IMMUNE RESPONSE TO VACCINES

WHAT IS A VACCINE?

Whole or a portion *of the* ***pathogen's structure*** *that upon administration* ***stimulates antibody production or cellular immunity*** *against the pathogen but* ***is incapable of causing severe infection.***

IMPORTANCE OF VACCINES

-- Vaccines are one of the **greatest achievements of medical science** (other is discovery of antibiotics).

-- Vaccines have destined dreaded diseases like **smallpox** to history and **polio** is on the verge of extinction.

-- At least **3 million lives are saved every year** and if vaccination is available to everyone the number will be **4.5 million**.

Triumph of Vaccines: Data from USA

Disease	Total cases	Year	Cases in 1994	% Change
Diphtheria	206,939	1921	2	-99.9%
Measles	894,134	1941	963	-99.9%
Mumps	152,209	1968	1537	-99.9%
Pertussis	265,269	1934	4617	-99.9%
Poliomyelitis	21,269	1952	0	-100%
Rubella	57,686	1969	227	-99.9%
Tetanus	1,560	1923	51	-99.9%

Vaccines: NIH report 2005

-- More than **seven million children**, under the age of 5, die every year as the result of infectious diseases.

-- **Nintey-nine percent** of those children live in **developing countries** around the world.

-- Existing vaccines are often **inadequately distributed** to the **poorest countries**.

-- An **ideal vaccine** would require **no more than three doses** and cost **$1 per dose**.

-- A **useful vaccine** could cost up to **$10.**

-- Every year **33 million infants still miss out** on immunization.

-- At least **1.5 million of them will die** of a vaccine-preventable cause before they reach their **5th birthday.**

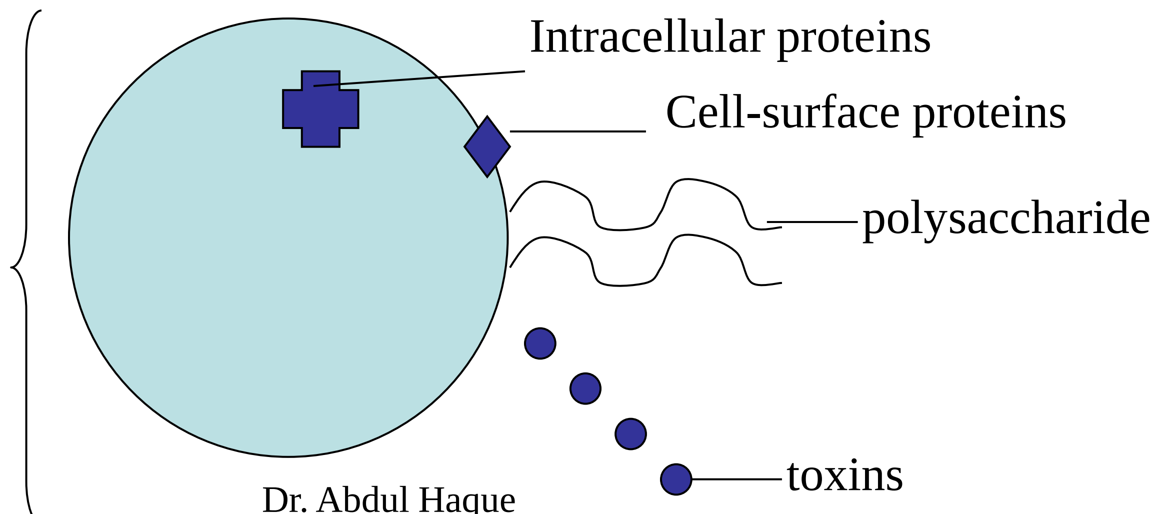
-- **Two out of every three** un-immunized children can be found in **five** countries -- India, Nigeria, China, Pakistan and Indonesia.

BASIC CONCEPT OF VACCINES

- Deliver to body something that **looks like the pathogen** but is **not pathogenic**.

- **It should induce protective immune response.**

Entire organism
• live (attenuated)
• killed



VACCINATION

-- It **protects** a recipient **from a pathogenic agent**.

-- Vaccines produce **active immunity.**

-- Immunity and immunologic memory is **similar to natural infection** but without risk of disease.

General rule

The **more similar** a **vaccine** is to the **natural disease**, the **better** is the **immune response** to the vaccine.

Features that characterize agents for which successful vaccines have been developed:

- The agent (pathogen) causes an **acute infection with clear symptoms**.

- The agent is **antigenically stable**.

- Or if there are **different serotypes** in the field, **each** remains essentially **antigenically stable.**

- It **induces** a **certain titre** of a specific antibody in a recipient.

- For inducing a **classical immune response** a vaccine should be able to induce **specific CD8+ T-cell response** in addition to a **CD4+ T-cell response.**

Example is smallpox virus. So it was easy to eliminate it.

The pathogenesis of a particular infection can influence the response to a vaccine

Three different situations are possible:

- Induction of **sufficient antibody production** at the **location of infection** (poliovirus, diphtheria, tetanus). It may have to be supplied in a **preformed state** for immediate action.

- In viral infections, if a secondary viremia follow the primary viremia (measles, mumps) it is important for a vaccine to induce a strong humoral and cellular response to **limit production of virus** at both the **primary and secondary sites**.

- If the infectious agent becomes largely **cell-associated**, it is desirable that vaccine is one that induces a **strong type 1 T-cell response** (pox virus, rabies virus, TB).

