have also joined the EU project SUPPORT-E (Supporting high-quality evaluation of COVID-19 convalescent plasma throughout Europe) where data on treatment with hyperimmune plasma should provide answers to questions of efficacy, dosage, and timing of use during the disease and enable standardisation and quality conditions for this new blood component. Data on plasma donations and clinical treatments are available in this European open-access database.


OK

Finančna sredstva EK s strani EC-ESI (ang. *Evropean Commision Emergency Support Instrument*) za doseganje strateške neodvisnosti pri zagotavljanju zdravil iz krvi v regiji smo poleg uvedbe programa uporabili tudi za povečanje števila odvzemnih mest, pridobitev potrebnih naprav za odvzem in shranjevanje plazme, potrebna testiranja za zagotovitev varne in kakovostne plazme, promocijo in motivacijo darovalcev ter razvoju klicno-naročniškega svetovalnega centra, kot to velja za sodobne klicne centre v drugih panogah.

To bo omogočalo celostno, poenoteno in standardizirano obravnavo krvodajalcev pred prihodom na odvzem krvi in sledljivost komunikacije s krvodajalcem, kar zagotavlja varno kri in varen odvzem kri. Naročniški sistem bo omogočil boljšo organizacijo in načrtovanje dela pa tudi hitro in učinkovito uravnavanje zalog krvi.

Projekt traja od 1. septembra 2020 do 15. oktobra 2021.

EC-ESI (European Commission Emergency Support Instrument) financial resources from the EC to achieve strategic independence in the supply of plasma-derived medicinal products in the region also launched the programme to increase the number of collection sites, procure the equipment for plasma collection and storage, conduct the tests to ensure safe and high-quality plasma, promote and motivate donors, develop a call-appointment counselling centre as is common in other industries for modern call centres.

This will allow comprehensive, uniform, and standardised blood donor management before blood donation, and traceability of communication with the blood donor, ensuring safe blood and safe blood donation. The appointment system will enable better organisation and planning of work and fast and efficient management of blood supplies.

The project lasted from 1 September 2020 to 15 October 2021.

5.

TRANSFUZIJSKA SLUŽBA V ŠTEVILKAH

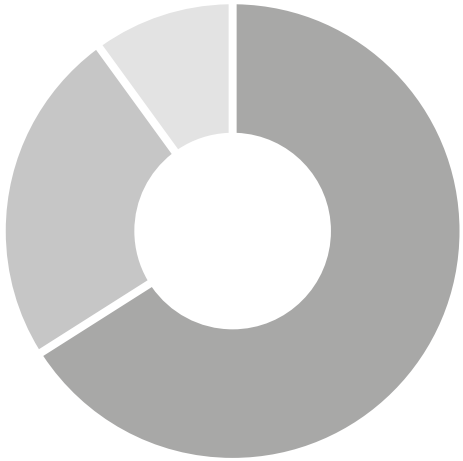
TRANSFUSION ACTIVITY IN FIGURES

OSEBNA IZKAZNICA
IDENTITY CARD

2.000.000
PREBIVALCEV / INHABITANTS

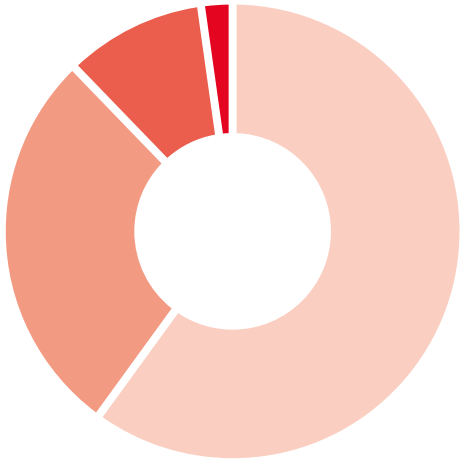
3 %
POPULACIJE SLOVENIJE DARUJE KRI
POPULATION OF SLOVENIA DONATES BLOOD

100 %
NEPLAČANIH, PROSTOVOLJNIH IN ANONIMNIH KRVODAJALCEV
VOLUNTARY, NON-REMUNERATED AND ANONYMOUS BLOOD DONORS



Delež števila odvzemov krvi po transfuzijskih službah
The share of collected blood by transfusion service

ZTM Ljubljana BTC Ljubljana	66 %
CTM Maribor TMC Maribor	24 %
CTM Celje TC Celje	10 %



