

VARIOUS APPLICATION OF ARTIFICIAL BLOOD

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INDEX

01

01

WHY

Artificial blood?

04

Future of

artificial blood

02

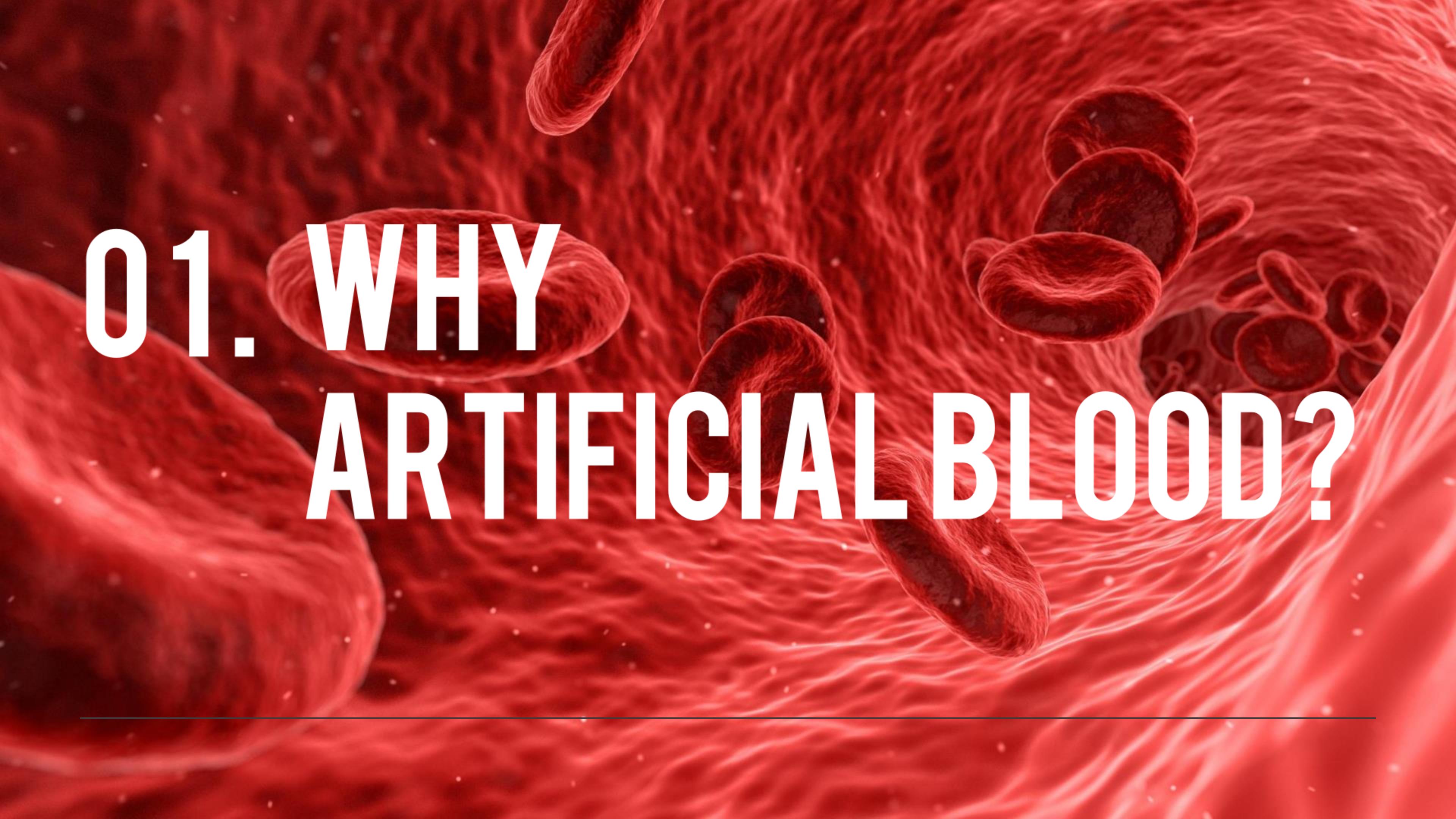
HOW

artificial blood?

03

History of

artificial blood



01. WHY ARTIFICIAL BLOOD?

For Blood Transfusion(수혈)

Blood is ONLY supplied by Blood Donation(헌혈),

BUT.....

SHORTAGE OF BLOOD IN KOREA

In Korea,

1020 generation is main source of blood

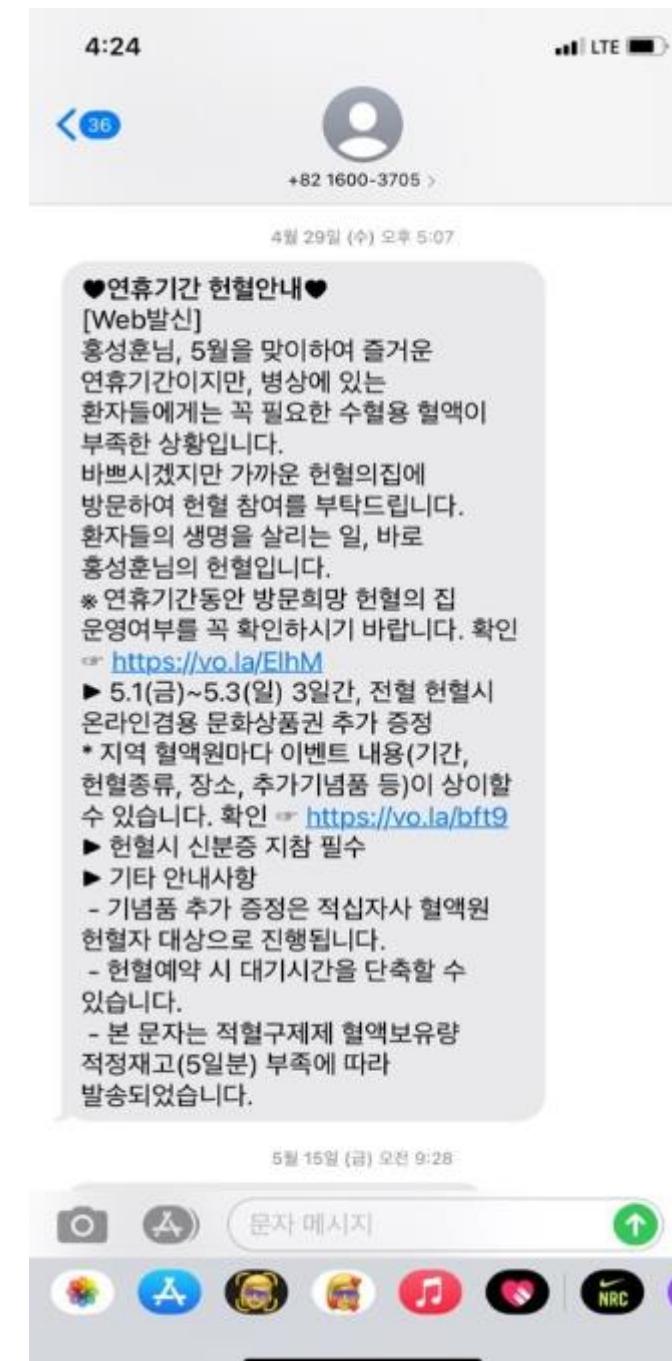
50+ generation is main demand of blood.

