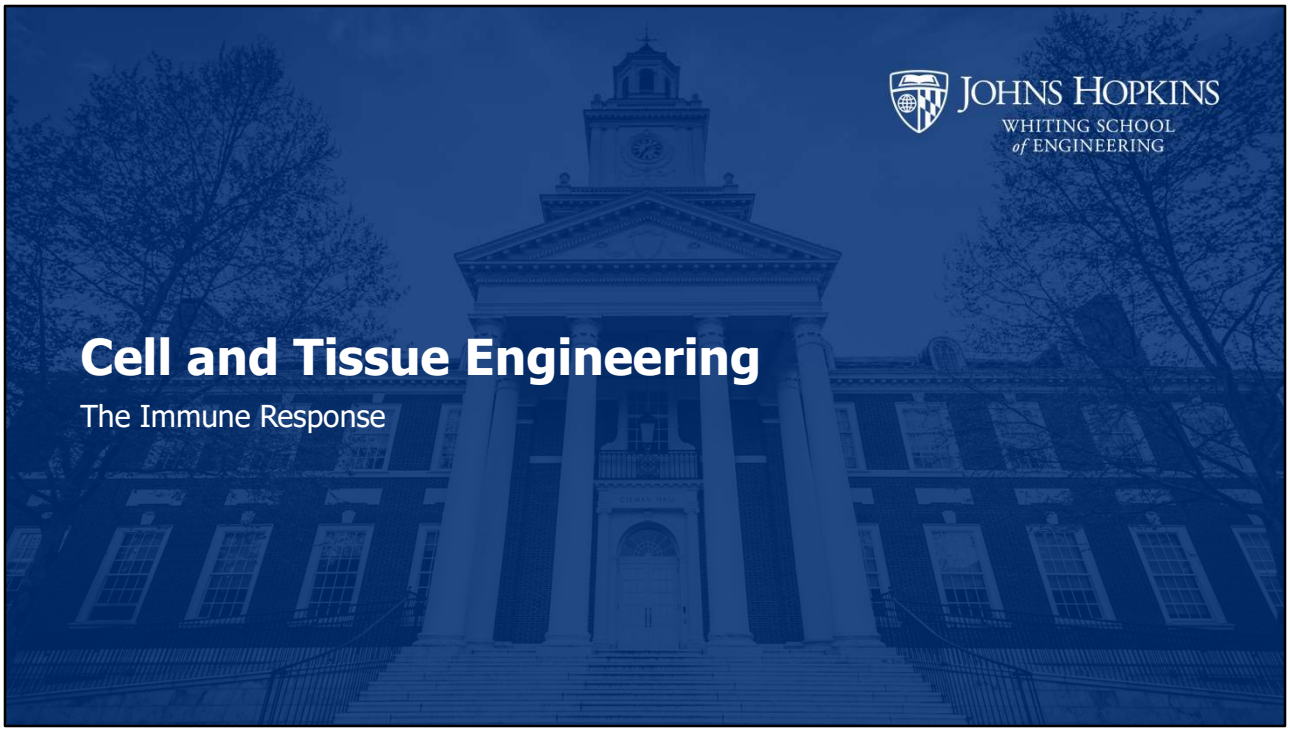
JOHNS HOPKINS
WHITING SCHOOL
of ENGINEERING
Cell and Tissue Engineering
The Immune Response

Battling the Immune Response??

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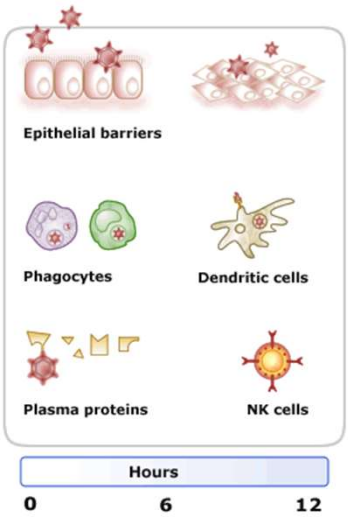
macleodcartoons.blogspot.com; http://animatedcliparts.net/dog-clip-art/

Your immune system is your body's defense against pathogens – **foreign** materials including **dirt**, **parasites**, **bacteria** and even **cancer** cells

Recent evidence suggests that children who grow up with pets at home (pets which expose them to more of the bad stuff) build stronger immune systems and develop fewer allergies.

