

Basics of cardiopulmonary bypass

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ABSTRACT

Cardiopulmonary bypass (CPB) provides a bloodless field for cardiac surgery. It incorporates an extracorporeal circuit to provide physiological support in which venous blood is drained to a reservoir, oxygenated and sent back to the body using a pump. Team effort between surgeon, perfusionist and anaesthesiologist is paramount for the successful use of CPB. However, it also has its share of complications and strategies to reduce these complications are the area of the current research.

Key words: Cardioplegia, cardiopulmonary bypass, heparin, oxygenator, protamine, ultrafiltration

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INTRODUCTION

Advances in cardiac surgery have been possible due to the development of cardiopulmonary bypass (CPB). CPB is a form of extracorporeal circulation whose function is circulatory and respiratory support along with temperature management to facilitate surgery on the heart and great vessels. The first successful human cardiac surgery using CPB was performed by John Gibbon in 1952^[1] for repair of the atrial septal defect. The safe conduct of CPB requires a team effort between the surgeon, perfusionist, and anaesthesiologist.

This article gives an overview of CPB, its components, setup, complications and anaesthesia management during CPB.

THE CPB CIRCUIT

CPB circuit includes pumps, cannulae, tubing, reservoir, oxygenator, heat exchanger and arterial line filter [Figure 1]. Modern CPB machines have systems for monitoring pressures, temperature, oxygen saturation, haemoglobin, blood gases, electrolytes as well as safety features such as bubble detectors, oxygen sensor and reservoir low-level detection alarm.

PUMP

Roller pump includes two rollers positioned on a rotating arm, which compress a length of tubing to produce forward flow. This action can produce haemolysis and tubing debris, the incidence of which increases with time. Hence, the use of roller pumps for longer procedures is discouraged. Centrifugal pump consists of impellers/stacked cones within housing. When rotated rapidly, negative pressure is created at one inlet, and positive pressure at the other, thus propelling the blood forward. They are afterload dependent, so if the patient's systemic vascular resistance (SVR) increases, the cardiac output generated will drop unless the flow through the pump is increased. Centrifugal pumps may improve platelet preservation, renal function and neurological outcomes in longer cases.^[2]

Table 1 provides a comparison between roller and centrifugal pumps.

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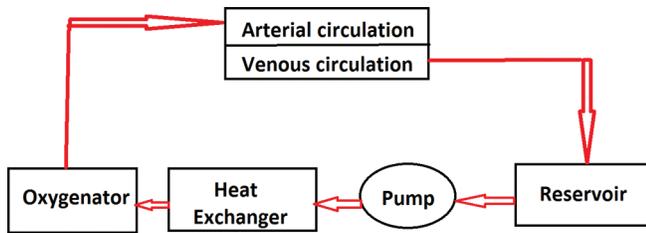


Figure 1: During CPB, venous blood is drained through gravity into a reservoir. The pump moves blood from the reservoir to the oxygenator through a heat exchanger, before returning it to the arterial circulation. Additional components include suckers (to remove blood from surgical field), vents (to decompress the heart), haemofilters (for ultrafiltration) and cardioplegia system

Table 1: Comparison of roller and centrifugal pumps

Roller pump	Centrifugal pump
Afterload independent	Afterload dependent
No flowmeter required	Needs flowmeter
Increase blood trauma and tubing debris	Decrease blood trauma and tubing debris
No backflow occurs	Retrograde flow possible if pump stops
Cheap	Expensive
Short-term use	Long-term use
Bulky	Portable
Circuit disruption from excessive line pressure	No disruption
Greater risk of air embolism	Lesser risk of air embolism
Priming volume less	Priming volume more

CANNULAE

Cannulae connect the patient to the circuit and hence to the CPB machine. They are made of polyvinylchloride (PVC) and are wire reinforced to prevent obstruction due to kinking. Venous cannulae: single-stage cannulae are used during most open-heart surgeries, where two cannulae are inserted into the superior and inferior vena cava and joined by a Y-piece. Dual-stage cannulae are used for most closed-heart procedures, where a single cannula is inserted into the right atrium. Drainage occurs through gravity. Vacuum applied to the reservoir allows the use of smaller cannulae and tubing, thus decreasing the circuit volume.