By low birth rate, and aging society,

1020 generation decreasing

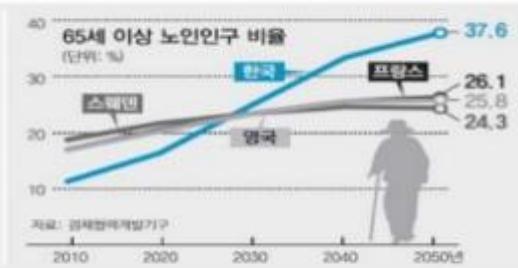
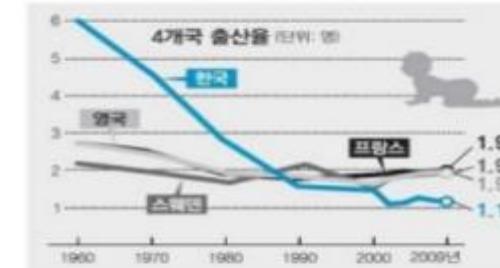
50+ generation increasing

RAPIDLY!!



1. 현재 상황 분석

(2) 고령화되는 사회



게다가 우리 나라는 이미 **초고령화 사회로 진입**

헌혈 가능한 젊은 인구는 감소하고 있는 반면,
혈액 수급을 필요로 하는 노인 인구는 늘어나고 있다.

1. 현재 상황 분석

(3) 10/20대의 헌혈 공급 의존도 높음



[연령별 헌혈자 비율]

이렇게 적은 헌혈을 안에서도 **약 80% 가량이 10-20대의 헌혈에 의존**하고 있다.

SHORTAGE OF BLOOD IN WORLD

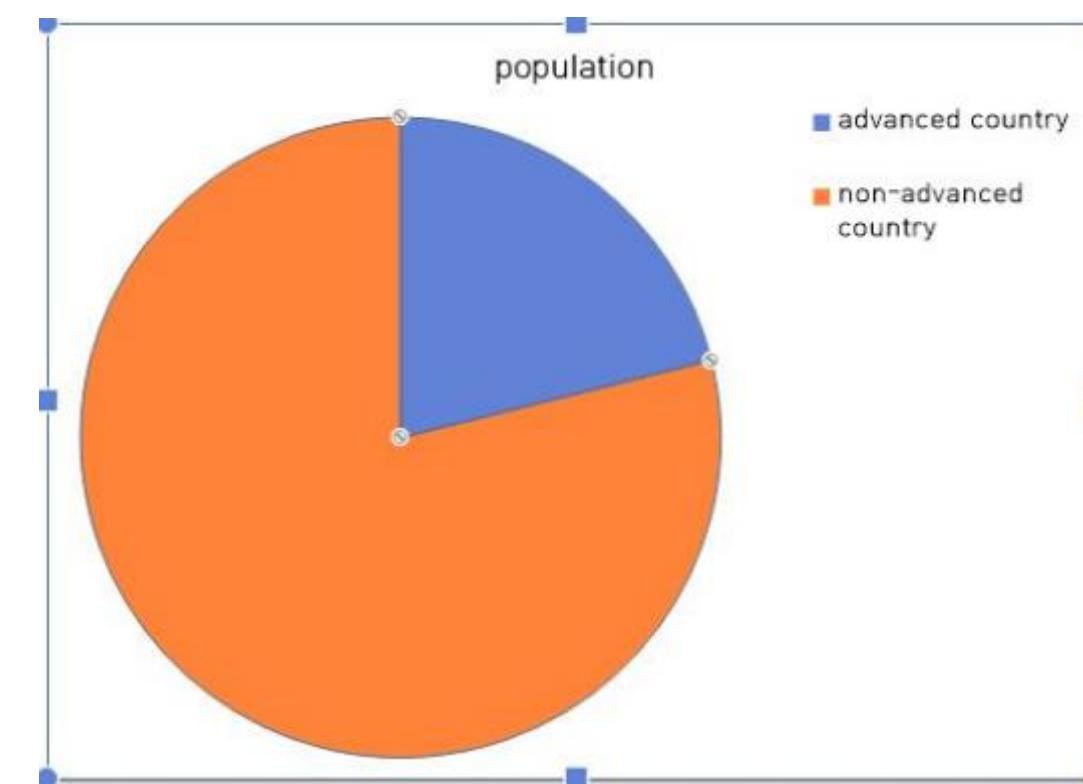
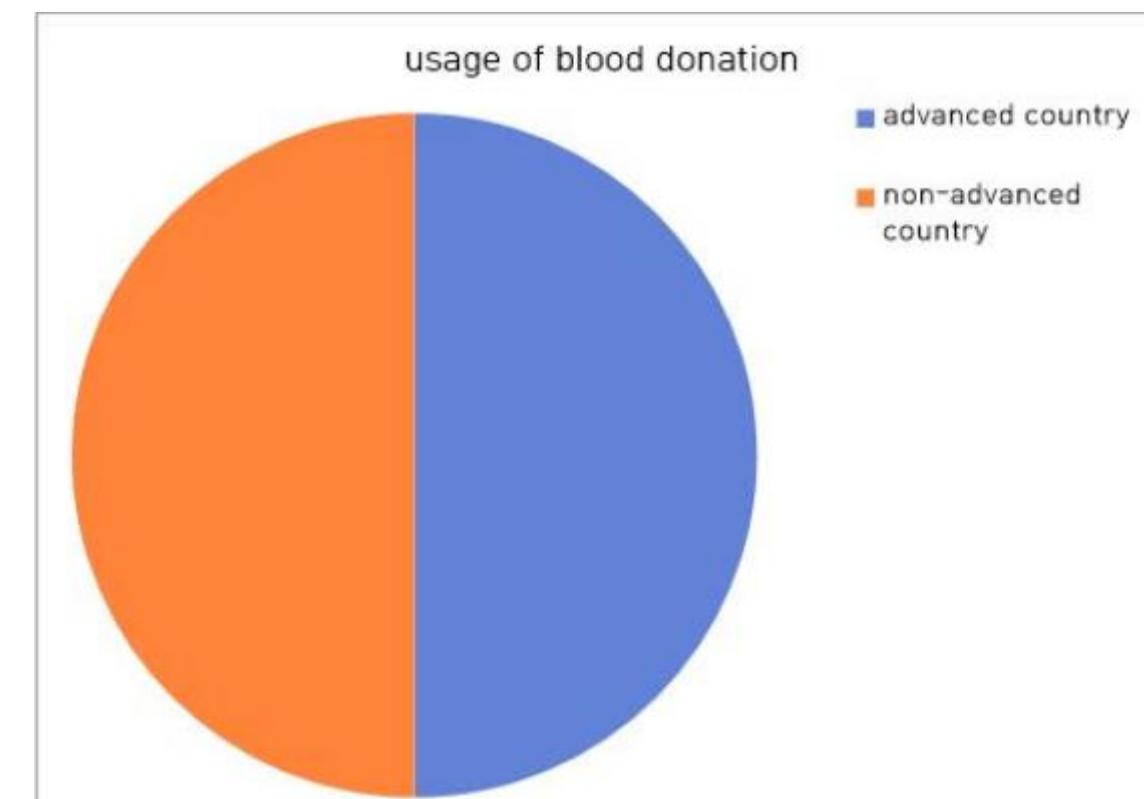
In WORLD,

