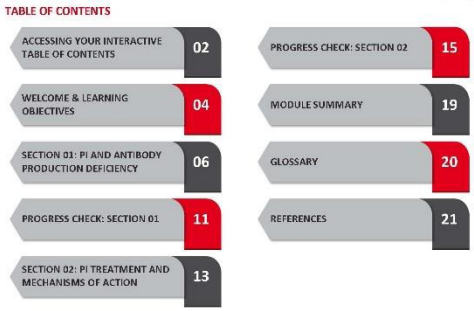
MECHANISM OF ACTION (MOA) OF IMMUNOGLOBULIN (IG) TREATMENT IN PRIMARY IMMUNODEFICIENCY

RARE DISEASE HUB

C-ANPROM/UK/IG/0028 February 2022

ACCESSING YOUR INTERACTIVE TABLE OF CONTENTS

For All Devices Using Adobe Acrobat Reader or Nuance Power PDF



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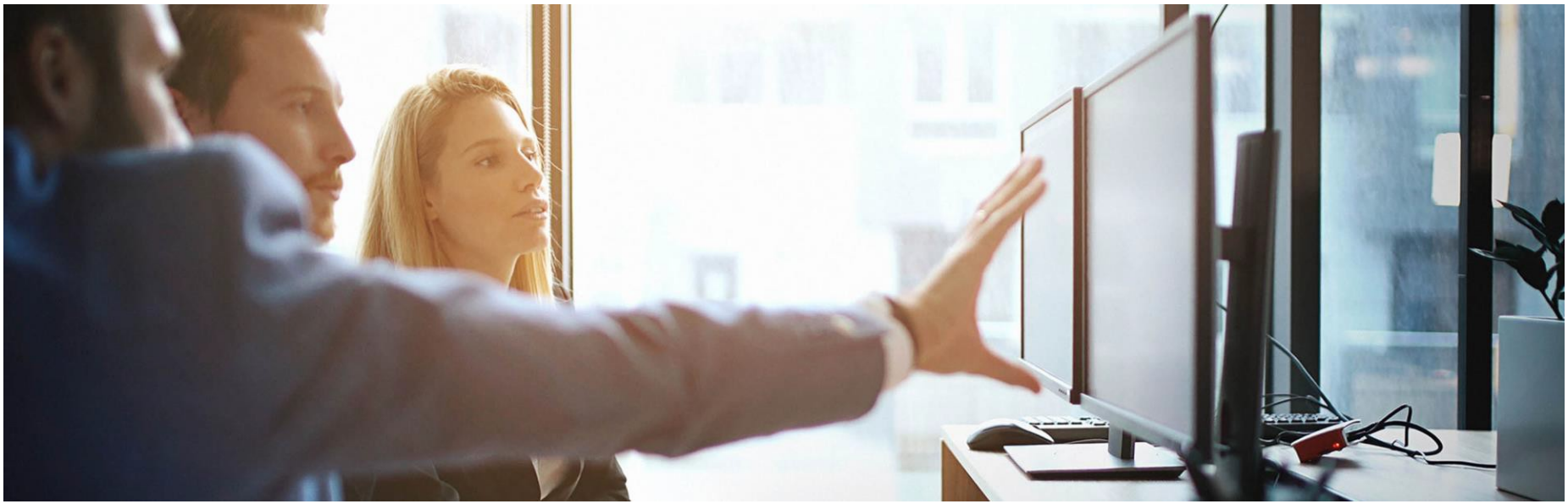
To quickly return to the Table of Contents from any location in the module, click on the icon found at the top right corner of every page.