It seems strange to block a defense system that is so critical to our survival – but **replacement organs** are equally **vital** to transplant patients' **survival**!

The Basics of Immunity – Innate Immunity



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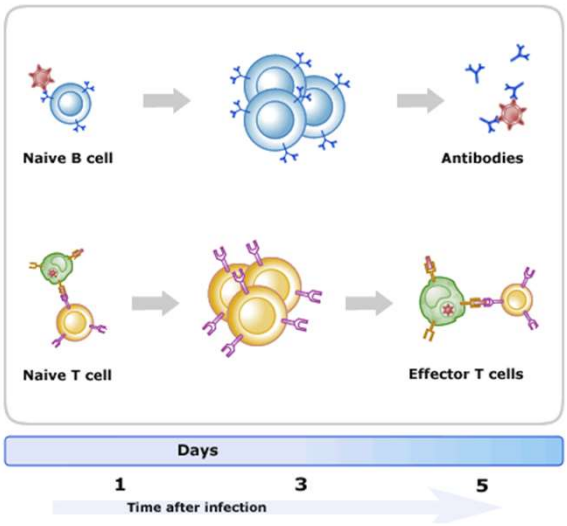
Before we start talking about **modulating** the immune response for tissue engineering we need to have a basic understanding of **what** the immune system is.

Your body's immune response is made of two components – **innate** and **specific** immunity.

In **innate** immunity there is no specific recognition of a foreign material, the **barrier** tissues (like the epithelial tissue) physically block entry, while other immune cells utilize the **chemical antimicrobials** or the complement cascade for destruction of microbial components.

The Basics of Immunity – Adaptive Immunity



Humoral

Cell-mediated

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The other hand of your immune system is specific – it is called **specific** or **adaptive** immunity.

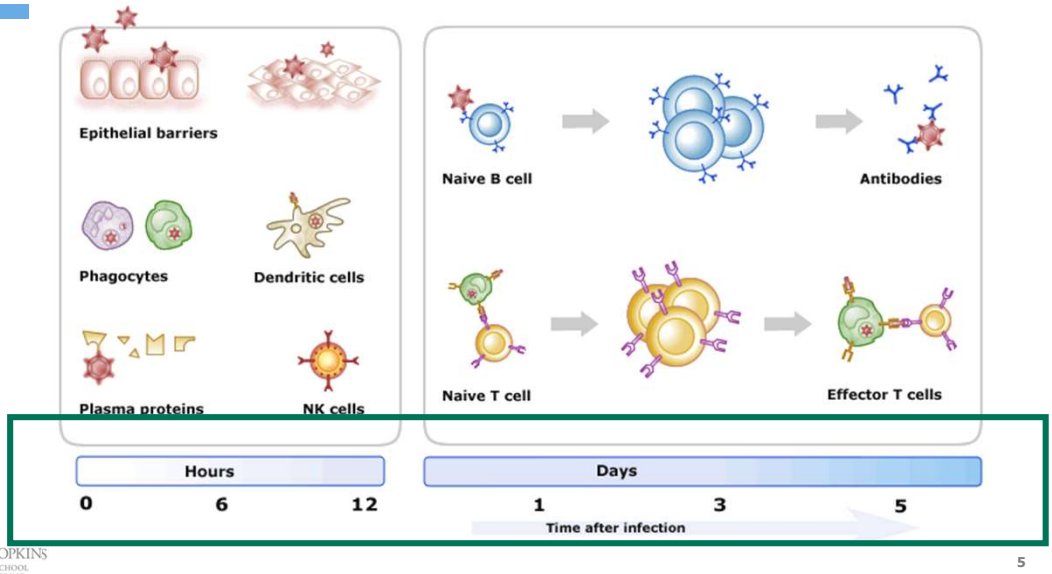
This system targets **specific pathogens** using **T**-cells and has **memory** so that it can easily launch a full-scale attack on something it has seen before.

In the **humoral** pathway B cells recognize foreign antigens and become activated. This causes them to **produce** and **secrete** antibodies specific to the antigen which activate the **complement** system and **tag** the foreigner for **phagocytosis**.

