Molecular and Cellular Immunology/Immunology

Course Introduction

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A brief history of immunology

- **Immunity:** comes from the Latin “immunis” meaning “exempt”
- Concept dates to 430 B.C. when Thucydides, the historian of the Peloponnesian War, wrote that those who had recovered from Plague could care for those with disease
- **Variolation** - used in ancient Asia; brought to Europe in 1721 by Lady Mary Wortley and subsequently used in the Revolutionary War
- **1796:** Jenner used cow pox to protect from smallpox. The term “vaccination” (“vacca” is Latin for “cow”) derives from this.

Figure 1-1
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History, cont.

- **1870's:** Koch proved that infectious diseases are caused by microorganisms- anthrax
- **1860's-1880's:** Louis Pasteur developed vaccines against cholera quite by accident - **attenuation**. Coined "vaccine" in honor of Jenner. Also made first anthrax and rabies vaccines.

THE GOAL OF IMMUNITY/

IMMUNIZATION: MEMORY

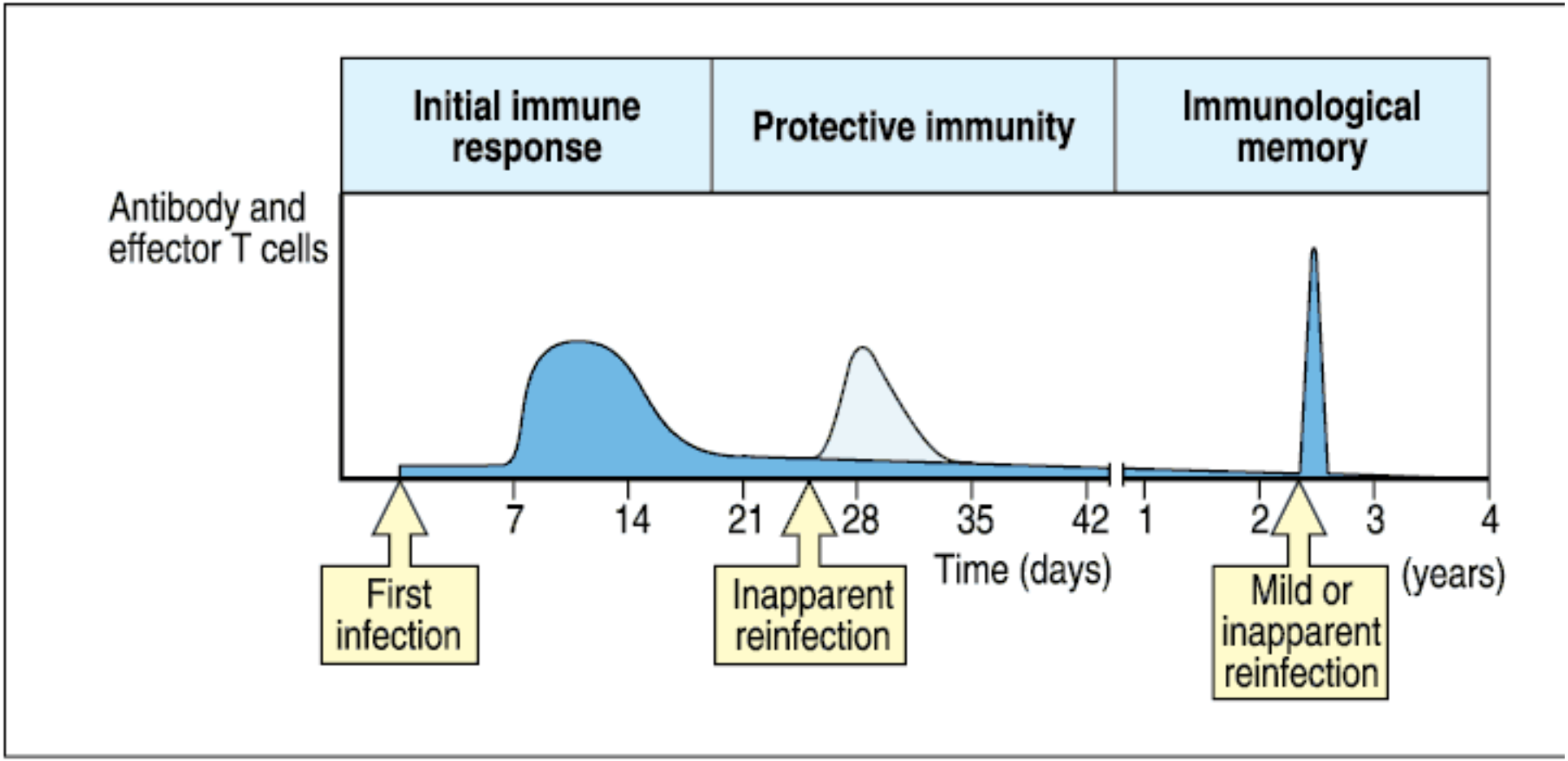

Fig 10.16 © 2001 Garland Science

TABLE 1-1 Cases of selected infectious disease before and after the introduction of effective vaccines