Pogostost darovanja krvi na leto
Frequency of blood donation per year

enkrat letno once a year	60 %
dvakrat letno twice a year	28 %
trikrat letno three times a year	10 %
štirikrat letno four times a year	2 %

krvodajalk in krvodajalcev letno
blood donors annually

~ 62.000

krvodajalcev
male blood donors

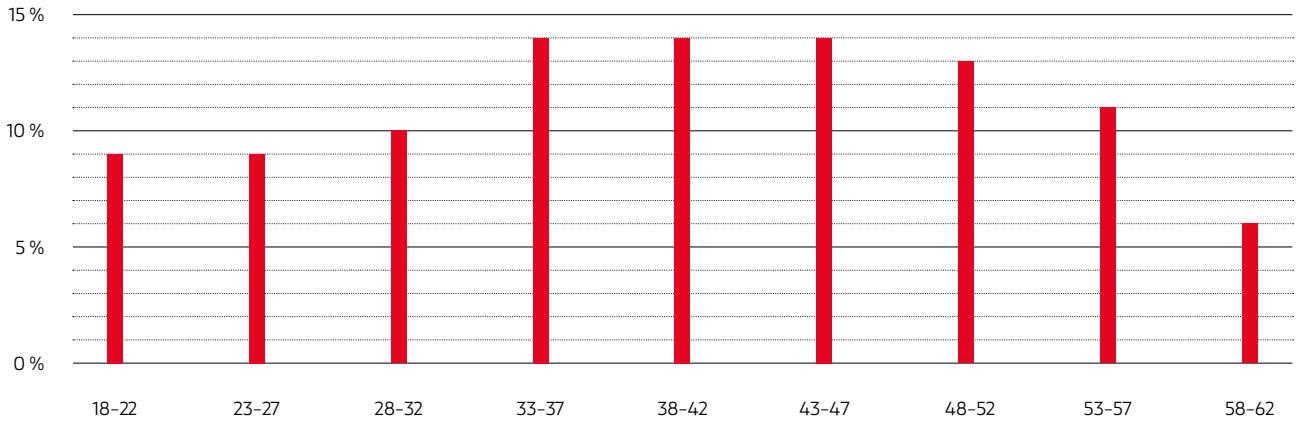
60 %

krvodajalk
female blood donors

40 %

novih krvodajalcev
new blood donors

~ 10 %



Starostna porazdelitev krvodajalcev
Age distribution of blood donors

ŠTEVILO PRIJAVLJENIH KRVODAJALCEV

NUMBER OF REGISTERED BLOOD DONORS

LETO / YEAR	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
ZTM Ljubljana / BTC Ljubljana	52.400	55.036	52.320	49.567	45.144	46.225	49.696	49.857	49.863	47.498	39.576
CTD Izola / TU Izola	6.383	6.843	5.952	5.994	5.861	5.573	5.758	5.399	5.216	5.325	4.985
CTD Jesenice / TU Jesenice	2.254	2.178	1.969	1.982	2.003	1.905	1.789	1.559	1.332	1.519	1.317
CTD Nova Gorica / TU Nova Gorica	3.663	3.886	3.757	3.690	3.613	3.136	3.270	3.340	3.167	3.185	3.095
CTD Novo mesto / TU Novo mesto	6.041	6.846	6.602	6.616	6.586	6.601	6.746	6.598	6.641	6.915	6.236
CTD Slovenj Gradec / TU Slovenj Gradec	3.379	3.328	3.010	2.861	2.873	2.879	2.917	2.903	2.711	2.679	2.792
CTD Trbovlje / TU Trbovlje	1.360	1.318	1.154	993	998	864	861	957	974	1.111	1.128
SKUPAJ ZTM / TOTAL BTC	75.480	79.435	74.764	71.703	67.078	67.183	71.037	70.613	69.904	68.232	59.129
CTM Maribor / TMC Maribor	15.121	15.739	14.823	15.195	15.377	14.948	15.236	15.070	14.272	14.457	12.806
ETD Murska Sobota / TU Murska Sobota	4.642	4.687	4.686	4.538	4.366	4.357	4.150	3.969	3.814	3.853	3.763
ETD Ptuj / TU Ptuj	4.203	4.167	4.276	3.938	3.883	3.911	3.951	3.919	3.879	3.824	3.408
SKUPAJ CTM MARIBOR / TOTAL TMC MARIBOR	23.966	24.593	23.785	23.671	23.626	23.216	23.337	22.958	21.965	22.134	19.977
CTM Celje / TC Celje	11.051	11.061	10.953	9.863	9.704	9.573	9.263	9.308	9.178	9.586	8.308
SLOVENIJA / SLOVENIA	110.497	115.089	109.502	105.237	100.408	99.972	103.637	102.879	101.047	99.952	87.414