There are 112.5 million units of blood
donation

Half of them : used in advanced country

population of advanced country : only 19%

27 countries in Africa : only 4 million units

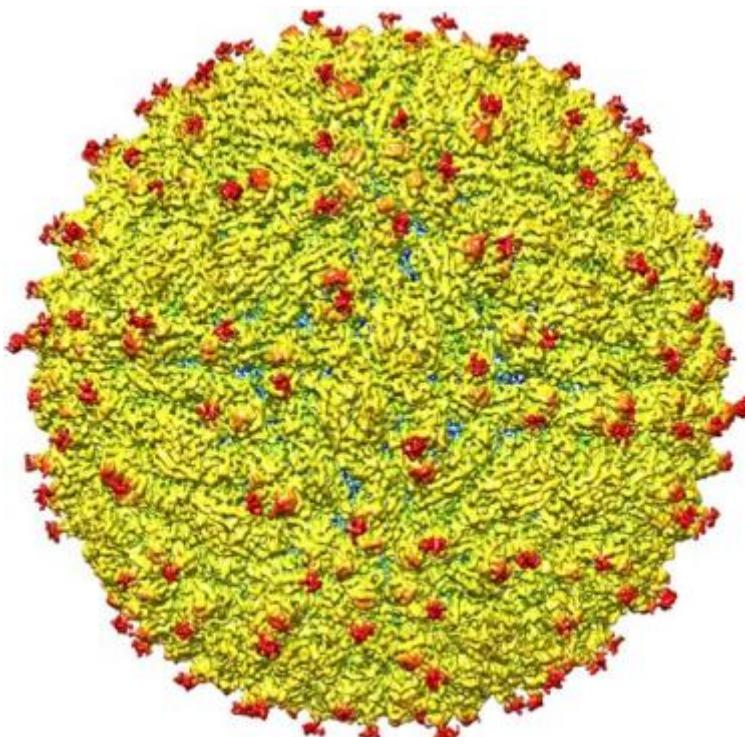
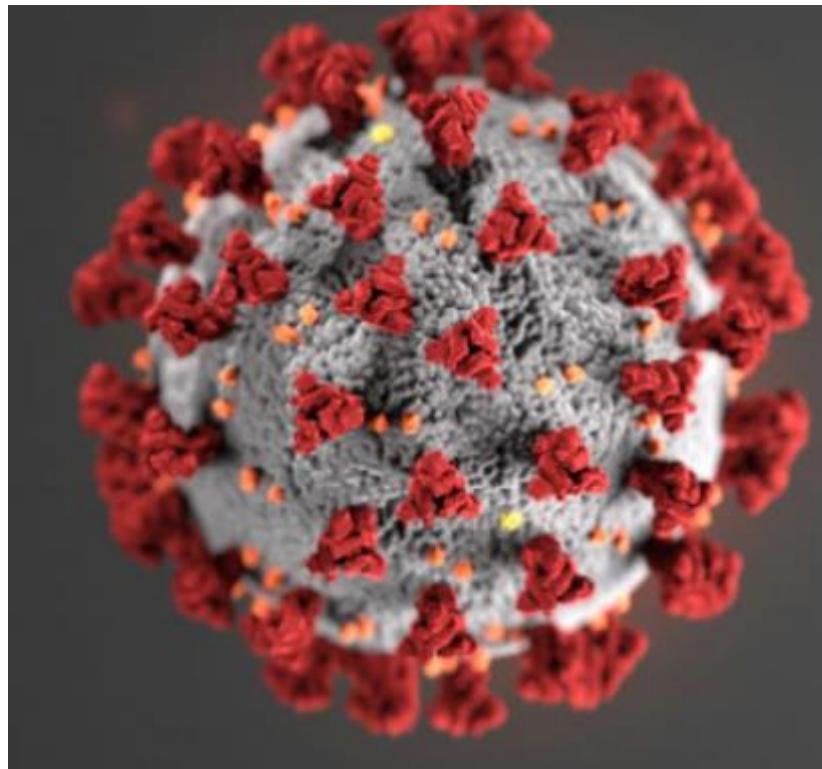


DRAWBACK OF BLOOD DONATION

Problem of Transfusion-transmitted infection
(수혈감염)

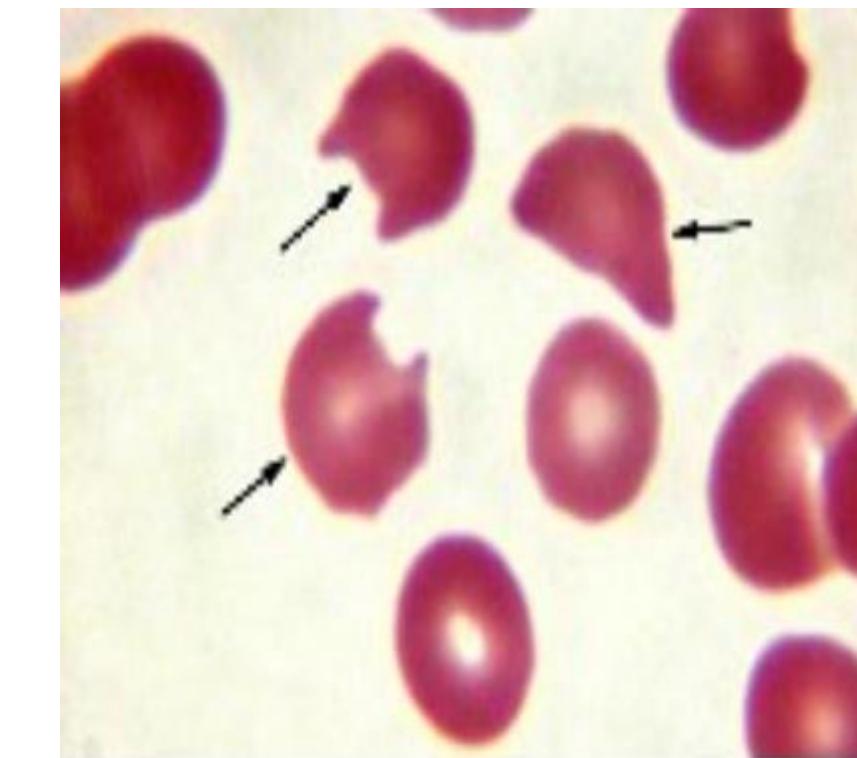
COVID19, Zica-virus... can be transmitted by
blood donation

To prevent this, A LOT OF inspection cost
is needed

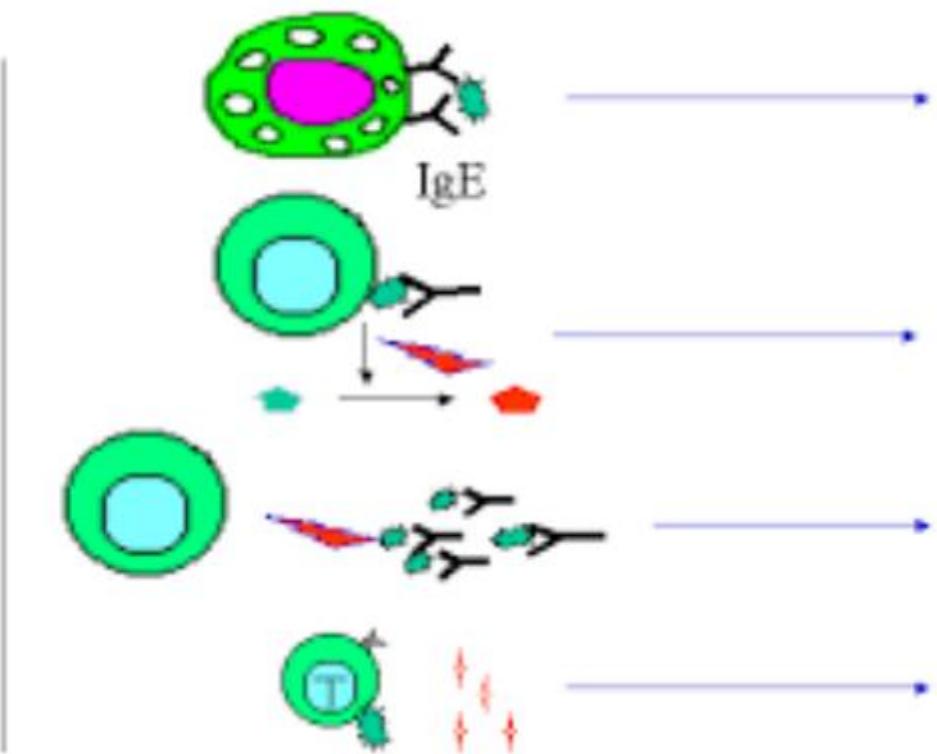


DRAWBACK OF BLOOD DONATION

Problem of ABO incompatible blood transfusion
(ABO 부적합 수혈)



Type I
Type II
Type III
Type IV



In developing country, several ABO incompatible blood transfusion happened

Lots of side effects

- hemolytic transfusion reaction(용혈수혈반응)
- allergic reaction(알레르기 반응)

....