An alternative site for cannulation is via the femoral vein in minimally invasive or redo surgeries, where a long cannula is inserted up to the right atrium. Transoesophageal echocardiography (TOE) helps in the assessment of its proper placement. A vent is required to drain the left side of the heart for blood draining through the bronchial and thebesian veins.

An arterial cannula is usually inserted into the ascending aorta. Alternate sites include the femoral,

innominate or axillary artery in situations such as emergency, redo surgery, minimally invasive surgery or to achieve regional perfusion in procedures that involve the ascending aorta and arch.

OXYGENATOR

Bubble oxygenators are largely of historical interest in the era of membrane oxygenators.

Membrane oxygenators consist of hollow microporous polypropylene fibres (100–200 μm internal diameter). Blood flows outside the fibre while gases pass inside the fibre, thus separating the blood and gas phases. They have lesser propensity for air embolism and give greater accuracy in blood gas control. Newer designs have an integrated filter to manage emboli, thus making additional arterial filters unnecessary.

A heat exchanger is integrated with the oxygenator and placed proximal to it to reduce the release of gaseous emboli due to alterations in the temperature of saturated blood.

TUBING

These are generally made of PVC, due to PVC's durability and acceptable haemolysis rate. Plasticisers like di(2-ethylhexyl) phthalate which are added to impart flexibility are potentially toxic and shown to leach from the tubing.^[3] Newer plasticisers such as dioctyl adipate have less leaching and are under investigation.

RESERVOIR

They collect the blood drained from the heart. Open reservoirs are more commonly used. They allow passive removal of entrained venous air along with the option of applying vacuum to assist drainage. They integrate a separate cardiotomy, and defoaming circuit to process suctioned blood. When they are used, a safe level of blood in the reservoir is maintained to avoid air entry into the arterial circuit.

Closed reservoirs have a limited volume capacity, but offer a smaller area of blood contact with artificial surfaces. This produces less inflammatory activation, better sterility and reduces post-operative transfusion.^[4] They, however, require a separate circuit for processing suctioned blood.

CARDIOPLEGIA SYSTEM

For intracardiac repair, cross-clamping the aorta is necessary, which renders the heart ischaemic. Cardioplegia is a method of myocardial protection where the heart is perfused with a solution to cause electromechanical arrest which reduces myocardial oxygen consumption. The cardioplegia cannula is inserted proximally while the aortic cannula is distal to the clamp. A separate pump delivers cardioplegia either antegrade into the aortic root or retrograde into the coronary sinus or both. TOE can guide in the placement of the balloon-tipped retrograde cannula into the coronary sinus. Retrograde cardioplegia alone results in inadequate right ventricle protection. Ostial cardioplegia is given when there is severe aortic regurgitation.

Cardioplegia can be crystalloid (cold) or blood-based (warm or cold); can be given continuously or intermittently. Potassium-based solutions are commonly used. Blood cardioplegia is a combination of oxygenated blood and crystalloid in a ratio ranging from 1:1 to 8:1. Substances such as bicarbonate, mannitol, magnesium, calcium, adenosine, procaine, glucose and glutamate may be added.

Other circuit components are the gas line and blender, which delivers fresh gas to the oxygenator in a controlled mixture. The set FiO_2 determines PaO_2 while total flow determines PaCO_2 on the bypass. The arterial line filter is present distal to the pump and removes particulate matter more than 20–40 μm in size.

Surface coating of the circuit with various materials has been attempted to improve biocompatibility, minimise inflammation and thrombus formation. Covalently-bonded heparin circuits have shown evidence in many studies of reduced inflammation and platelet activation resulting in lesser bleeding and transfusions.^[5-8] Some newer coatings include poly-2-methoxyethylacrylate, phosphorylcholine and trillium. The clinical benefits of one type of coating over another remain controversial.^[9]

CONDUCT OF CPB

Priming

The deairing of CPB circuit is done by priming solutions, consisting of a mixture of crystalloids and colloids. Priming causes haemodilution which improves flows

during hypothermia. Heparin 3–4 units/ml is added to the prime. Depending on the pre-bypass haemoglobin and priming volume, addition of external blood may be required to maintain a target haematocrit on bypass (21%–24% in adults and 28%–30% in children). The following equations are used.