ŠTEVILO NOVIH KRVODAJALCEV

NUMBER OF NEW BLOOD DONORS

LETO / YEAR	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
Slovenija / Slovenia	12.503	12.781	10.706	10.369	9.596	8.654	9.548	9.514	9.822	9.324	6.643

ŠTEVILO ODVZEMOV POLNE KRVI

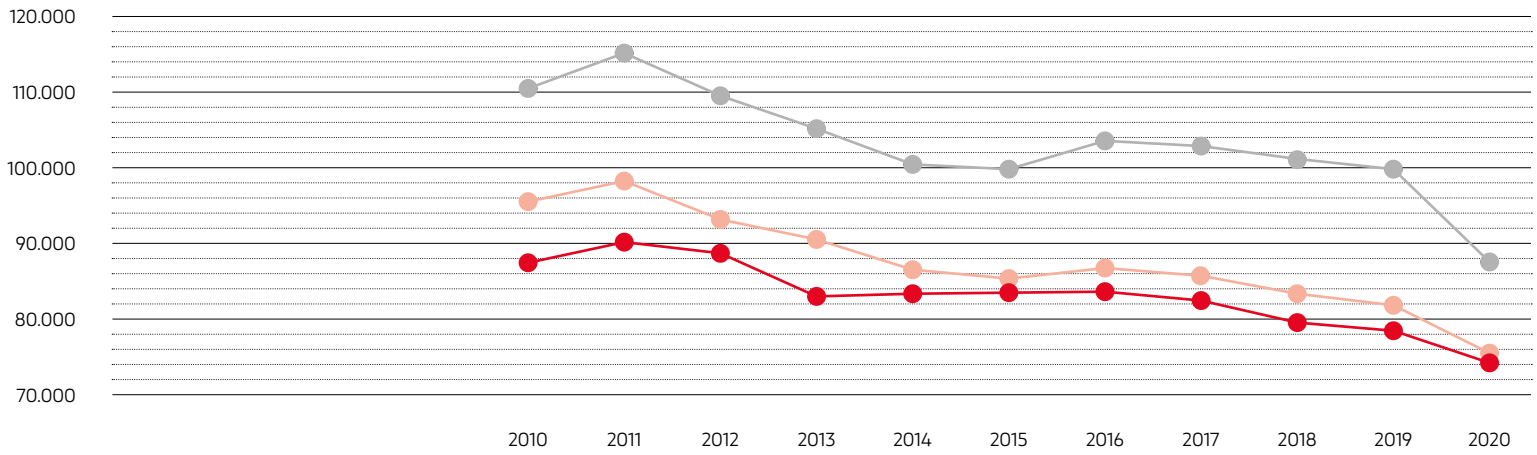
NUMBER OF WHOLE BLOOD UNITS COLLECTED

LETO / YEAR	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
ZTM Ljubljana / BTC Ljubljana	42.491	44.205	41.945	39.242	36.817	36.547	38.275	38.579	37.631	35.736	32.195
CTD Izola / TU Izola	5.991	6.329	5.523	5.227	5.354	5.090	5.331	4.953	4.820	4.936	4.650
CTD Jesenice / TU Jesenice	2.050	1.842	1.777	1.778	1.816	1.761	1.640	1.402	1.195	1.334	1.215
CTD Nova Gorica / TU Nova Gorica	3.436	3.630	3.475	3.432	3.382	2.923	3.027	3.109	2.943	2.989	2.862
CTD Novo mesto / TU Novo mesto	5.472	5.954	5.710	5.800	5.760	5.718	5.882	5.727	5.755	6.025	5.530
CTD Slovenj Gradec / TU Slovenj Gradec	3.116	3.049	2.721	2.503	2.461	2.538	2.580	2.543	2.415	2.294	2.500
CTD Trbovlje / TU Trbovlje	1.316	1.250	1.116	934	973	802	803	895	843	961	1.001
SKUPAJ ZTM / TOTAL BTC	63.872	66.259	62.267	58.916	56.563	55.379	57.538	57.208	55.602	54.275	49.953
CTM Maribor / TMC Maribor	13.325	13.748	12.733	14.811	13.531	13.256	13.253	12.712	12.332	12.044	11.141
ETD Murska Sobota / TU Murska Sobota	4.333	4.333	4.385	4.376	4.079	4.082	3.862	3.677	3.498	3.593	3.564
ETD Ptuj / TU Ptuj	3.831	3.831	3.824	3.922	3.502	3.692	3.681	3.568	3.455	3.450	3.116
SKUPAJ CTM MARIBOR / TOTAL TMC MARIBOR	21.489	21.912	20.942	23.109	21.112	21.030	20.796	19.957	19.285	19.087	17.821
CTM Celje / TC Celje	10.240	10.136	9.890	8.611	8.934	8.986	8.662	8.726	8.394	8.579	7.864
SLOVENIJA / SLOVENIA	95.601	98.307	93.099	90.636	86.609	85.395	86.996	85.891	83.281	81.941	75.638