Antigen (on RBC)	Type A	Type B	Type AB	Type O
Antibody (in plasma)	Anti-B Antibody	Anti-A Antibody	Neither Antibody	Both Antibodies
Blood Donors	Cannot have B or AB blood Can have A or O blood	Cannot have A or AB blood Can have B or O blood	Can have any type of blood Is the universal recipient	Can only have O blood Is the universal donor

02

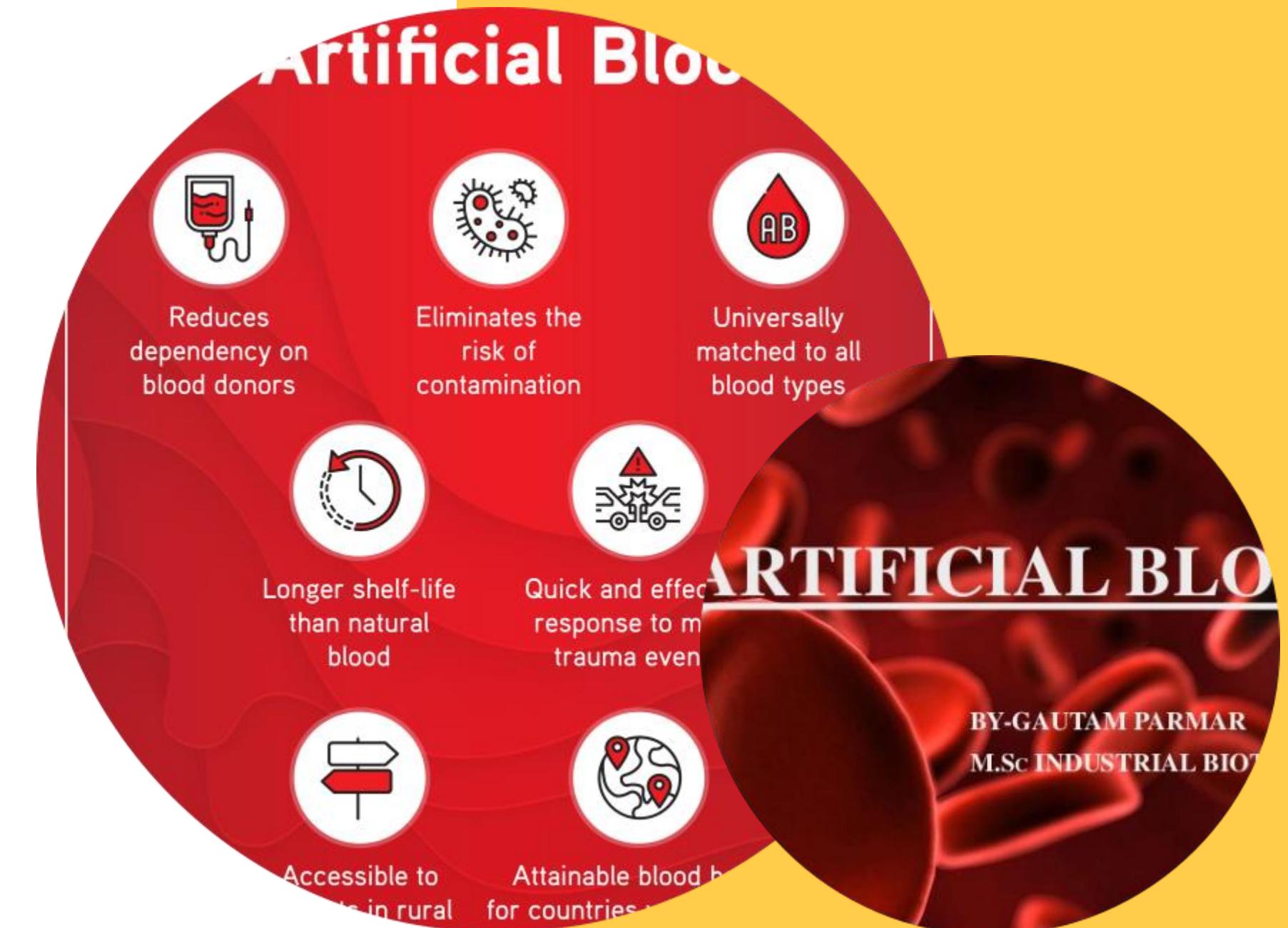
HOW
ARTIFICIAL BLOOD?

Function and Characteristics of Artificial Blood

06 FUNCTION

artificial blood cell function

oxygen carrying capacity



Two kinds Artificial O₂ carriers

07

HEMOGLOBIN BASED O₂ CARRIERS

Made based on hemoglobin

08

PERFLUOROCARBON EMULSIONS

Made into emulsion and used

infusion in low doses

A) Hemoglobin based O₂ carriers

WHY HBOC?

A)

reduce tissue damage

supplies oxygen to tissues

less side effects than clinical benefits.

01

USE

- # alternative to red blood cells
- major surgery
- patients with severe trauma
- carrier of oxygen

02

STERILIZATION

- # can be sterilized
- prevent the spread of germs and viruses
- avoiding the risk of infection of diseases

03

STORAGE

- General blood
 - stored in a refrigerator of 2 to 6 oC for up to 42 days at the most
- HBOC
 - stored at room temperature for up to 3 years from 1 year.

Function and Characteristics of HBOC

04

TRANSFUSION

-
- # immediate transfusion in emergency
 - no need for cross-matching
 - can be used regardless of blood type

05

INDOOR

-
- HBOC
 - effective in indoor oxygen concentrations.
 - perfluorocarbon solutions
 - no effective

06

LOW VISCOSITY

-
- # low viscosity
 - effectively used for shock, stroke, myocardial infarction, multi organ failure

manufacturing process of HBOC

MANUFACTURING PROCESS OF HBOC

Hemoglobin

- # red blood cells of human or animal
- # recombinant technology

refining

- # necessary both before and after the transformation of the chromosomes
- # non-chromatic cell debris & non-modified tetramic hemoglobin.

modification

- # intramolecular crosslinking, polymerization, conjugation to macromolecules
 - # transformation by genetic manipulation
 - # microcapsulation.
-
-

03. HISTORY OF ARTIFICIAL BLOOD



HOW IS IT POSSIBLE??