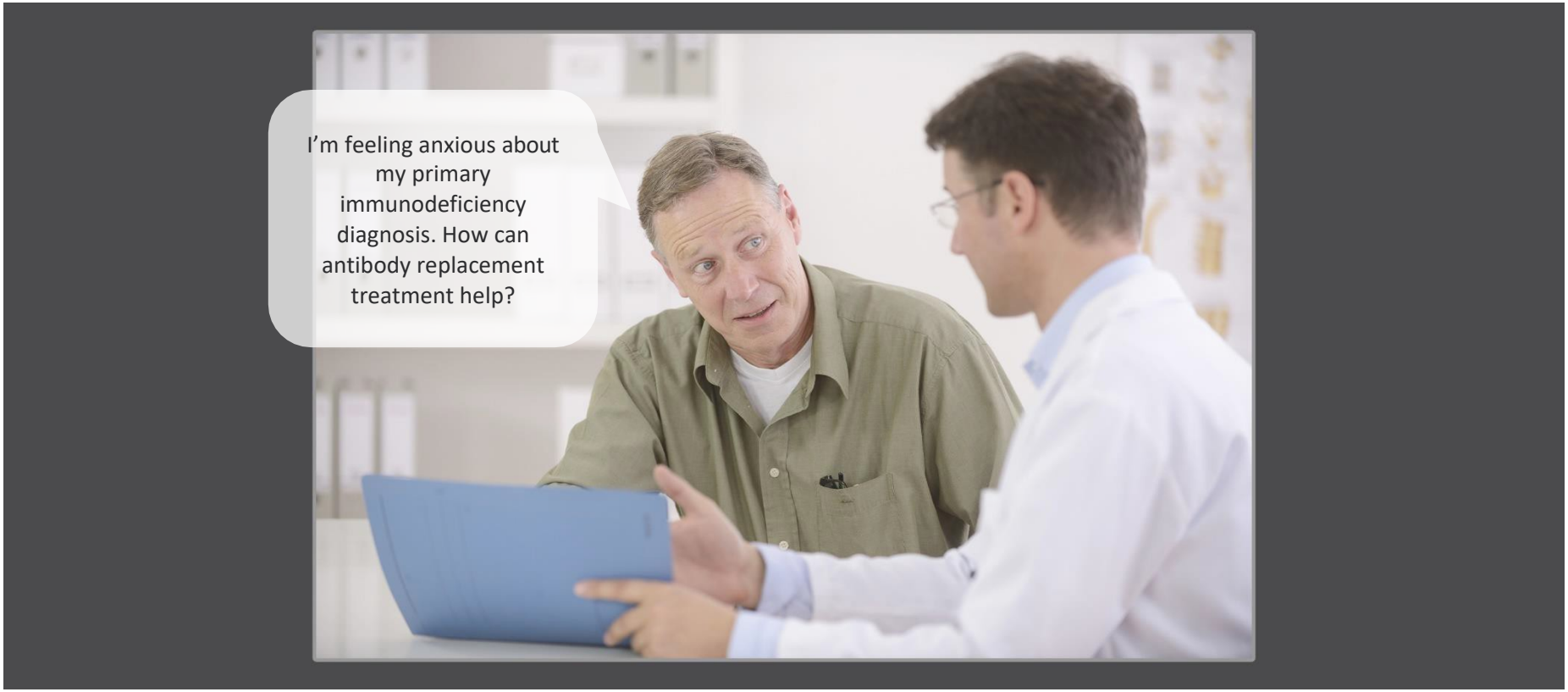
TABLE OF CONTENTS



WELCOME & LEARNING OBJECTIVES

Upon completion of this module, you will be expected to demonstrate that you can…

- Describe primary immunodeficiency (PI) in terms of antibody production deficiency
- Explain the mechanism of action by which IG replacement is used to treat patients with PI with antibody deficiencies



Welcome to the Mechanism of Action (MOA) of Immunoglobulin (IG) Treatments in Primary Immunodeficiency module!