PRIKAZ GIBANJA PRIJAV KRVODAJALCEV, ŠTEVILA ODVZEMOV KRVI IN IZDAJ KONCENTRIRANIH ERITROCITOV

PRESENTATION OF REGISTERED BLOOD DONORS, THE NUMBER OF COLLECTED BLOOD UNITS AND NUMBER OF CONCENTRATED ERYTHROCYTES UNITS ISSUED

LETO / YEAR	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
Prijave / Registered blood donors	110.497	115.089	109.502	105.237	100.408	99.972	103.637	102.879	101.047	99.952	87.414
Št. odvzemov polne krvi / The number of whole blood units collected	95.601	98.307	93.099	90.636	86.609	85.395	86.996	85.891	83.281	81.941	75.638
Izdaja KE / The number of issued concentrated erythrocytes units	87.451	90.282	88.791	83.069	83.200	83.455	83.702	82.562	79.619	78.473	74.372



ŠTEVILO OPRAVLJENIH PLAZMAFEREZ

NUMBER OF PLASMAPHERESIS PERFORMED

*** Vključena HCP** /
* HCP included

LETO / YEAR	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
ZTM Ljubljana / BTC Ljubljana	512	711	623	902	100	565	1.919	1.950	2.514	2.723	1.848*
CTM Maribor / TMC Maribor	65	10	0	0	0	0	0	0	0	7	13
CTM Celje / TC Celje	0	0	0	0	0	0	0	0	0	0	0
SLOVENIJA / SLOVENIA	577	721	623	902	100	565	1.919	1.950	2.514	2.730	1.861

ŠTEVILO OPRAVLJENIH TROMBOCITAFEREZ

NUMBER OF PLATELETS APHERESIS PERFORMED

LETO / YEAR	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
ZTM Ljubljana / BTC Ljubljana	1.611	1.724	2.104	1.999	1.915	2.274	2.421	2.635	2.580	1.525	918
CTM Maribor / TMC Maribor	135	192	239	115	76	49	59	62	61	79	13
SLOVENIJA / SLOVENIA	1.746	1.916	2.343	2.114	1.991	2.323	2.480	2.697	2.641	1.604	931

ŠTEVILO IZDANIH ENOT KONCENTRIRANIH ERITROCITOV (KES/KEF)

NUMBER OF ISSUED UNITS OF CONCENTRATED RED BLOOD CELLS

LETO / YEAR	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
Skupaj ZTM Ljubljana / Altogether BTC Ljubljana	59.570	60.479	59.909	55.312	53.470	53.727	55.199	55.125	53.676	52.449	49.547
Skupaj CTM Maribor / Altogether TMC Maribor	20.708	22.293	20.827	20.695	21.332	21.403	20.660	19.394	18.230	18.198	17.026
CTM Celje / TC Celje	7.173	7.510	8.055	7.062	8.398	8.325	7.843	8.043	7.708	7.826	7.799
SLOVENIJA / SLOVENIA	87.451	90.282	88.791	83.069	83.200	83.455	83.702	82.562	79.614	78.473	74.372

ŠTEVILO IZDANIH ENOT KONCENTRIRANIH TROMBOCITOV IZ POLNE KRVI (KT)

NUMBER OF ISSUED POOLED PLATELET UNITS

LETO / YEAR	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
Skupaj ZTM Ljubljana / Altogether BTC Ljubljana	4.569	5.006	5.340	5.551	5.238	5.502	7.561	7.833	7.225	6.623	6.540
Skupaj CTM Maribor / Altogether TMC Maribor	1.816	2.092	2.090	1.997	1.864	1.796	2.135	1.862	1.493	1.453	1.347
CTM Celje / TC Celje	416	550	485	514	624	733	713	723	673	805	576
SLOVENIJA / SLOVENIA	6.801	7.648	7.915	8.062	7.726	8.031	10.409	10.418	9.391	8.881	8.463

ŠTEVILO IZDANIH ENOT KONCENTRIRANIH TROMBOCITOV IZ TROMBOFEREZE (KT)

NUMBER OF ISSUED APHERESIS PLATELET UNITS

LETO / YEAR	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
Skupaj ZTM Ljubljana / Altogether BTC Ljubljana	2.355	2.484	3.120	2.891	2.611	2.714	2.832	2.917	2.806	1.664	1.040
Skupaj CTM Maribor / Altogether TMC Maribor	122	158	236	117	76	42	76	62	93	90	20
CTM Celje / TC Celje	1	1	4	0	0	0	0	0	0	0	0
SLOVENIJA / SLOVENIA	2.478	2.643	3.360	3.008	2.687	2.756	2.908	2.979	2.899	1.754	1.060