In 1966, prof. L.C. Clark made a mouse
SURVIVE UNDERWATER

PFC liquid : supplying air to mouse's lung

Scientists begin focusing on this liquid : **PFC**
(PerFluoroCarbons)



ARTIFICIAL BLOOD AS OXYGEN CARRIER

Main Roles of BLOOD

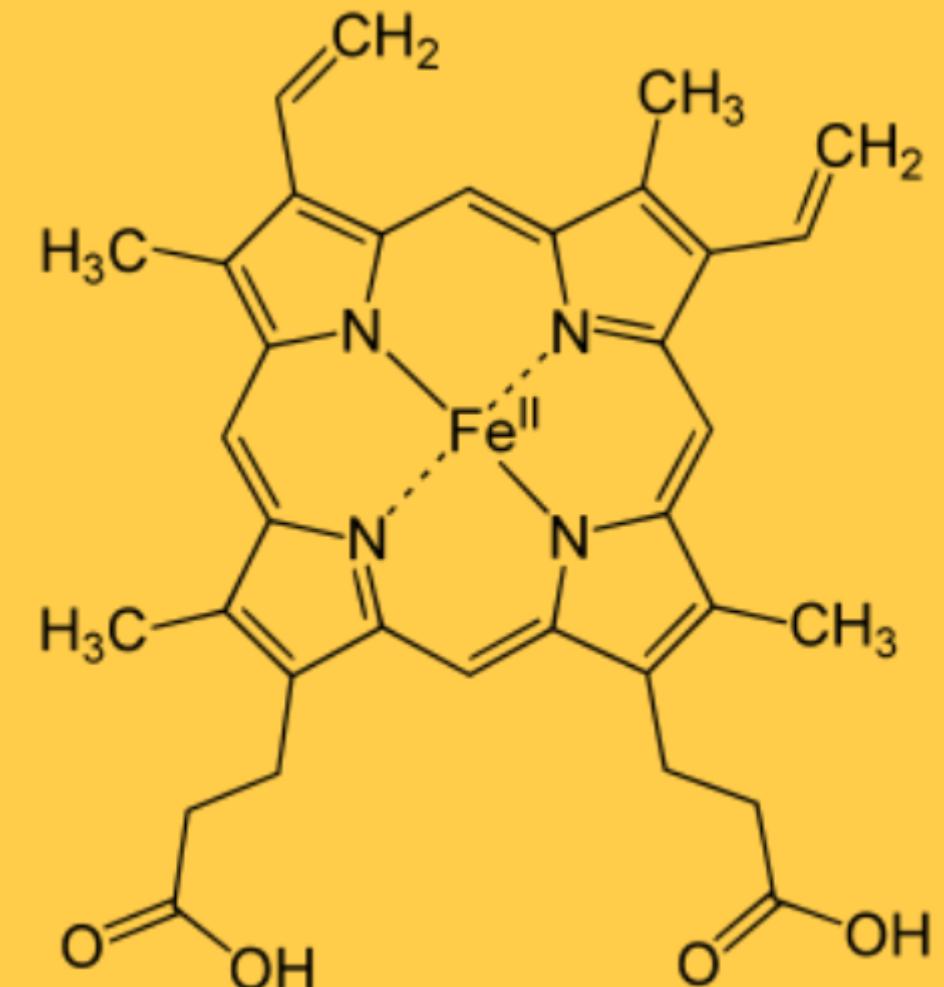
oxygen carrier(hemoglobin)/carbon dioxide remover

nutrient carrier

hormone carrier

...

Scientists start expecting **Artificial blood**
: OXYGEN CARRIER

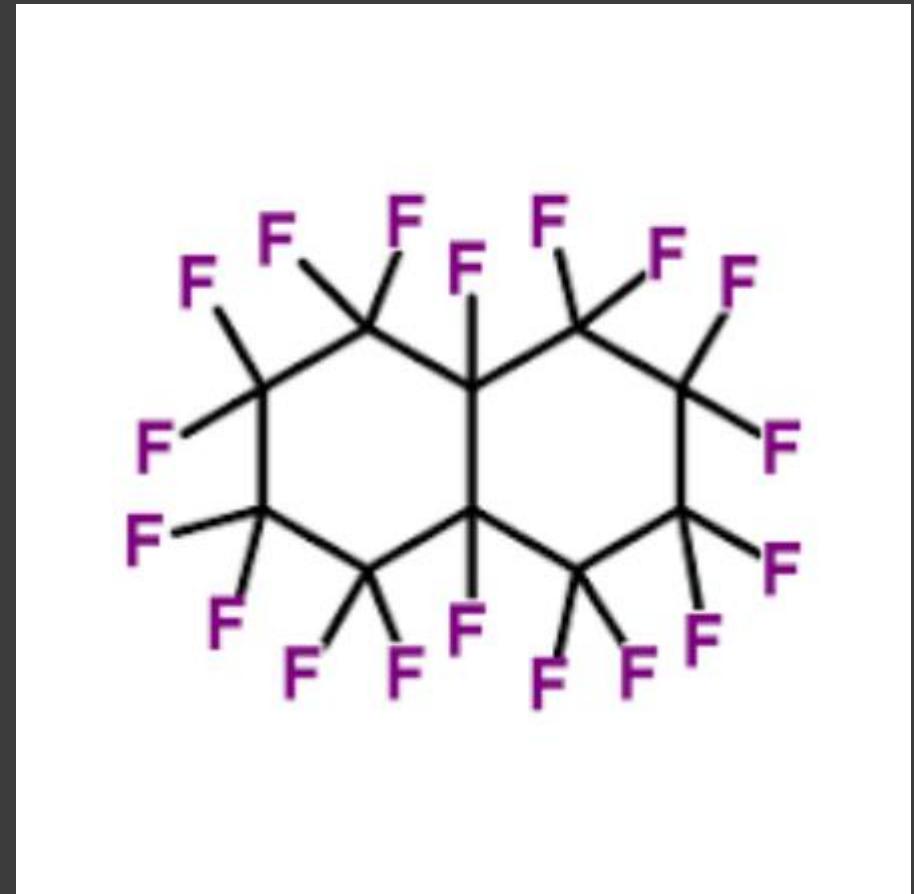
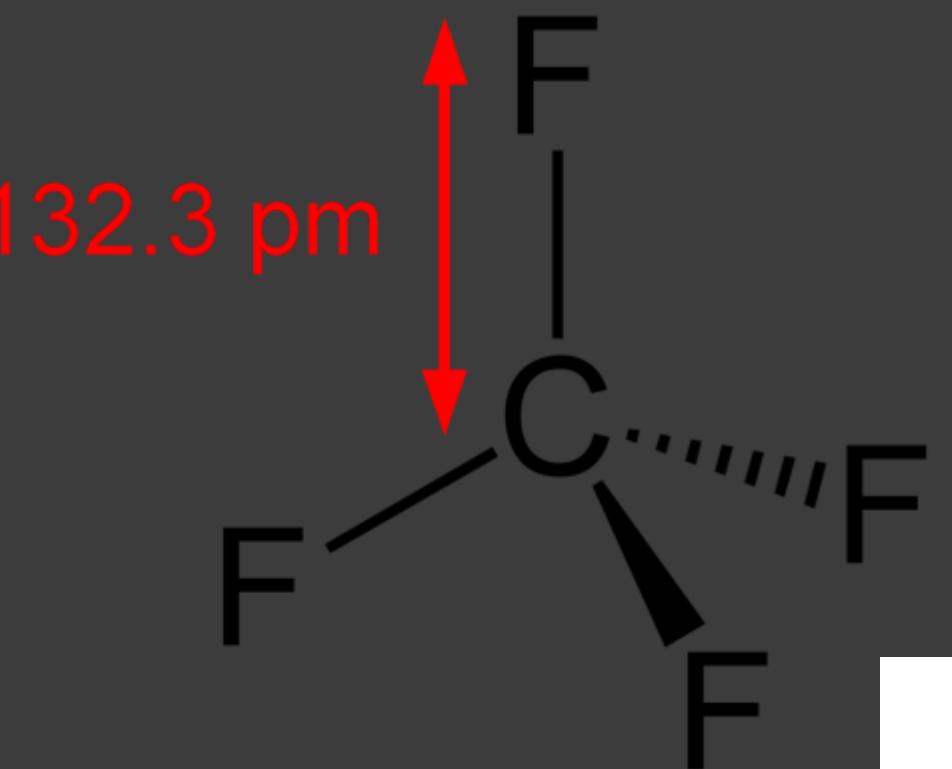