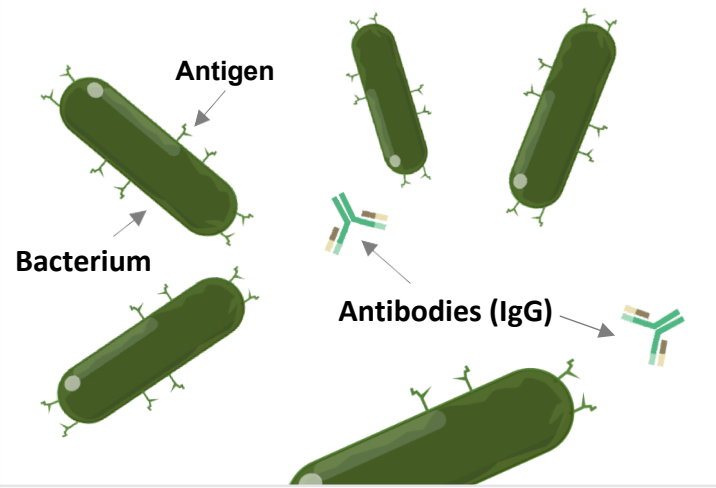
Lawrence has been recently diagnosed with primary immunodeficiency (PI). He’s feeling anxious about his diagnosis and wants to know how the IG replacement treatment he has been prescribed can help his PI condition. This module will explain the MOA by which IG treats patients with PI.

SECTION 01:
PI AND ANTIBODY PRODUCTION DEFICIENCY

Overview of PI

Primary Immunodeficiency (PI):

- More than 350 forms
- One or more **immune system** components are missing or malfunctioning
- Patients have increased susceptibility to **infections** from **pathogens** such as bacteria, viruses, fungi, or parasites
  - Including infections of the skin, respiratory system, ears, brain, spinal cord, urinary or gastrointestinal tracts



- Infections can be difficult to cure, unusually severe, or be caused by unusual organisms

Primary immunodeficiency

The primary immunodeficiency diseases are a group of disorders caused by basic defects in immune function that are intrinsic to, or inherent in, the cells and tissues of the immune system. Can be abbreviated as PI, PID and PAD.

Immune system

Bodily system responsible for identifying an antigen as abnormal or foreign and preventing it from harming the body; includes the thymus gland, spleen, lymph nodes, lymphocytes, and antibodies.

Infections

Diseases caused by microorganisms, especially those that release toxins or invade body tissues.

Pathogen
Any microorganism capable of producing disease.

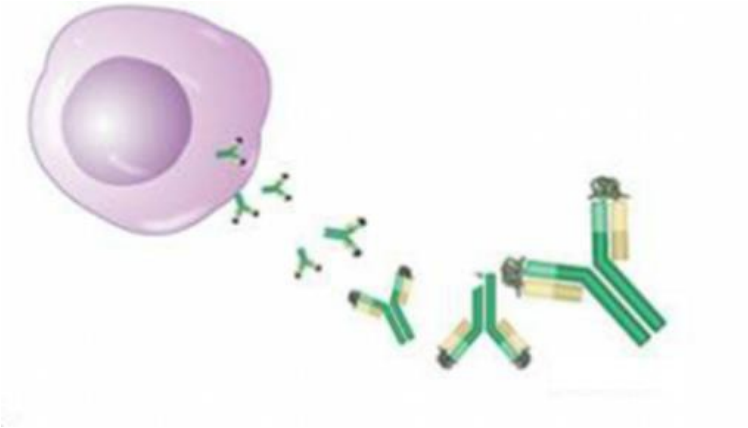
Antigen
Any substance that is capable of activating an immune response or binding with an antibody.

Antibody Production and Deficiencies

Humoral immunity disorders affect **B cell** differentiation and antibody production. These disorders account for approximately half of all PI cases.

In normal **antibody** production:

- B cells transform into **plasma cells**
- Plasma cells produce **immunoglobulin** to fight pathogens



Antibody
Immunoglobulin molecule produced by B lymphocytes (also known as B cells) that combine specifically with an antigen to destroy or control it.

B cell
Type of lymphocyte that identifies antigens and differentiates into antibody-producing plasma cells or memory cells.

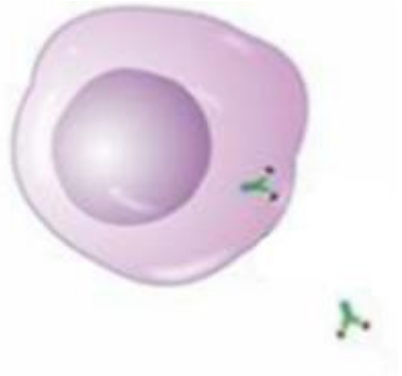
Plasma cell
A cell derived from a B cell that has been sensitised to a specific foreign antigen and produces antibodies to that particular antigen. It may be found in the blood or in tissue fluid.