Total circulating volume (TCV) = Patient's blood volume + priming volume

Target haematocrit (Hct) on CPB = Patient's blood volume (PBV) \times Hct/TCV

Blood required on prime = (Target Hct \times TCV) – (Pt. Hct \times PBV)/Hct of donor blood

Cardiac index of a 70 kg adult with normal metabolism at 37°C is 2.2–2.4 L/m²/min. For each 1°C decrease in temperature, the required cardiac output reduces by 7%, and the pump flow can be reduced by an equivalent factor. Knowing the body surface area (BSA) of the patient, the required pump flow is as follows:

Pump flow rate = BSA \times Cardiac index

Initiation of CPB

Heparin 300 U/kg IV is administered before arterial cannulation with a target ACT (measured after 3 min) of more than 480 s. During arterial cannulation, systolic pressure should be 90–100 mm Hg to reduce the risk of aortic dissection. The aortic cannulation is done first to provide volume resuscitation in case of hypotension associated with venous cannulation. Once the aortic cannula is connected to the tubing, line pressure is checked to rule out dissection. After venous cannulation, venous clamp is gradually released to establish full CPB and then ventilation is discontinued.

Anticoagulation

Clotting on CPB is life-threatening. Activated clotting time (ACT) is a point-of-care test used to assess the adequacy of heparinisation. Normal ACT ranges from 80 to 120 s.^[10] It can also be affected by haemodilution and hypothermia. ACT must be monitored every 30–40 min during bypass.

Automated devices to measure ACT include the Hemochron® and the HemoTec® device. The Hemochron and HemoTec ACT values are not inter-changeable, with the Hemochron value being longer, especially in children.^[11,12]

Other methods to titrate anticoagulation include the heparin dose-response curve and the Hepcon device, which measures plasma heparin concentration.

Altered heparin response with failure to achieve target ACT may be seen in some patients, with response to additional doses of heparin ultimately achieving the target ACT. Heparin resistance is failure to achieve target ACT despite high doses of heparin (800–1000 U/kg).^[13] Causes include elderly age, recent heparin exposure, nitroglycerin infusion, thrombocytosis and antithrombin III deficiency (congenital/acquired).^[14] Treatment is the administration of antithrombin III concentrates (1000 units) or fresh frozen plasma (2–4 units).^[15]

Further exposure to heparin is a concern in patients with heparin-induced thrombocytopenia requiring CPB. Alternative anticoagulants include lepirudin, argatroban, danaparoid, and bivalirudin, all which have no specific reversal agents. Bivalirudin has the advantage of a short half-life of 24 min^[16] due to metabolism by bivalirudin-bound thrombin. Hence, care must be taken to prevent stasis in the circuit as bivalirudin will be consumed in static blood if not continuously circulated.

Anaesthesia and monitoring on CPB

Perfusion pressure is used as a surrogate marker of organ perfusion and should be maintained between 50 and 70 mmHg. Hypertensive patients and those at risk for stroke require higher flows and perfusion pressures to maintain organ perfusion.^[17] Cerebral oximetry, evoked potentials and transcranial Doppler can be used to assess the adequacy of cerebral blood flow. Mixed venous oxygen saturation monitoring can provide an estimate of the balance between global oxygen delivery and demand. Mixed venous oximetry of 70% or greater is maintained, but even this does not guarantee adequate perfusion of all tissue beds.^[18]

Blood level in the reservoir should be monitored to prevent air embolism. Central venous pressure (CVP) should be low. High CVP indicates a poor venous return. Monitoring of aortic line pressure, blood temperature and integrity of gas supply to the oxygenator is essential. Glucose is maintained between 120 and 180 mg/dL.^[19] Anaesthesia can be maintained by inhalational route or total intravenous anaesthesia can be given. Volatile anaesthetics provide cardioprotective effects through preconditioning. Nitrous oxide is avoided during CPB to prevent an increase in the size of air emboli. Anaesthetic requirements are reduced with

hypothermia, however drug pharmacokinetics are also altered due to haemodilution and altered metabolism leading to variable effect.