WHAT IS PFC? (플루오린화탄소)

PerFluoroCarbon : C_xF_y

About Artificial blood

- C₁₀F₁₈(perfluorodecaline) : oxygen solubility ↑ ↑
(water X20 / EVEN blood X2)
- Not soluble in water (non-polar structure)



WHAT IS PFC? (플루오린화탄소)

High oxygen solubility

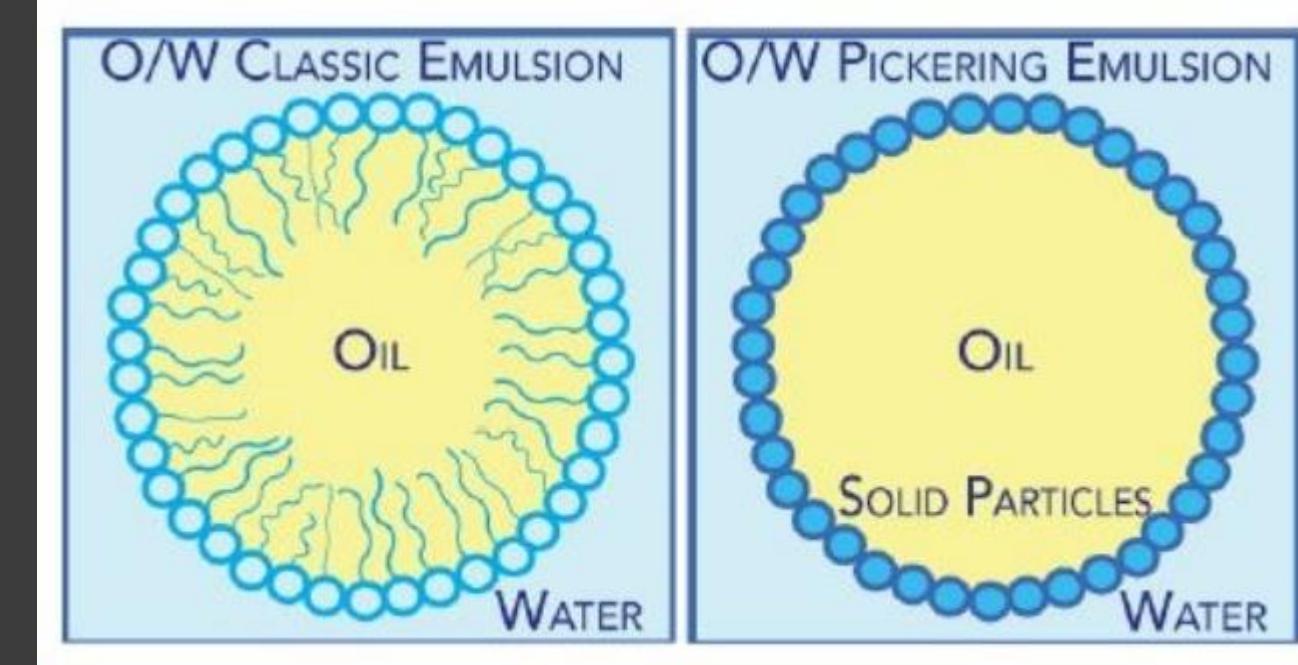
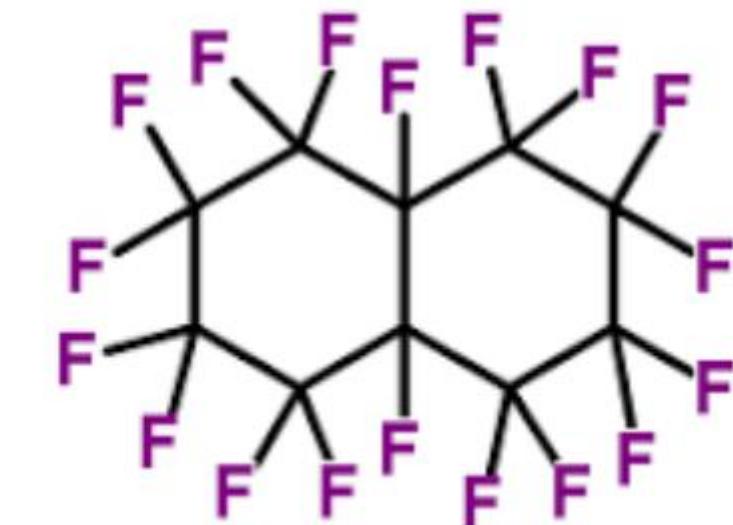
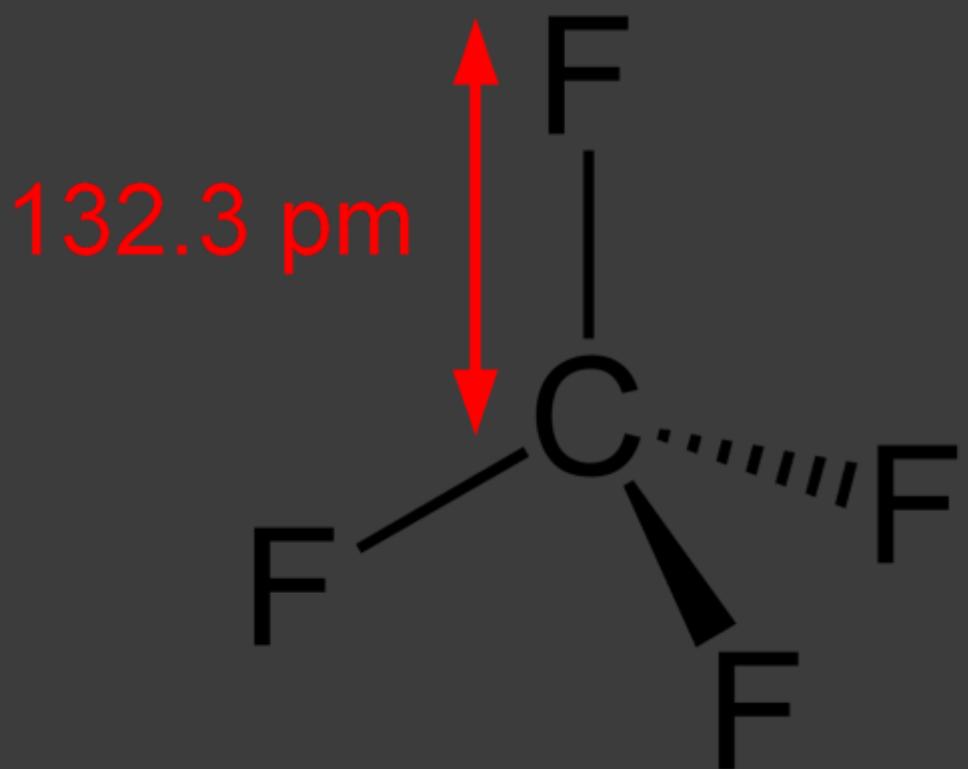
-> Best Material for OXYGEN CARRIER

Not Soluble in Water

-> If inserted in blood vessel in original form

harden / BLOCK BLOOD VESSEL!