Immunoglobulin
Any of a diverse group of plasma polypeptides that binds antigenic proteins and serves as one of the body's primary defences against disease. There are five types of immunoglobulins (IgA, IgD, IgE, IgG, and IgM). Also known as antibodies. IG (or Ig) is frequently used as a general term when referring to treatment with IgG.

Antibody Production and Deficiencies (Cont.)

Antibody production deficiency results when antibody production is impaired and antibodies are missing and/or not working properly:

- Due to missing or malfunctioning immune system components that normally help with antibody production
  - Usually caused by defects in B cells; sometimes **T cell** defects may also be present
- As a result, antibodies are missing and/or not working properly
- Accounts for approximately 50% of PI cases
- Includes **common variable immunodeficiency (CVID)**, specific antibody deficiency (SAD), and **X-linked agammaglobulinemia (XLA)**



Antibody production deficiency
The most common form of PI, in which antibody production is impaired, resulting in missing and/or malfunctioning antibodies.

Common variable immunodeficiency (CVID)
A frequently diagnosed primary immunodeficiency, especially in adults, characterised by low serum levels of immunoglobulins, which causes an increased susceptibility to infection. While it is thought to be caused by genetic defects, the exact cause is unknown in a majority of cases.

X-linked agammaglobulinemia (XLA)
An inherited primary immunodeficiency disease in which patients lack the ability to produce antibodies.

T cell
Type of lymphocyte that responds to specific antigens with the assistance of antigen-presenting cells via cell-mediated immunity. May be further categorised by function as T helper cell or cytotoxic T cell.

PI Diagnosis

- PI is usually detected only when the patient has experienced recurrent severe infections
- According to the Immune Deficiency Foundation (IDF):
  - Patients are diagnosed, on average, 12.4 years after the onset of symptoms
  - More than half of patients reported permanent impairment including reduced lung and digestive function and impaired hearing
- As a result, patients may have experienced permanent impairment before they are diagnosed
- Diagnosis may be a relief after years of suffering with illnesses, as steps can then be taken to help manage the patient's condition
- Important signs that may indicate PI include:
  - Recurrent, unusual, or difficult to treat infections
  - Poor growth or loss of weight
  - Recurrent pneumonia, ear infections, or sinusitis
  - Multiple courses or antibiotics or IV antibiotics necessary to clear infections
  - Recurrent deep abscesses of the organs or skin
  - A family history at PI
  - Swollen lymph glands or an enlarged spleen
  - Autoimmune disease

PROGRESS CHECK

QUESTION ONE

Think about how you would complete the following question, then select the Check Your Answer button.

Which of the following statements describes the antibody production deficiency disease state?

A B cells don't make enough antibodies and/or the antibodies that are produced don't function properly, so the immune system cannot produce effective responses to pathogens.

B B cells always make enough antibodies, but those antibodies attack endogenous complement, so the immune system cannot produce an effective response to pathogens.

C T cells make low levels of antibodies, but the antibodies have an extended half-life that produces effective responses to some pathogens.

D T cells make low levels of antibodies and/or the antibodies that are produced don't function properly, so the immune system cannot produce effective responses to pathogens.

CHECK YOUR ANSWER

PROGRESS CHECK (CONT.)

ANSWER: QUESTION ONE

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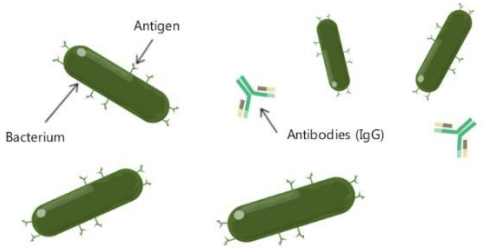
SECTION 02:
PI TREATMENT AND MECHANISMS OF ACTION