IMMUNOLOGIC MEMORY

*The **most effective vaccines** are those which induce **strong immunologic memory**.*

B-CELL MEMORY

- **Memory B cells** are formed in the **germinal centers (GCs) of lymphoid tissue.**

- Rapidly dividing B cells, the **centrocytes**, in the GC undergoes **somatic hypermutation** in **BCR**.

- Subsequently cells with Ig receptors of **higher affinity** are selected by the retained antigen to undergo **further differentiation.**

- Most of these selected cells become **antibody secreting cells (ASC)** i.e., **plasma cells**, most of which migrate to the **bone marrow**.

- Other cells become **memory cells**, which **circulate around the body.**

- When these cells **return to antigen-containing lymphoid tissue**, the **cycle of differentiation may begin again**, resulting in the **production of more antibodies.**

- The purpose of a **boosting dose** of antigen is to induce the **differentiation of existing B memory cells** by **replenishing** the **antigen depot** in GCs.

T-CELL MEMORY

- There are **significant differences** in this respect **between B and T cells**.

- Unlike the B cell receptor, there is **no somatic hypermutation** to increase the affinity of the TCR during this expansion phase.

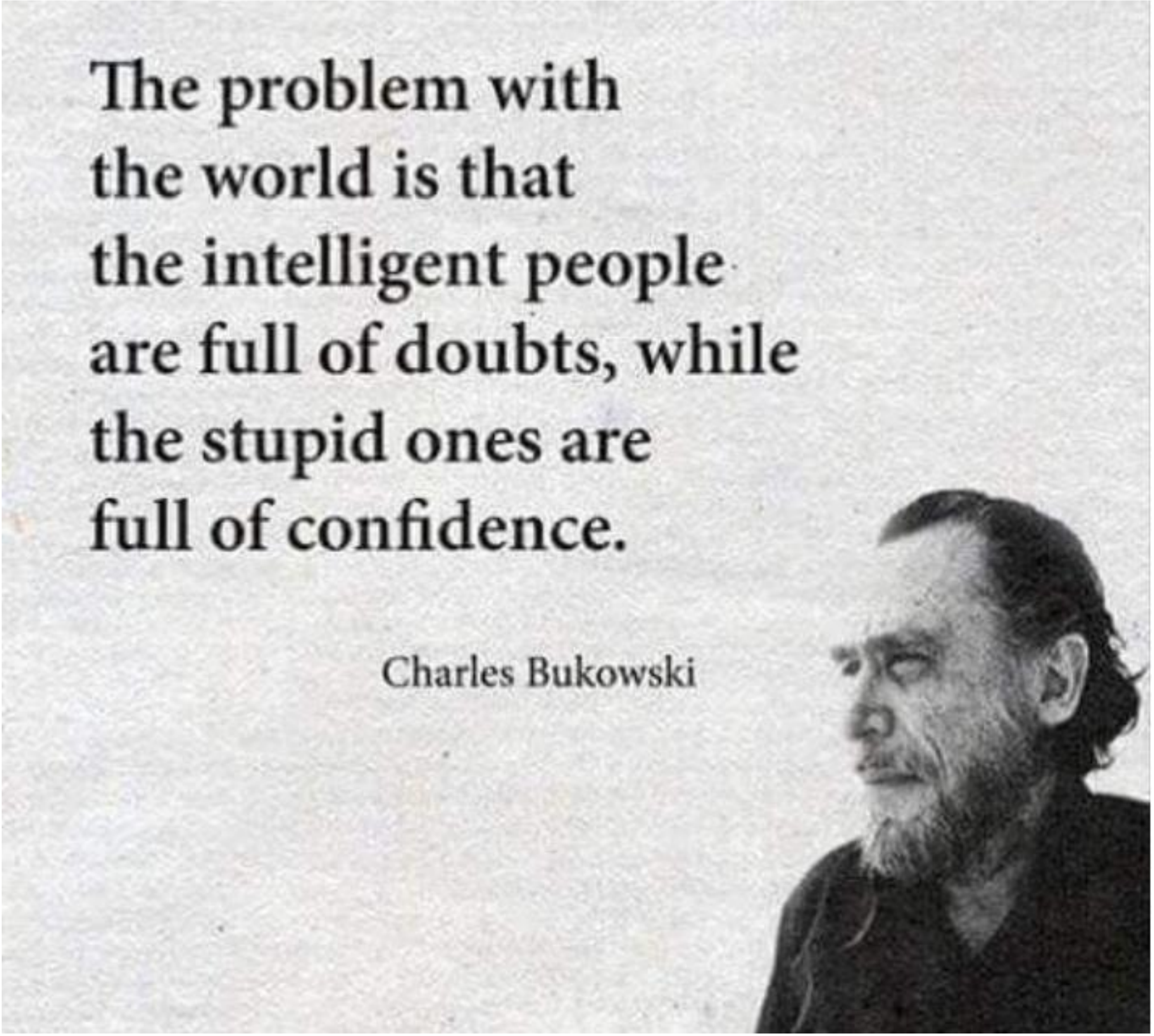
- Persistence of specific intact antigen is **not required** for long-term **cytotoxic T cell** memory.

- Therefore memory T-cell formation is **not limited** to any particular site.

- **Memory T cells** can be stimulated by APCs.

- **Naive T cells** require from **6 to greater than 30 hours** of stimulation by APCs to become fully activated.

-- **Memory T cells** are activated within **2 hours**.


The problem with
the world is that
the intelligent people
are full of doubts, while
the stupid ones are
full of confidence.
Charles Bukowski

German police dogs …. Final examination


Thank You!