-> need to be transformed into an EMULSION(유제)
in size 0.4mm



DEVELOPMENT OF EMERSION BUT.....

In 1968, prof. Gayer succeeded to develop
Emulsion of PFC

He replaced all of blood in mouse
by PFC emulsion, and **mouse SURVIVED** for 8 hrs!

Eye of 'Bloodless' mouse : WHITE(x blood)



DEVELOPMENT OF EMERSION BUT.....

PFC emulsion of Geyer has serious problem

:It's easy to be **accumulated in organ**

Other developments of PFC afterward have **many side effects**

(cause stroke, thrombopenia(혈판감소증)....)

->All of developments : SUSPENDED

Many advantages(long shelf life, x ABO incompatible transfusion....)

->Still research about PFC is on progress

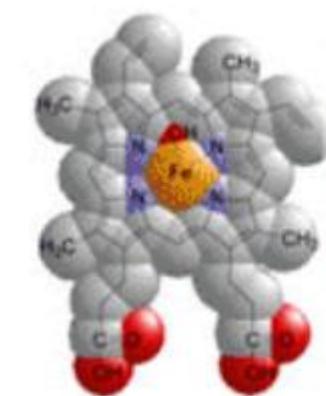


HEMOGLOBIN BASED OXYGEN CARRIER (HBOC)

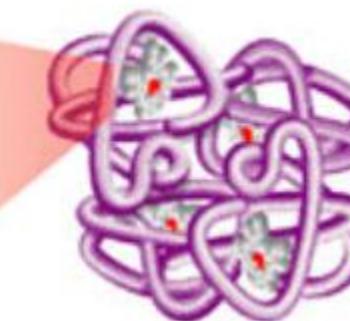
Hemoglobin : main oxygen carrier in Red Blood Cell

Scientists start to focus on

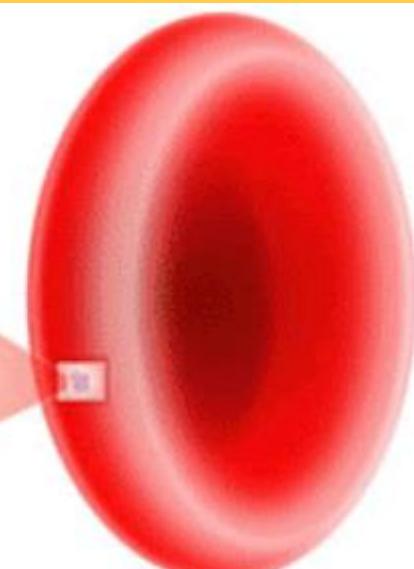
possibility of HEMOGLOBIN as an oxygen carrier.....



Heme



Hemoglobin



Erythrocyte

HEMOGLOBIN BASED OXYGEN CARRIER (HBOC)

HBOC had several problems

: vasoconstriction(혈관수축)

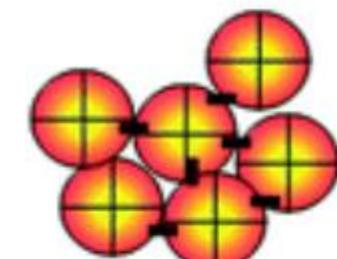
: cause oxygen radical(활성 산소)-> high blood pressure / nephrotoxic(신독성)

...

Scientists tried hard to solve these side effects...

-> There are 4 generations of HBOC

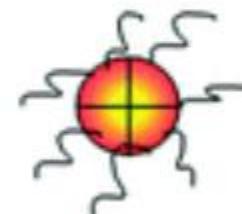
1st Generation modified hemoglobin (1st reports)



PolyHemoglobin (nanobiotechnology based)

1964 Chang (diacid)

1971 Chang (glutaraldehyde)



Conjugated Hb

1964 Chang (polyamide)

1968 Wong (dextran)

1970 Abuchowski & Davis (PEGylation)

1980 Iwashita (polyethylene glycol)



Crosslinked tetrameric Hb

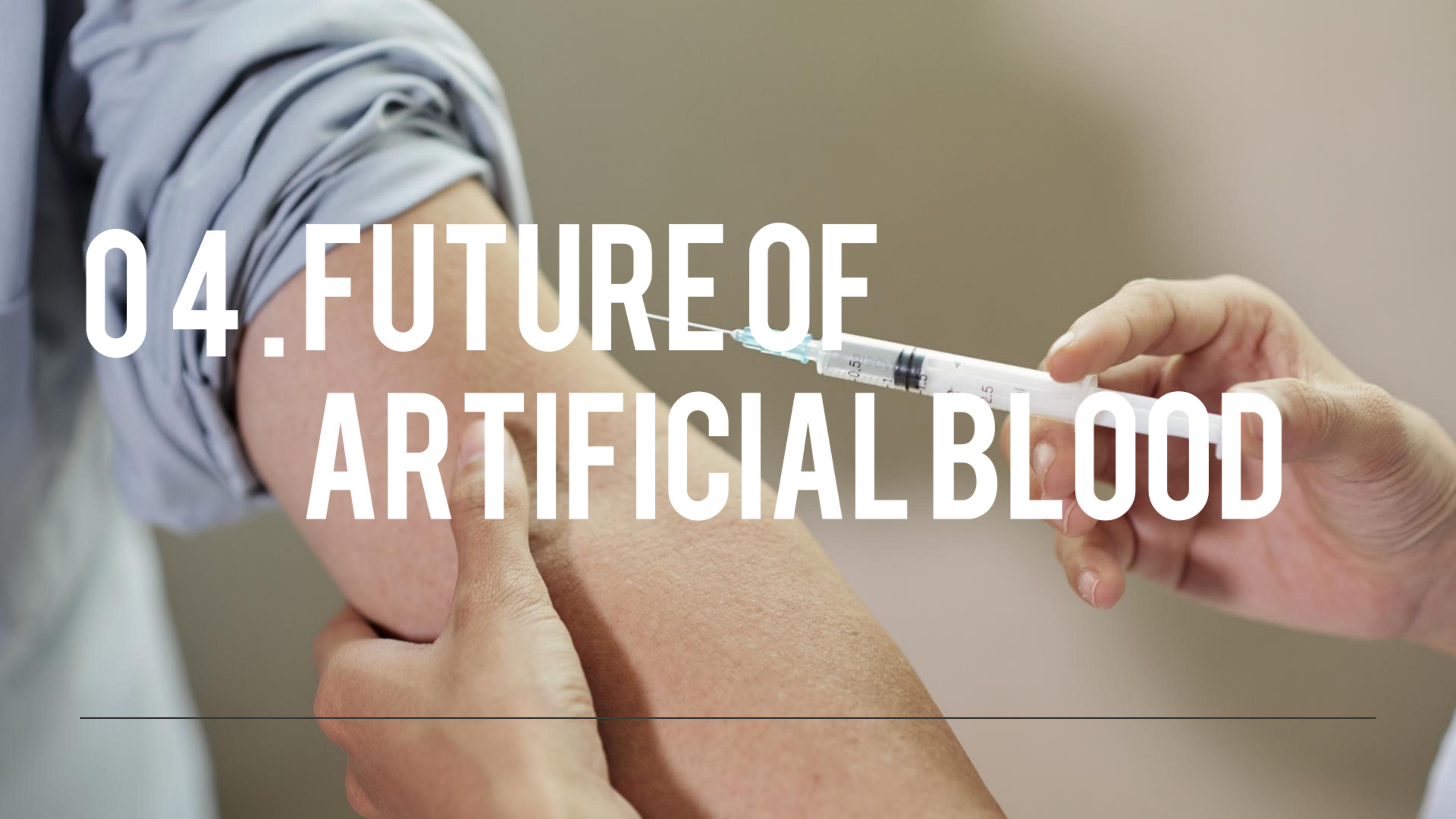
1968 Bunn & Jandl

1979 Walder (diaspirin)



Recombinant Human Hb

1990 Hoffman



04. FUTURE OF ARTIFICIAL BLOOD

**WHO IS HONORED 2012 NOVEL PRIZE IN
PHYSIOLOGY OR MEDICINE??!!!**

JOHN GURDEN & SHINYA YAMANAKA

They got a Novel Prize in Physiology and Medicine in 2012

for Induced Pluripotent Stem Cell

(유도줄기세포, 역분화줄기세포)