IG Replacement Treatment in PI

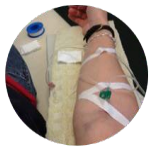
- IG replacement therapy is used to treat antibody production deficiency
- Goal of treatment: to prevent and/or reduce recurrent or severe infections

- Patient receives IgG antibodies to a wide variety of bacterial and viral agents
- This helps replace the patient's missing and/or malfunctioning IgG antibodies, and therefore helps patients to fight infections

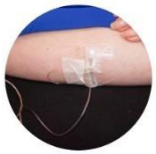


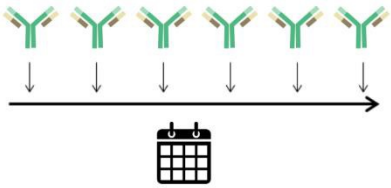
- IG treatment does not stimulate the patient's immune system to make enough functioning antibodies, and the infused dose provides only temporary protection and is metabolised by the body over time
- Therefore, patients require repeated IG infusions at regular intervals (e.g., daily to once a month)
- Routine IG infusions can provide protection from infections in patients with PI

Intravenous (IV)



Subcutaneous (SC)





PROGRESS CHECK

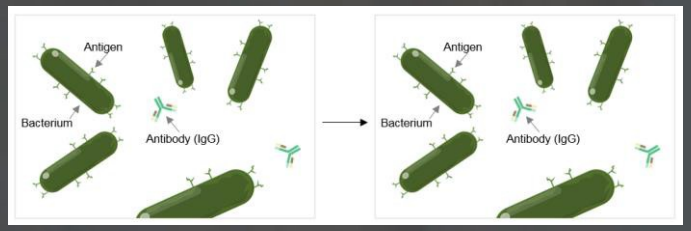
QUESTION TWO

Think about how you would complete the following question, then select the Check Your Answer button.

Which of the following pairs of images best depicts the effects of IG replacement treatment in patients with PI?

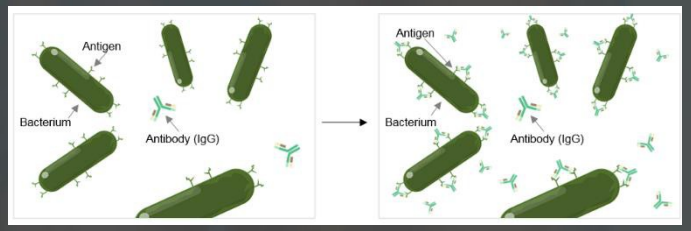
A

Before IG treatment | After IG treatment



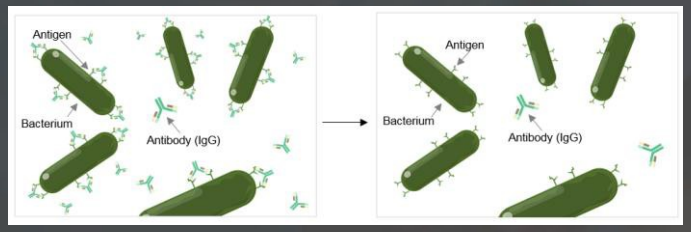
C

Before IG treatment | After IG treatment



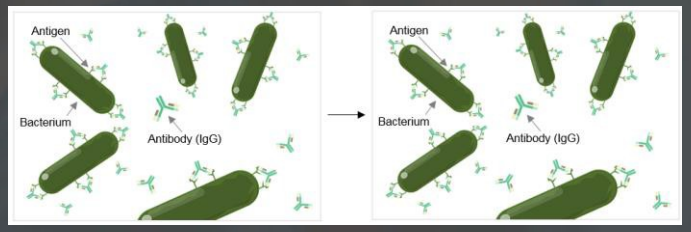
B

Before IG treatment | After IG treatment



D

Before IG treatment | After IG treatment



CHECK YOUR ANSWER

PROGRESS CHECK (CONT.)