Temperature management

Hypothermia is frequently used during CPB for its presumed organ protective effects. Blood viscosity increases with hypothermia and allows maintenance of a higher perfusion pressure despite haemodilution. However, hypothermia reversibly inhibits the clotting factors and platelets. Currently, the data are inconclusive regarding the superiority of hypothermic over the normothermic bypass.^[20] Rather than the absolute temperature, the rate of rewarming and cerebral hyperthermia have been shown to be more important to prevent cerebral injury.^[21–23]

Core temperature monitoring sites include the rectum, urinary bladder, oesophagus and pulmonary artery. Nasopharyngeal temperature gives an estimate of cerebral temperature.

Acid-base management

This is particularly important in hypothermic CPB and deep hypothermic circulatory arrest (DHCA). With cooling, CO₂ becomes more soluble in the blood (partial pressure decreases) causing alkalosis. The “alpha” in alpha-stat, refers to the alpha-imidazole ring of histidine, which is an important intracellular buffer. The constancy of the charge state of this ring is important in the regulation of pH-dependent cellular processes. In alpha-stat, pH is not corrected, and PaCO₂ is allowed to fall with hypothermia. Blood gases measured at 37°C are uncorrected. Alpha-stat maintains limits microemboli by maintaining cerebral autoregulation. Inhomogeneous cerebral cooling is the disadvantage of alpha-state management.

The pH-stat maintains a constant pH and PaCO₂ with hypothermia. CO₂ is added to the oxygenator causing increased cerebral blood flow and cooling. Prolonged pH-stat management can lead to severe acidosis, so a switch to conventional alpha-stat during the rewarming phase is required.

In adults with moderate hypothermia, alpha-stat is beneficial.^[24] In infants, brain injury is more associated with hypoperfusion so pH-stat is useful.^[25,26] If DHCA is used, a cross-over strategy can be employed, with pH-stat in the initial phase of cooling, followed by a switch to alpha-stat. This maximises cerebral cooling and avoids severe acidosis with prolonged pH-stat.^[27]

Ultrafiltration

Ultrafiltration during and after CPB removes inflammatory mediators and excess fluid thereby producing haemoconcentration. Conventional ultrafiltration uses a haemofilter inserted into the bypass circuit. Modified ultrafiltration (MUF) is used after completion of the surgical repair before protamine administration, with blood removed from the arterial line and returned to the venous line after passing through the haemofilter. It was first described by Naik *et al.* in 1991.^[28] Many randomised controlled studies have shown decreased blood loss and transfusions,^[29-31] especially with MUF in paediatric patients.^[32]

Weaning

Weaning is the process where extracorporeal support is gradually withdrawn as the heart takes over the circulation. Several steps are required for successful completion of weaning.

The use of hypothermia requires a period of rewarming. Rapid rewarming and hyperthermia are associated with cerebral injury. Nasopharyngeal temperature should not exceed 37°C, although authors accept temperature range of 35.5°C–36.5°C. Temperature gradient between the heater and venous blood should not exceed 10°C. The high gradient between core and peripheral temperature can lead to after drop in temperature. Use of vasodilators can help in homogenous rewarming and to increase venous capacitance during transfusion of circuit blood. Supplemental doses of anaesthetics are administered; acid-base balance, electrolytes, PaO₂, PaCO₂, sugar and haematocrit are kept within normal limits. Serum potassium of 4.5–5 mmol/L is targeted to help prevent arrhythmias.

After open-heart procedures, deairing of the heart is done. TOE is useful to assess the adequacy of deairing. Air embolism, frequently involving the right coronary artery due to its anterior location, can cause arrhythmias, ST-elevation and myocardial dysfunction. It is treated by increasing the perfusion pressure and maintaining pulsatile perfusion by partially clamping the venous line.

Heart rate, rhythm and contractility are assessed. Sinus bradycardia is treated with atropine and/or beta-adrenergic agonists while epicardial pacing is used for persistent atrioventricular block. Removal of the aortic cross-clamp can be associated with ventricular fibrillation, especially in conditions causing left ventricular hypertrophy like severe aortic stenosis.

Defibrillation is achieved using internal paddles with the biphasic energy of 5–20 J. Antiarrhythmics such as amiodarone, lidocaine and magnesium^[33] can be added for persistent dysrhythmias. Mechanical ventilation is started, and the perfusionist gradually occludes venous return and fills the heart while incrementally reducing pump flows.