ŠTEVILO IZDANIH ENOT SVEŽE ZAMRZNJENE PLAZME (SZP)

NUMBER OF ISSUED FRESH FROZEN PLASMA UNITS

LETO / YEAR	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
Skupaj ZTM Ljubljana / Altogether BTC Ljubljana	18.595	19.147	19.143	17.029	13.356	13.461	15.654	13.584	11.823	9.943	9.882
Skupaj CTM Maribor / Altogether TMC Maribor	9.187	9.398	9.354	9.089	8.431	7.127	7.400	4.638	3.303	34.06	2.589
CTM Celje / TC Celje	2.097	1.762	2.074	1.767	1.145	1.027	913	1.002	911	785	709
SLOVENIJA / SLOVENIA	29.879	30.307	305.71	27.885	22.932	21.615	23.967	19.224	16.037	14.134	13.180

POGOSTNOST ZAZNAVANJA PROTITELES VSEH OZNAČEVALCEV OKUŽB PRI KRVODAJALCIH V OBDOBJU OD 2010 DO 2020

FREQUENCY OF VIRAL MARKERS DETECTION IN BLOOD DONORS IN THE PERIOD FROM 2010 TO 2020

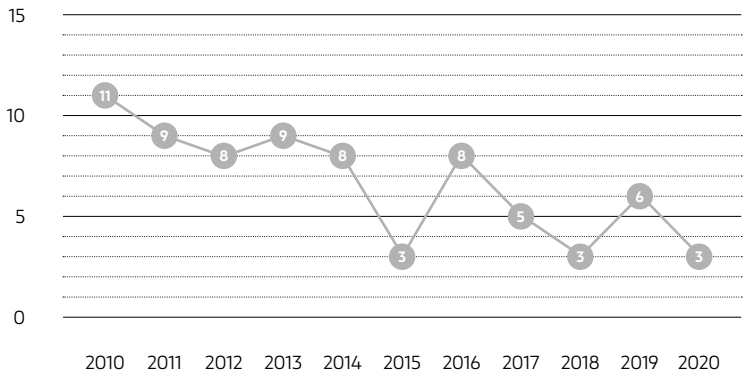
		ŠT. ODKRITIH KRVODAJALCEV / NUMBER OF DETECTED DONORS	**LETNO POVPREČJE** / ANNUAL AVERAGE	**POGOSTNOST NA 100.000 ODVZETIH ENOT** / OCCURRENCE AT 100.000 COLLECTED UNITS	**PREVALENCA POJAVNOSTI MED ODVZETIMI ENOTAMI** / PREVALENT OCCURRENCE AMONG THE COLLECTED UNITS
Hepatitis B	**HBsAg**	73	6	$9{,}0/10^5$	1 : 11.090
	HBV DNA	40	3	$4{,}9/10^5$	1 : 20.239
Hepatitis C	**Anti-HCV**	25	2	$3{,}1/10^5$	1 : 32.382
	samo HCV RNA	0	0	/	/
HIV	**Anti-HIV 1/2/O in p24**	15	1	$18{,}5/10^5$	1 : 53.970
Sifilis	**Anti Treponema pallidum**	72	6	$8{,}9/10^5$	1 : 11.244

ŠT. TESTIRANIH ENOT / THE NUMBER OF TESTED UNITS **809.553**

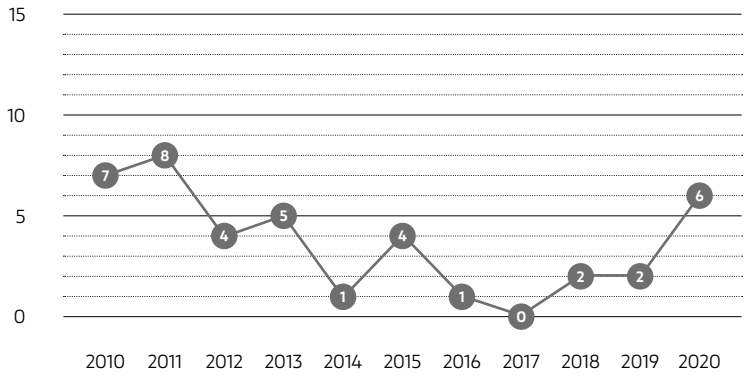
POGOSTNOST ZAZNAVANJA NEUSTREZNIH ENOT KRVI ZARADI VSEBNOSTI OZNAČEVALCEV OKUŽB MED LETOMA 2010 IN 2020