ANSWER: QUESTION TWO

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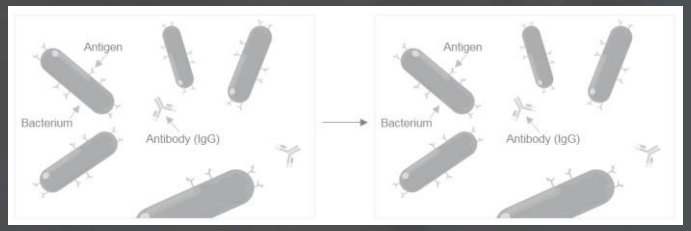
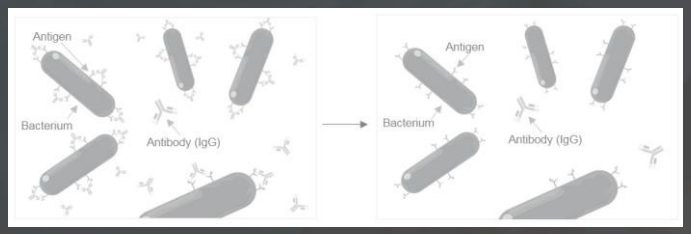


B

Before IG treatment | After IG treatment



C

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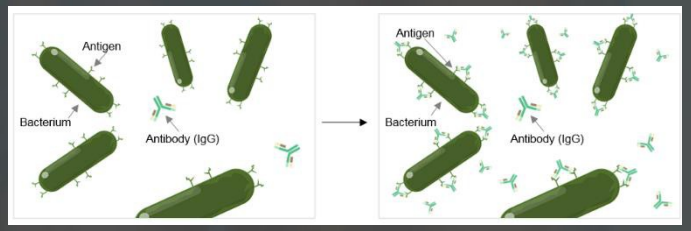
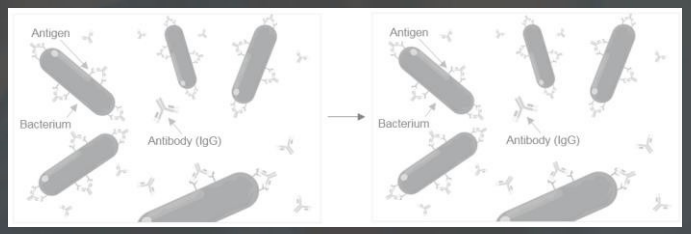


Very few antibodies | Many more antibodies

D

Before IG treatment | After IG treatment



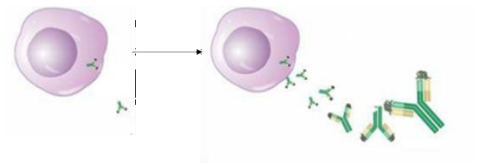
PROGRESS CHECK

QUESTION THREE

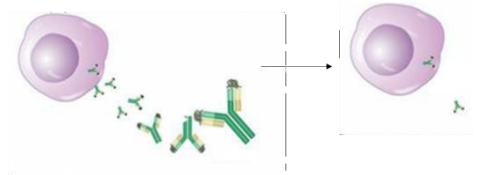
Think about how you would complete the following question, then select the Check Your Answer button.

Which of the following statements about IG replacement treatment is correct?

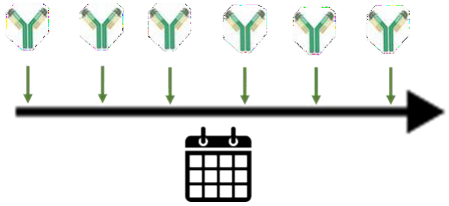
A IG treatment corrects the B cell defects seen in antibody production deficiency.



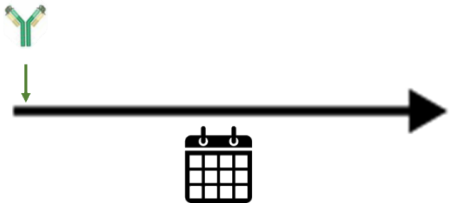
B IG treatment reduces the number of antibodies produced by B cells.



C Since infused doses of IG provide only temporary protection and are metabolised by the body, patients with PI receive infusions at regular intervals (e.g., daily to once a month).



D Since IG treatment causes long-term stimulation of antibody production, only one infusion is required.



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PROGRESS CHECK (CONT.)