Difficulties in weaning manifested by systemic hypotension may be due to either hypovolaemia, ventricular dysfunction or low SVR. Hypovolaemia is treated by giving controlled boluses of blood from the circuit. Low SVR is treated with vasopressors such as phenylephrine, noradrenaline or vasopressin. The need for inotropes should be evaluated by visually assessing contractility and with TOE. Prior left ventricular dysfunction, severe pulmonary hypertension, inadequate myocardial protection and prolonged cross-clamp time are factors to consider in determining the post-bypass use of inotropes. A variety of inotropes are available, but the evidence base to advocate one inotrope over another is lacking. Inodilators such as milrinone, dobutamine and levosimendan can be used in the setting of ventricular dysfunction with increased afterload. Use of levosimendan may be associated with a reduction in mortality.^[34]

In spite of all measures, if the patient fails to wean, mechanical support devices like intra-aortic balloon pump, ventricular assist device or extracorporeal membrane oxygenation should be considered.

After separation from CPB, heparin is reversed with protamine in a ratio of 1:1–1:3. Protamine is administered over 10–15 min. Protamine can cause various reactions, namely type I (hypotension, due to fast infusion), type II (anaphylaxis) and type III (pulmonary hypertensive crisis). Depending on severity, these reactions can be managed with stopping protamine, fluids, vasoconstrictors/inotropes or return to bypass. Once protamine administration is complete, ACT is checked to confirm normalisation. Additional protamine should be given if circuit blood containing heparin is transfused. High doses of protamine also cause anticoagulation. Residual re-heparinisation may also occur as the drug emerges out of poorly perfused compartments, especially in obese patients (heparin rebound).

The final step is arterial decannulation. Post CPB, radial arterial catheters may underestimate central aortic

systolic pressure (but mean pressure is equivalent), due to vasodilation and arteriovenous shunting in the upper limb.

COMPLICATIONS

Mechanical complications

Arterial cannulation can be associated with bleeding, cannula malposition causing selective cerebral perfusion, plaque dislodgement and dissection. Dissection presents as low arterial pressure, high arterial line pressure (>300 mmHg), loss of venous return and bluish discoloration of the vessel. It can be diagnosed with TOE. Repair of the dissection is necessary under DHCA. Venous cannulation can be associated with bleeding, cannula malposition/air lock causing an inadequate return, leading to cerebral and splanchnic congestion. Massive air embolism is due to pumping from an empty reservoir. Treatment is cessation of the pump and commencing retrograde cerebral perfusion.

Other complications include oxygenator failure, pump malfunction, clotting in the circuit, tubing rupture, gas supply failure and electrical failure due to which hand cranking must be available at all times.

Systemic complications

CPB causes qualitative and quantitative platelet dysfunction. The concentration of pro-coagulants decreases due to haemodilution. Inflammatory, coagulation, complement and fibrinolytic pathways are activated. Thromboelastography can help in knowing the cause of bleeding diathesis. Bleeding is greater with prolonged bypass time, redo-surgery and preoperative use of anticoagulants. Studies have shown decreased blood loss and transfusion requirement in cardiac surgery patients with prophylactic anti-fibrinolytics.^[35,36] Effective fibrinolysis inhibition requires a loading dose of 10 mg/kg for tranexamic acid (TA) followed by 1 mg/kg/h or 50 mg/kg of epsilon-aminocaproic acid followed by infusion of 25 mg/kg/h.^[37] High doses of TA may increase the risk of seizures (~5%–7%).^[38]

Inflammatory response and hypotension can cause acute kidney injury (AKI). Risk factors are prolonged bypass time, sepsis and diabetes. Treatment includes maintenance of high perfusion pressure, use of early biomarkers to detect AKI and dialysis.

The spectrum of cerebral injury ranges from cognitive dysfunction to stroke. The strategy

includes maintenance of higher perfusion pressure, adequate Hct, and alpha stat management. TOE along with epiaortic ultrasound can be used to detect calcification/atherosclerosis of the ascending aorta so that such sites can be avoided for cannulation.