	ANNUAL CASES/YR		CASES IN 2004
Disease	Prevaccine	Postvaccine	Reduction (%)
Smallpox	48,164	0	100
Diphtheria	175,885	0	100
Measles	503,282	37	99.99
Mumps	152,209	236	99.85
Pertussis (whooping cough)	147,271	18,957	87.13
Paralytic polio	16,316	0	100
Rubella (German measles)	47,745	12	99.97
Tetanus ("lockjaw")	1,314 (deaths)	26 (cases)	98.02
Invasive hemophilus influenzae	20,000	172	99.14

SOURCE: Adapted from W. A. Orenstein et al., 2005. *Health Affairs* 24:599.

Table 1-1
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More History

- 1890: Von Behring and Kitasato - discovered substances in serum that bound to pathogens and neutralized toxins, precipitate toxins, lyse and clump bacteria
- 1930: discovery of antibodies as the source of this

Humoral vs. Innate Immunity

- Metchnikoff: discovered cells that could engulf microoranisms: phagocytic cells that he called “macrophages: - the beginning of innate and cell-mediated immunity
- Body fluids: “humours”, so serum factors (i.e. antibodies) were “humoral immunity”

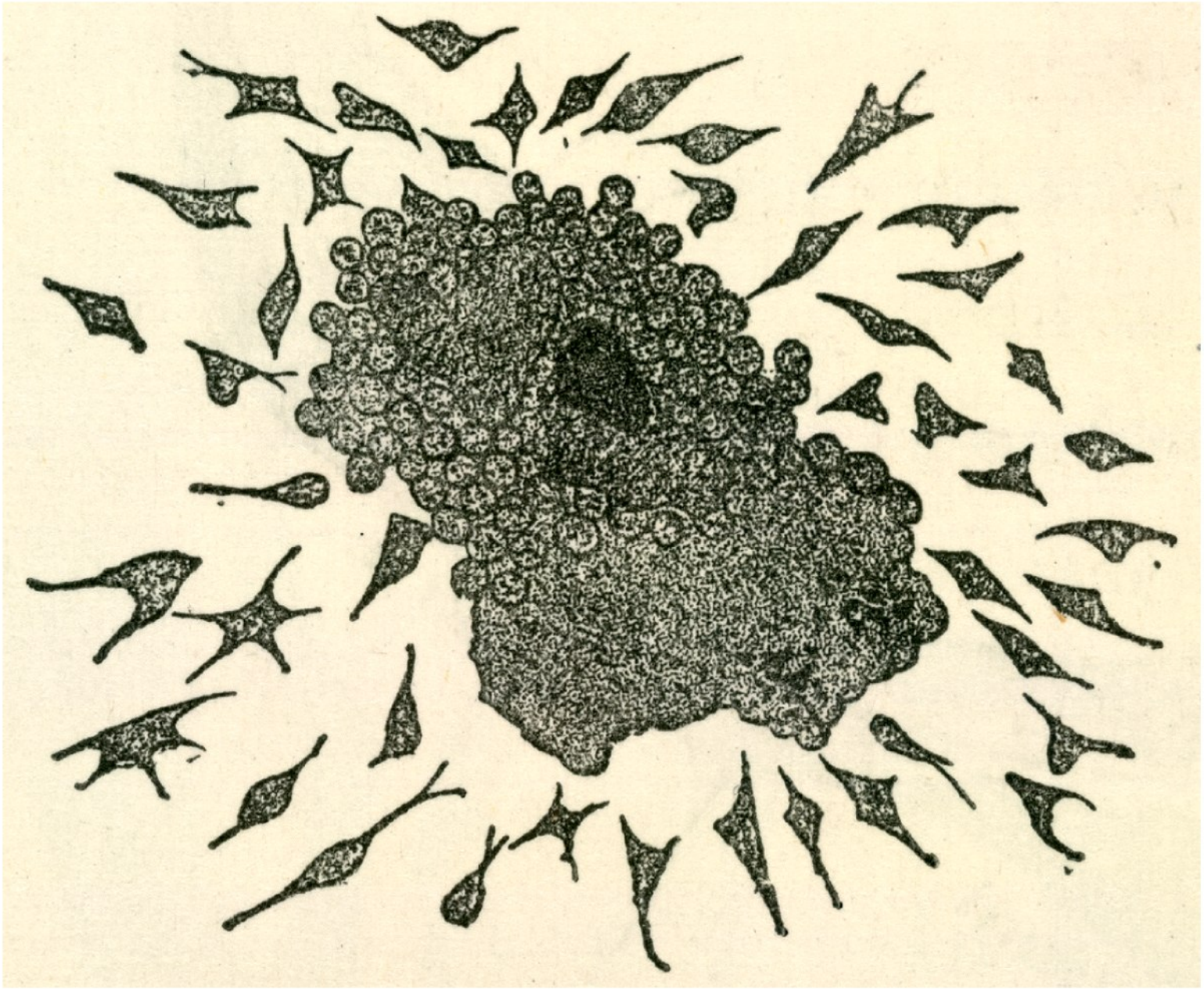

Figure 1-3
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Antibodies: competing theories

- Selection vs. instruction hypotheses for antibodies
- 1900: Paul Ehrlich and the “side-chain” hypothesis or the “selection” hypothesis
  - The immune system selects the antibody based on “lock and key” fit