FREQUENCY OF DETECTING UNSUITABLE UNITS OF BLOOD DUE TO THE CONTENT OF INFECTIOUS MARKERS BETWEEN 2010 AND 2020

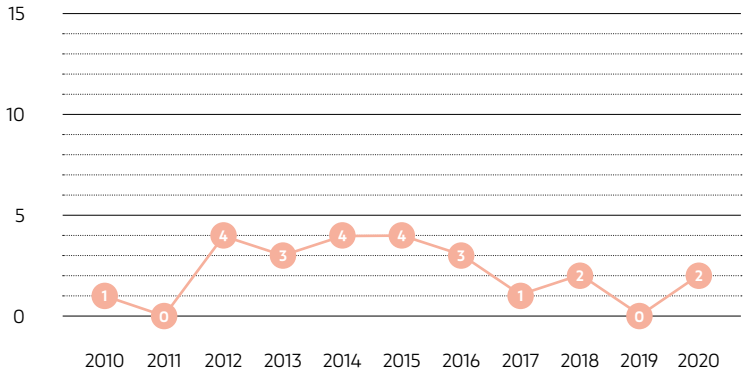
Hepatitis B: HBsAg



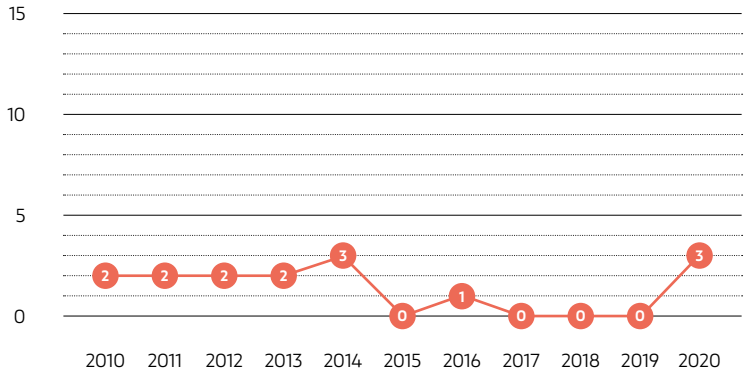
HBV DNA (OBI)



Hepatitis C: anti-HCV



AIDS: anti-HIV



Sifilis: anti-Treponema pallidum

V SKLOPU IMUNOHEMATOLOŠKIH PREISKAV SMO ZA BOLNIKE OPRAVILI:

WITHIN THE IMMUNO-HEMATOLOGICAL TESTS FOR PATIENTS, WE PERFORMED:

* **Opravlja ZTM** /
* Performed by BTC Ljubljana

LETO / YEAR	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Navzkrižnih preizkusov / Cross-match tests	135.766	143.288	136.792	132.575	131.464	130.074	140.616	130.090	123.643	123.797	116.462
Določitev krvne skupine ABO, RhD in Kell / Determination of blood group ABO, RhD and Kell	74.898	76.789	71.398	66.650	71.892	64.163	64.710	65.291	63.963	64.606	59.614
Coombsovih testov / Coombs tests	70.293	90.836	94.270	96.183	94.560	93.392	94.456	88.778	90.515	87.979	82.802
Sspecifikacij eritrocitnih protiteles / Erythrocyte antibodies specifications	1.925	2.553	2.512	2.729	2.607	2.647	2.838	2.889	3.069	2.833	2.584
Preiskav pred injiciranjem Ig anti-D / Tests before Ig anti-D injection	6.624	6.851	8.387	8.553	8.354	8.475	8.984	8.114	8.194	8.715	7.438
***Trombocitnih preiskav** / *Platelet tests	1.152	1.247	1.063	914	962	929	1.061	1104	1.022	1.240	1.538
***Granulocitnih preiskav** / *Granulocytic tests	59	459	84	184	181	189	46	99	73	139	117
***Molekularnobioloških preiskav** / *Molecular-biological tests	229	351	189	328	439	329	211	382	730	3.380	3.186
***Molekularnobioloških preiskav - določitev plodovega genotipa RhD** / Foetal genotyping RhD										3.012	2.822