If the antigen is **intracellular** instead of extracellular then your body uses **the cell-mediated** pathway. In this pathway T cells or T lymphocytes identify foreign antigens presented by infected macrophages.

Helper T cells can aid in destruction of the intracellular antigen or **cytotoxic T cells** will destroy the infected cell all together.

The Basics of Immunity - Timing



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Depending on the times since exposure you may be in a different phase of the immune response. **Hyper acute** responses happen in seconds to minutes – this is mainly the **innate** response.

Humoral and cell-mediated acute responses happen in **days or weeks**. Some of this depends on whether it is a first time or repeat exposure.

Vaccines may be coming to your mind now – an early exposure to an weakened or inactivated **antigen** that allows your body to respond with an adaptive immune response later.

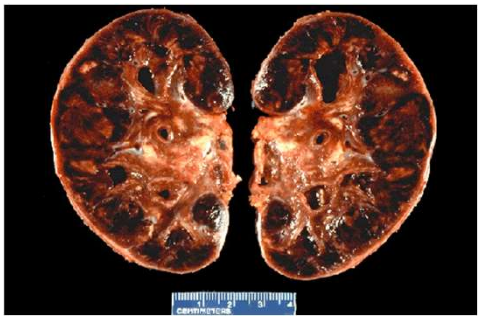
Instead of an adaptive immune response of 3 week, after **exposure** you body can mount the same defense in **just 1/3 the time.**

Mechanisms of Rejection

Hyperacute – minutes to hours

Acute - weeks

Chronic – months to years



Transplant Compatibility Table

RECIPIENT Blood Type	DONOR Blood Type			
	A	B	AB	O
A	Yes	No	No	Yes
B	No	Yes	No	Yes
AB	Yes	Yes	Yes	Yes
O	No	No	No	Yes

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http://library.med.utah.edu/WebPath/RENAHTML/RENAL110.html; http://www.renalresource.com/booklets/KFTO.php

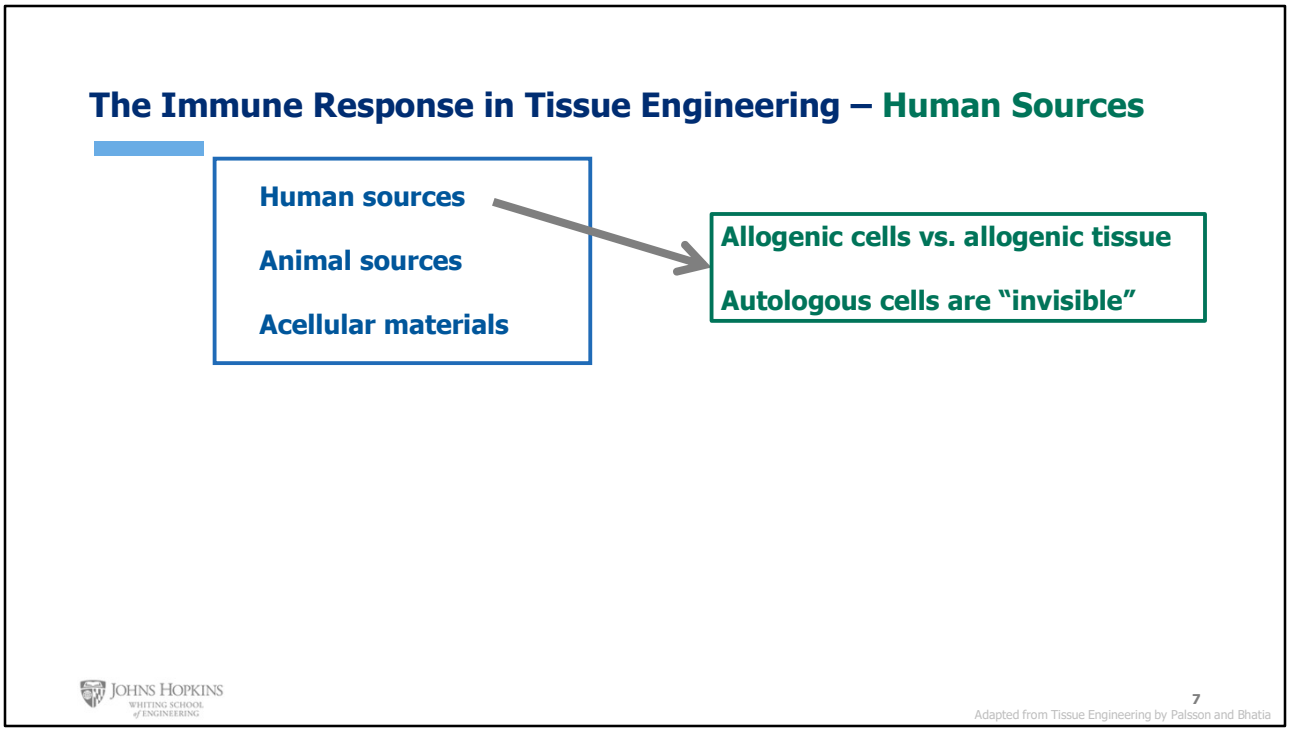
When transplants are conducted with **natural** or **engineered** tissue there is always a risk of **rejection** by the body – by the immune system.