Contact of blood with artificial surfaces, ischaemia-reperfusion injury, endotoxaemia and operative trauma can cause systemic inflammatory response after CPB. Acute phase reaction is initiated by the release of complement, cytokines, endotoxins and NO leading to increased capillary permeability. Rewarming can cause stress response and release of inflammatory mediators. The role of steroids is controversial in view of the lack of adequate benefit and flaring of postoperative infection.^[39,40]

Subclinical myocardial injury can occur due to cross clamping of the aorta in spite of cardioplegia. Stunning of the myocardium is responsible for immediate dysfunction. Factors include metabolic acidosis, preoperative ventricular function, reperfusion injury and inflammatory mediators. Optimisation of electrolytes, temperature and pH helps to reduce arrhythmias.

Acute respiratory distress syndrome can be present due to the effects of CPB. Anaesthesia-induced atelectasis and reduced mucociliary clearance further contribute to acute lung injury. As a result atelectasis and pleural effusions are common pulmonary abnormalities after cardiac surgery. Therefore, lung protective lung strategies are required in the pre- and post-operative periods of cardiac surgery.

Vasoplegia is characterised by severe, vasopressor-resistant vasodilation due to activation of nitric oxide synthase, vascular smooth muscle ATP-sensitive potassium channels and relative deficiency of vasopressin. Treatment includes fluid resuscitation and vasopressors such as phenylephrine, norepinephrine and vasopressin. Methylene blue (1.5 mg/kg IV) acts as a competitive inhibitor of nitric oxide and can be used as a rescue drug.

CONCLUSION

CPB has made increasingly complex cardiac surgeries possible in the current era. Over the years, CPB has undergone immense modifications in the form of novel defoaming agents, heparin coated circuitry, ultrafiltration, miniaturised circuit design, integrated

arterial filters with oxygenator. However it is not without its share of side effects, it is important to continue to search for strategies to further minimise them for better outcomes.

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Announcement

CALENDAR OF EVENTS OF ISA 2017

The cut off dates to receive applications / nominations for various Awards / competitions 2017 is as below. Hard copy with all supportive documents to be sent by Regd. Post with soft copy (Masking names etc.) of the same by E Mail to secretaryisanhq@gmail.com. The masked soft copy will be circulated among judges. Only ISA members are eligible to apply for any Awards / competitions. The details of Awards can be had from Hon. Secretary & also posted in www.isaweb.in

Cut Off Date	Name of Award / Competition	Application to be sent to
30 June 2017	Bhopal Award for Academic Excellence	Hon. Secretary, ISA
30 June 2017	Late Prof. Dr. A .P. Singhal Life Time Achievement Award	Hon. Secretary, ISA
30 June 2017	Rukmini Pandit Award	Hon. Secretary, ISA
30 June 2017	Dr. Y. G. Bhoj Raj Award	Hon. Secretary, ISA
30 Sept. 2017	Kop's Award	Chairperson, Scientific Committee ISACON 2017
30 Sept. 2017	ISACON Jaipur Award	copy to Hon. Secretary, ISA Chairperson, Scientific Committee ISACON 2017
30 Sept. 2017	Prof. Dr. Venkata Rao Oration 2017	copy to Hon. Secretary, ISA Hon. Secretary, ISA
30 Sept. 2017	Ish Narani Best poster Award	Chairperson, Scientific Committee ISACON 2017
30 Sept. 2017	ISA Goldcon Quiz	Chairperson, Scientific Committee ISACON 2017
10 Nov. 2017	Late Dr. T. N. Jha Memorial Award & Dr. K. P. Chansoriya Travel Grant	Hon. Secretary, ISA, copy to Chairperson Scientific Committee of ISACON 2017
20 Oct. 2017	Awards (01 Oct 2016 to 30 Sept 2017)	Hon. Secretary, ISA
(Report your monthly activity online every month after logging in using Secretary's log in ID)		
1.	Best City Branch	
2.	Best Metro Branch	
3.	Best State Chapter	
4.	Public Awareness – Individual	
5.	Public Awareness – City / Metro	
6.	Public Awareness - State	
7.	Ether Day (WAD) 2017 City & State	
8.	Membership drive	
9.	Proficiency Awards	

Send hard copy (where ever applicable) to
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 Nullippady, Kasaragod 671 121.
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