OPRAVLJENE PREISKAVE, TESTI IN STORITVE, KI SO VEZANI NA DOLOČANJE TKIVNE SKLADNOSTI

PERFORMED HISTOCOMPATIBILITY TESTING

LETO / YEAR	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Storitev, ki podpirajo transplatacijo organov / Services which support organ transplantation	10.565	9.681	8.591	11.035	10.430	12.770	11.117	8.726	15.223	14.814	11.561
Storitev, ki podpirajo transplatacijo KMC / Services which support HSC transplantation	3.187	1.735	1.905	1.858	3.005	1.944	1.736	1.753	2.279	1.690	1.297
Tipizacij HLA za register Slovenija Donor / HLA typing for the Slovenia Donor registry	1.602	2.117	1.499	1.000	3.071	2.306	1.386	1.272	2.956	3.630	1.298
Storitev za diagnostiko (avtoimunskih bolezni) / Diagnostic services (autoimmune disease)	828	717	408	132	155	74	89	73	76	61	51
Storitev za register Slovenija Donor / Services for the Slovenia Donor registry	635	559	264	257	304	227	209	279	304	267	115

STORITVE NA ZTM, OPRAVLJENE V SKLOPU TERAPEVTSKIH STORITEV

SERVICES AT BTC IN LJUBLJANA, PERFORMED WITHIN THE SPECIAL THERAPEUTIC SERVICES

LETO / YEAR	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
Avtologni odvzemi krvotvornih matičnih celic / Autologous haematopoietic stem cell sampling	147	162	181	177	163	188	153	218	158	176	174
Alogenski odvzemi krvotvornih matičnih celic / Allogeneic haematopoietic stem cell withdrawals	25	18	16	14	16	21	28	21	21	14	22
Granulofereze / Granulopheresis	31	37	84	86	67	94	70	65	106	35	7
Limfofereze (donorski limfociti, celične terapije) / Lymphopheresis (donor lymphocytes, cell therapies)	1	3	3	0	1	1	1	1	1	2	2
Terapevtske trombofereze / Therapeutic thrombopheresis	0	0	0	0	0	0	0	0	0	7	0
Terapevtske levkofereze / Therapeutic leukapheresis	5	13	16	4	4	0	0	3	0	4	6
Postopek koncentriranja kostnega mozga / Process of concentrating bone marrow	1	2	0	4	2	0	0	0	0	3	1
Transfuzije krvotvornih matičnih celic/ donorskih limfocitov / Haematopoietic stem cell/ donor lymphocyte transfusions	90	79	75	68	69	86	109	111	118	104	146
Fotofereze / Photopheresis				214	447	632	614	803	1.048	952	792

LETO / YEAR	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
Terapevtski odvzemi polne krvi / Number of whole blood draws	250	277	289	275	286	333	433	524	546	372	346
Odvzemi avtologne krvi (avtotransfuzija) / Autologous blood sampling (autotransfusion)	205	195	124	124	59	32	29	31	30	22	27
Odvzemi krvi za avtologni oz. alogenski serum / Blood sampling for autologous or allogeneic serum	16	14	10	10	8	26	19	42	9	75	130
Pregledi darovalcev granulocitov / Screenings of granulocyte donors								169	348	208	37
Pregledi darovalcev/bolnikov za odvzem KMC/ MNC/DLI* / Examinations of donors/patients for HSC/MNC/DLI withdrawal *								1.178	1.347	1.268	1.128

*

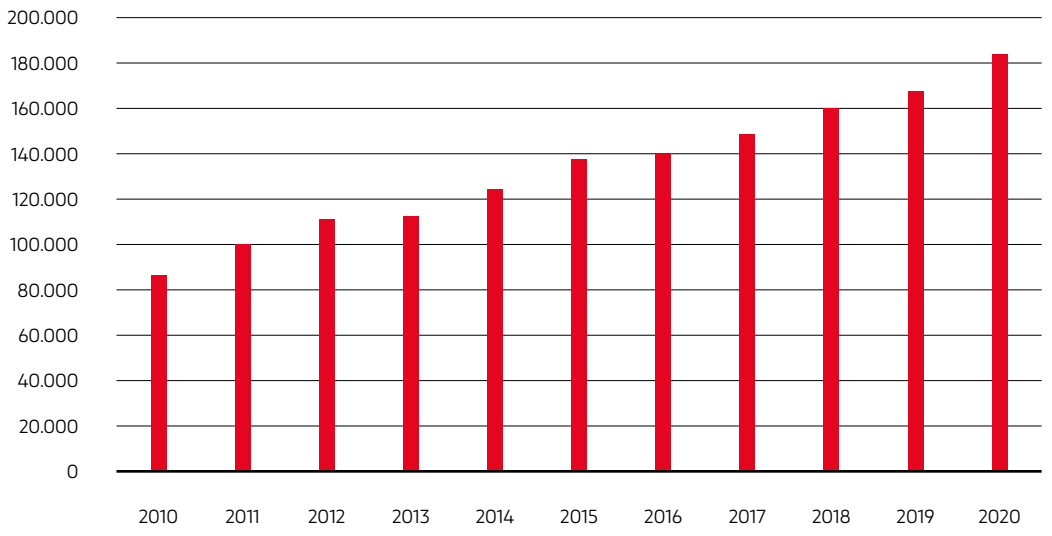
KMC – krvotvorne matične celice
MNC – mononuklearne matične celice
DLI – donorski limfociti