The **kidneys** I'm showing you here were removed due to rejection, you can see that they are round and no longer kidney shaped due to swelling. The dark areas are indicative of **hemorrhages** and tissue **breakdown**.

Just as the immune response can happen at different time scales -- ranging from hyperacute to acute to chronic -- so do the graft rejection mechanisms.

As you'll read in the text this week, **blood typing** can help eliminate acute responses.

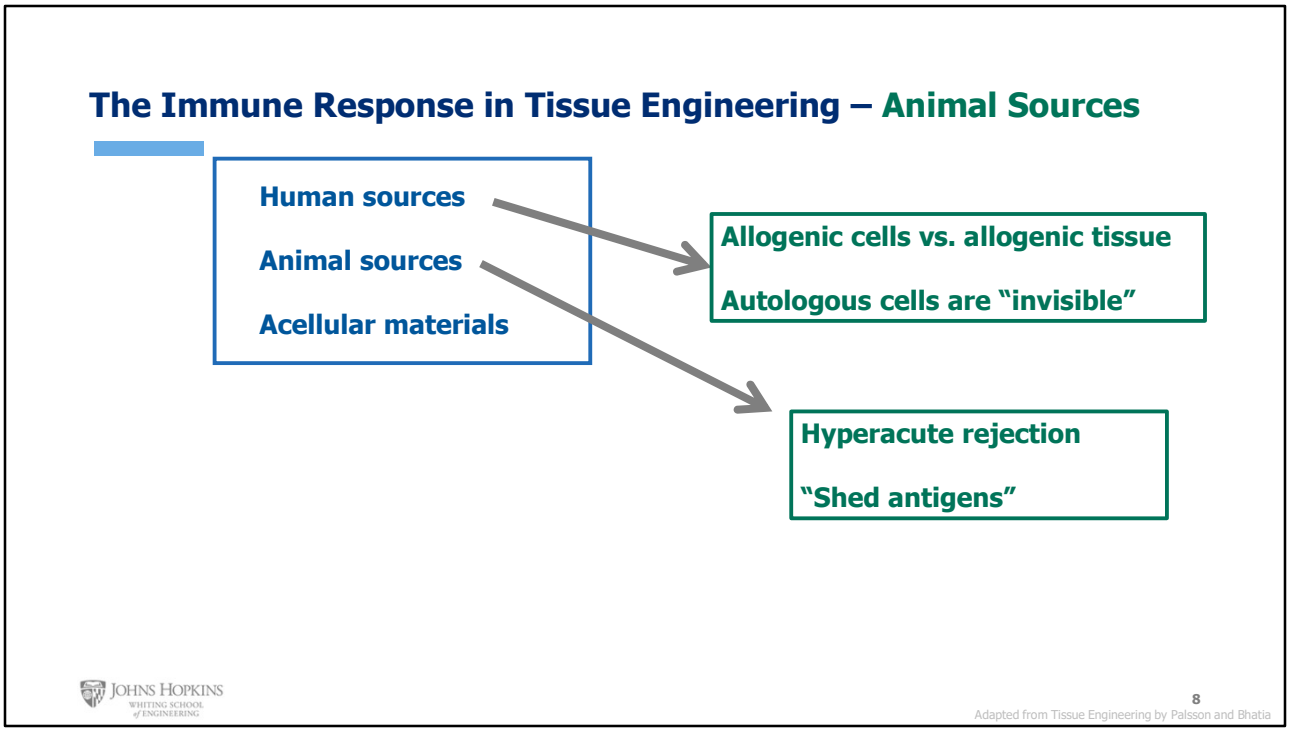
Tissue typing MHCs (major histocompatibility complexes) helps to **eliminate** rejection that occurs in the **acute time** frame. Less is known about **mediating chronic** rejection.