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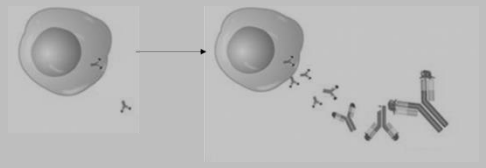

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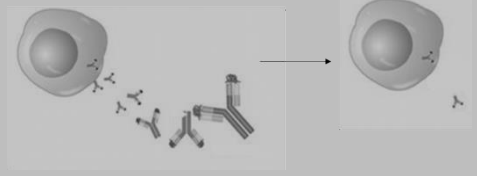

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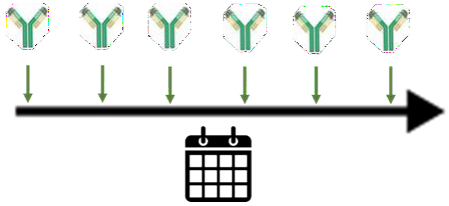

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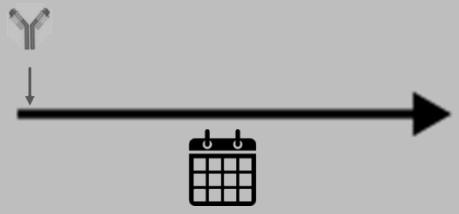


MODULE SUMMARY

Primary Immunodeficiency

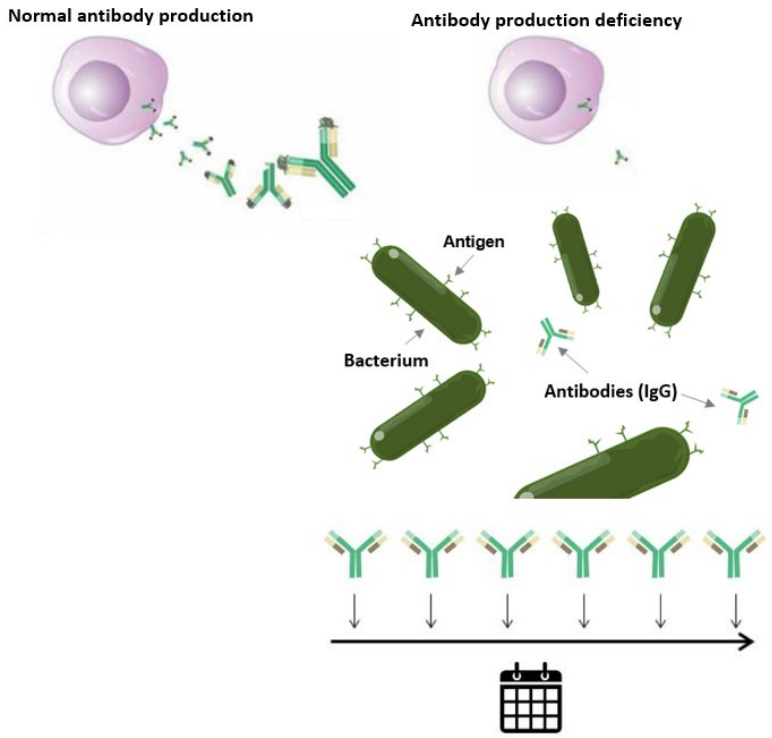
- More than 350 forms
- Immune system component(s) are missing, are not functioning, or are not functioning adequately enough to allow patients to fight off infection from pathogens

Antibody Production Deficiency

- Accounts for approximately 50% of all PI cases
- Associated with missing and/or malfunctioning antibodies
- Mostly caused by defects in B cells, which are responsible for antibody production, although T cell function may also be abnormal in some patients

Management of PI with IG Treatment

- IG treatment is used to treat antibody production deficiency
- Goal of IG treatment is to prevent and/or reduce recurrent or severe infections
- IG infusion helps replace the missing and/or malfunctioning antibodies
- This helps patients with PI fight off infections
- IG must be periodically replenished through regular IG infusions
- Routine IG infusions can provide protection from infections in patients with PI



GLOSSARY

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