HSC – haematopoietic stem cells
MNC – mononuclear stem cells
DLI – donor lymphocytes

PODATKI O SHRANJEVANJU CELIC V TEKOČEM DUŠIKU MED LETOMA 2010 IN 2020

DISPLAY OF CELL STORAGE IN LIQUID NITROGEN IN THE YEARS FROM 2010 TO 2020

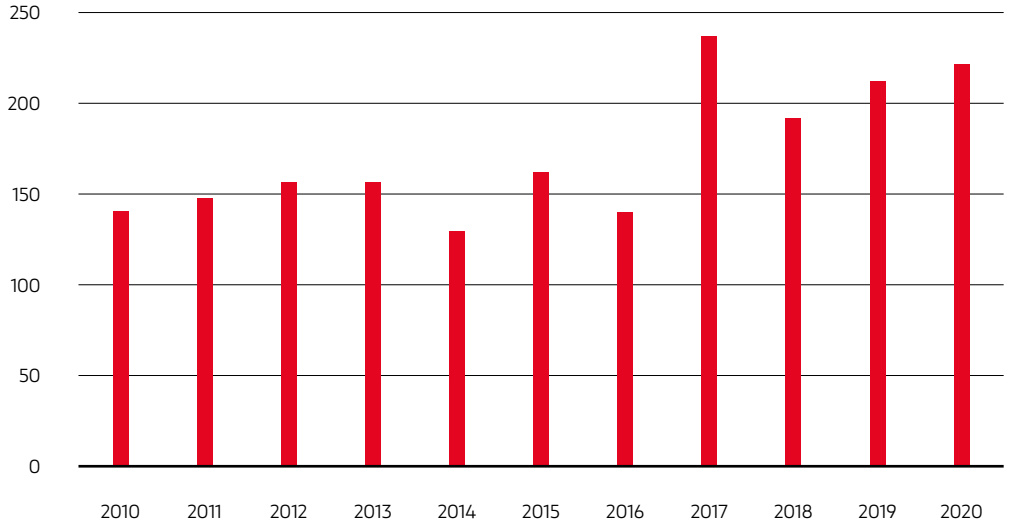
Os y: 365 dni x št. bolnikov /
Y-axis: 365 days x no. patients



PODATKI O ZAMRZOVANJU CELIC MED LETOMA 2010 IN 2020

DISPLAY OF CELL FREEZING IN THE PERIOD FROM 2010 TO 2020

Os y: št. zamrzovanj na leto /
Y-axis: number of freezes per year



NEŽELENE TRANSFUZIJSKE REAKCIJE GLEDE NA VRSTO REAKCIJE V SLOVENIJI MED LETOMA 2011 IN 2020

NUMBER AND TYPE OF REPORTED ADVERSE REACTIONS TO BLOOD TRANSFUSION IN SLOVENIA / HEAMOVIGILANCE BETWEEN 2011 AND 2020

LETO / YEAR	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
Hemoliza / Haemolysis	3	7	1	1	2	0	0	2	1	0
GVHD – reakcija presadka proti gostitelju / GvHD	0	0	0	0	0	0	0	0	0	0
TRALI – s transfuzijo povzročena akutna okvara pljuč / TRALI	1	1	2	1	0	0	0	0	0	3
TACO – volumska preobremenitev / TACO	10	13	9	8	5	11	5	8	3	7
PTP – posttransfuzijska purpura / PTP	0	0	0	0	0	0	0	0	0	0
Alergija / Allergy	57	66	49	58	53	51	34	35	39	21
Anafilaksija / Anaphylaxis	7	5	3	3	0	4	0	1	0	0
NHV – nehemolitična vročinska reakcija / Non-hemolytic transfusion reaction	52	60	34	38	53	60	38	47	36	37
Bakterijska okužba / Bacterial infection	0	0	0	1	0	0	0	0	0	0
Virusna okužba / Viral infection	1	0	3	2	1	2	1	0	0	0
Hipotenzija / Hypotension	0	2	1	1	3	0	0	3	3	1
Dispneja / Dyspnea	4	3	0	1	1	1	1	0	2	0
Drugo / Other	7	5	11	5	1	0	2	1	0	0
SKUPAJ / TOTAL	142	162	113	118	119	129	81	97	84	69

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