When engineering tissue replacements or cellular therapies, we must consider **rejection** of both the **cells** and the **materials** we use.

When considering using materials from human sources take into account that **allogenic human cells** will induce a smaller immune response than **whole allogenic tissue**. There are several reasons for this including the potential to **encapsulate** and **shield** cells from the host immune system and the **reduced amount of MHC** which helps reduce the onset of acute rejection.

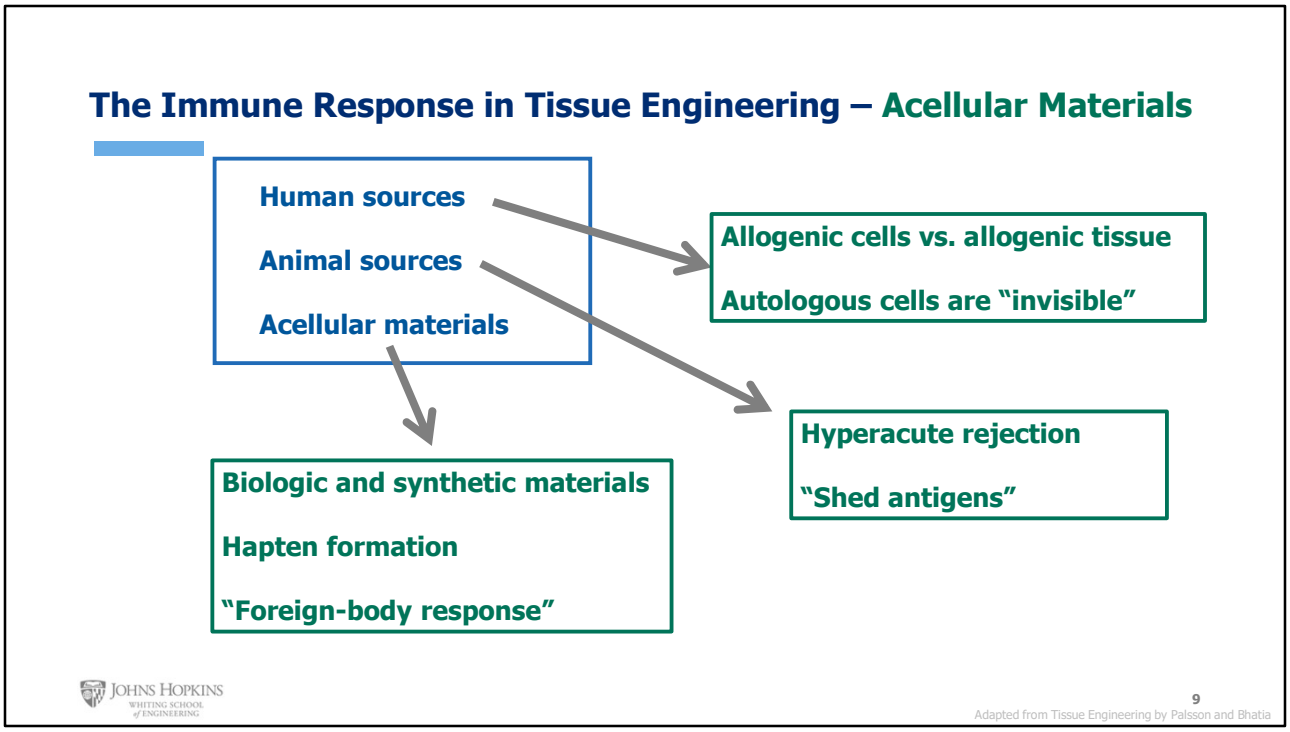
Although **autologous** cells should be invisible -- if the cells have been genetically modified and they produce a foreign protein -- they may be seen as foreign themselves.