Scientists begin focusing on relationship of
Induced Pluripotent Stem Cell and Artificial Blood



WHAT IS INDUCED PLURIPOTENT STEM CELL? (역분화줄기세포)

Conventional Stem Cell : embryonic stem cell / adult cell

embryonic cell -> ethical problem (destroy fertilized egg)

adult cell -> less number of cell it can be developed

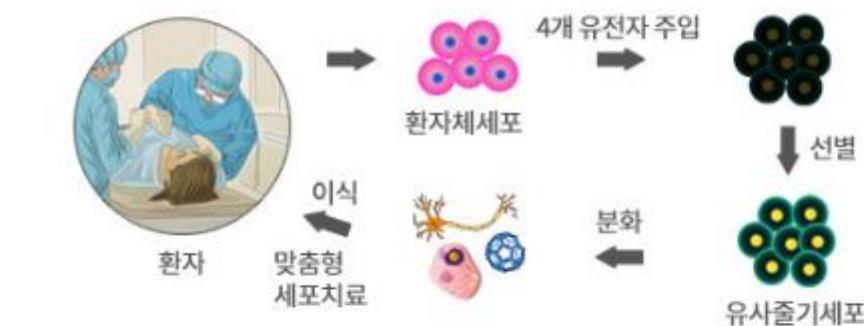
IPS -> dedifferentiation of somatic cell(체세포) of patient

: solve ethical problem of embryonic stem cell, and limit of adult stem cell



유도만능줄기세포 VS 체세포 복제 배아줄기세포

분화가 끝난 체세포줄기세포를 분화이전의 세포 단계로 되돌린 세포이다



GOOD!

- 수정란을 사용하지 않아 윤리적 문제 없음
- 다양한 세포로 분화 가능

BAD!

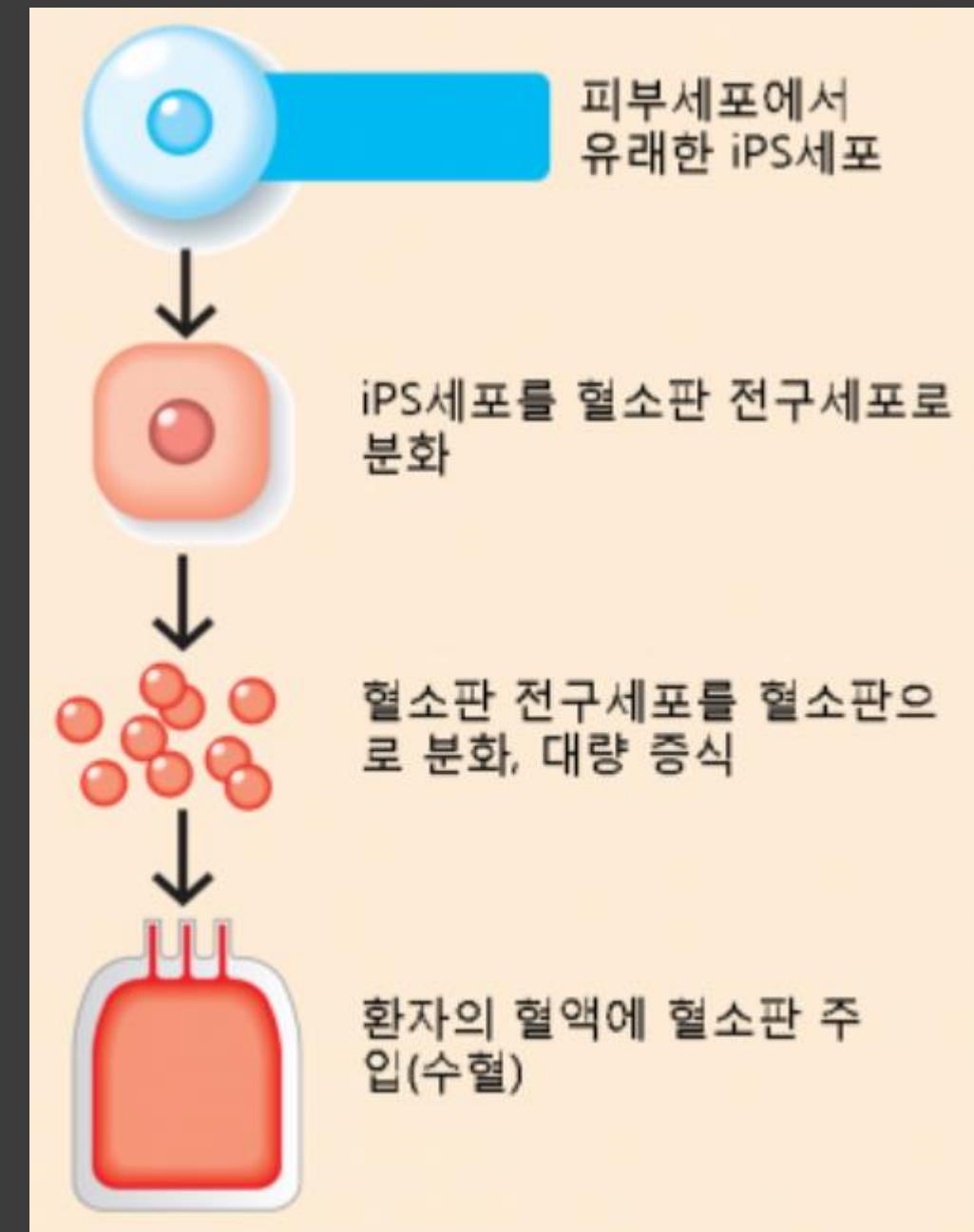
- 임이 발생할 수 있어 임상적용이 어려움
- 분화과정에서 조기 노화가 나타나 분화 및 증식 능력 제한

WHAT IS INDUCED PLURIPOTENT STEM CELL? (역분화줄기세포)

Scientists are trying to develop new artificial blood by IPS

Conventional artificial blood : only as oxygen carrier

artificial blood by IPS : expected to be able to carry out all of blood's roles



manufacturing process of HBOC

REFERENCE

- * https://ko.wikipedia.org/wiki/%EB%8C%80%EC%B2%B4_%ED%98%88%EC%95%A1
 - * [http://www.ksbm.or.kr/pub/16%20\(4\)%20152-156.pdf](http://www.ksbm.or.kr/pub/16%20(4)%20152-156.pdf)
 - * <https://synapse.koreamed.org/upload/SynapseData/PDFData/0119JKMA/jkma-52-168.pdf>
-

THANKYOU

이종현, 홍성훈