The rejection mechanism for **xenografts** is **hyperacute**

Although Researchers are working on humanizing cells from other animals through the presentation of human antigens. So far none of the efforts have been able to overcome The lack of human complement cascade or MHC proteins.

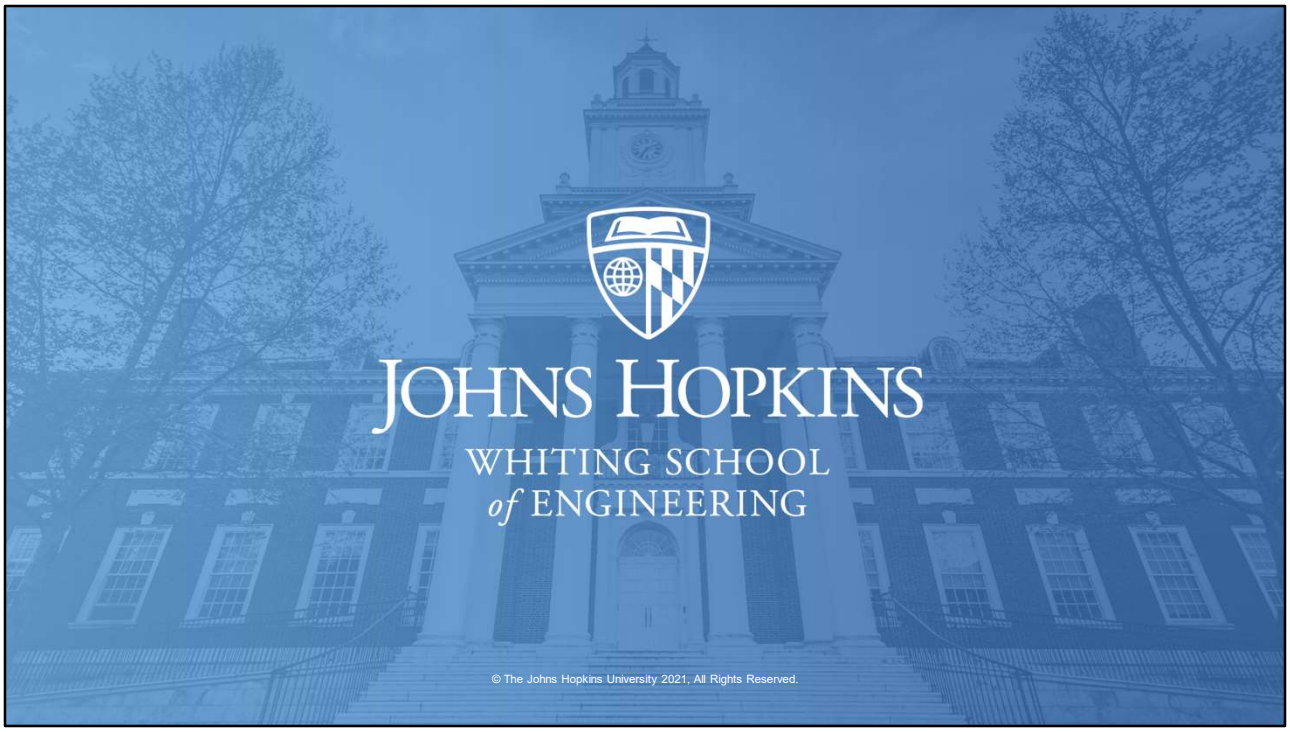
Additionally, any secreted proteins by xenograft cells can travel through the circulation and be recognized by the human immune system, thus activating the adaptive immune response.



Acellular materials that we discussed earlier – both biologic and synthetic materials can also active the adaptive immune response.

In addition to responses to the material alone, we must also consider immune responses to **hapten** – haptens are combinations of foreign and host material that although unreactive alone, are immunogenic when combined.

Mismatched chemical and mechanical properties between the host tissue and implanted material can cause the **foreign body response** – this is where the body walls-off the foreign material, encapsulating it with a fibrous shell that blocks all cell migration and nutrient diffusion.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