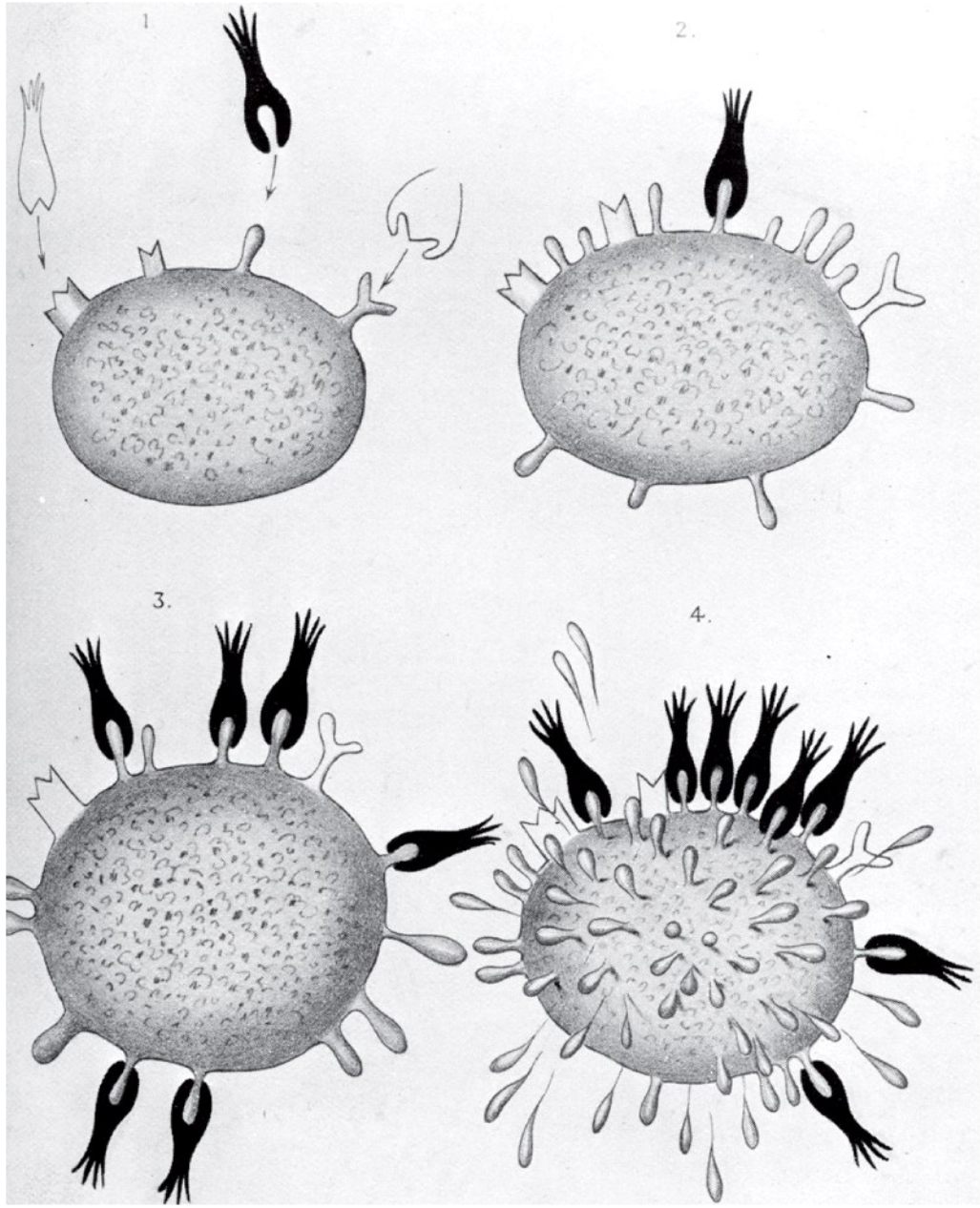

Figure 1-4
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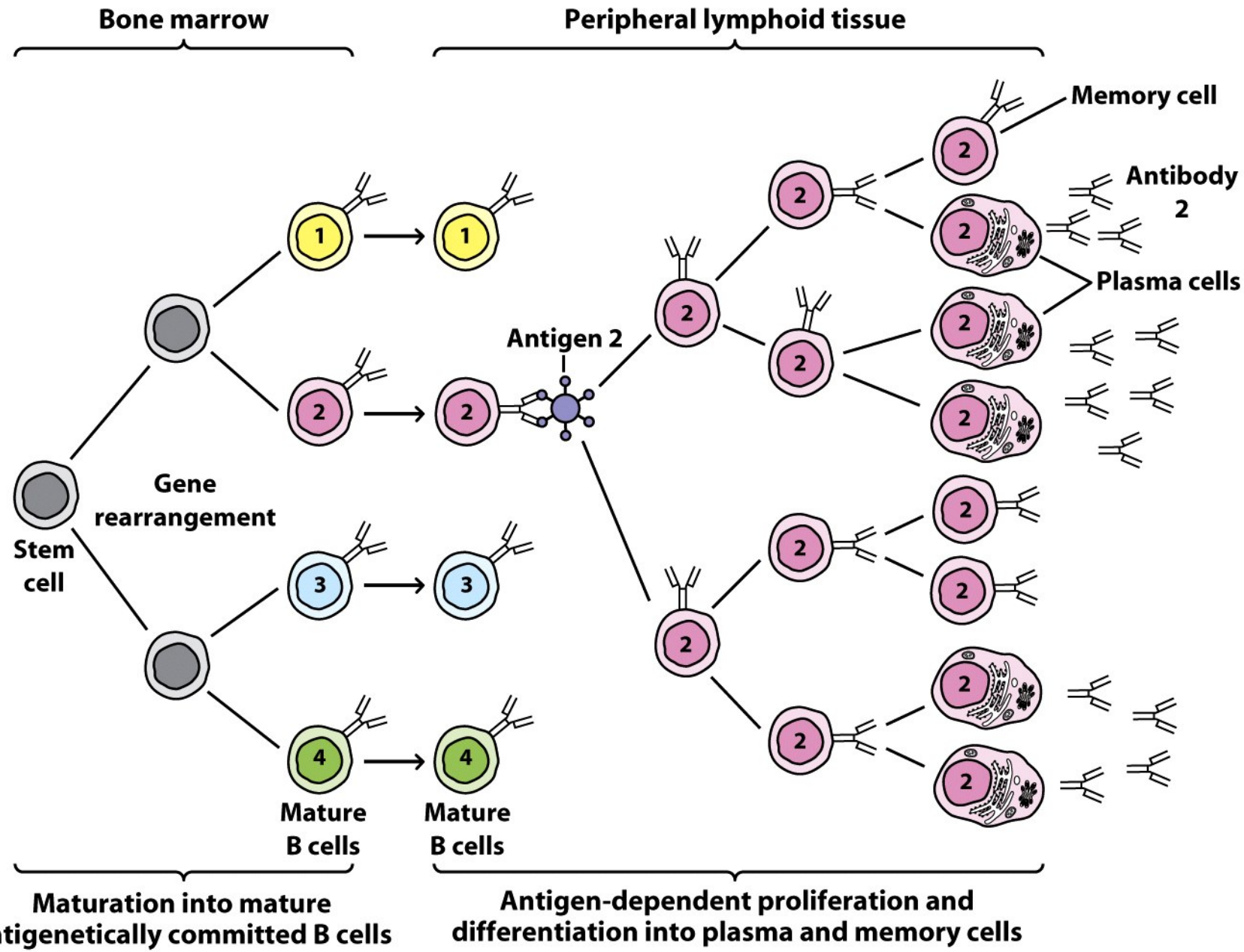

Figure 1-12
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- Clonal selection: 1950’s (Jerne, Talmadge and Burnet)
- Lymphocytes: discovered in the 1950’s
- Generation of Diversity: Genetic recombination of antibodies and the T cell receptor; 1970s-early1980s
- Monoclonal antibodies: 1975
- MHC restriction: 1976

Major groups of human pathogens	Examples of diseases
Viruses	Polio, smallpox, influenza, measles, AIDS
Bacteria	Tuberculosis, tetanus, whooping cough
Fungi	Thrush, ringworm
Parasites	Malaria, leishmaniasis

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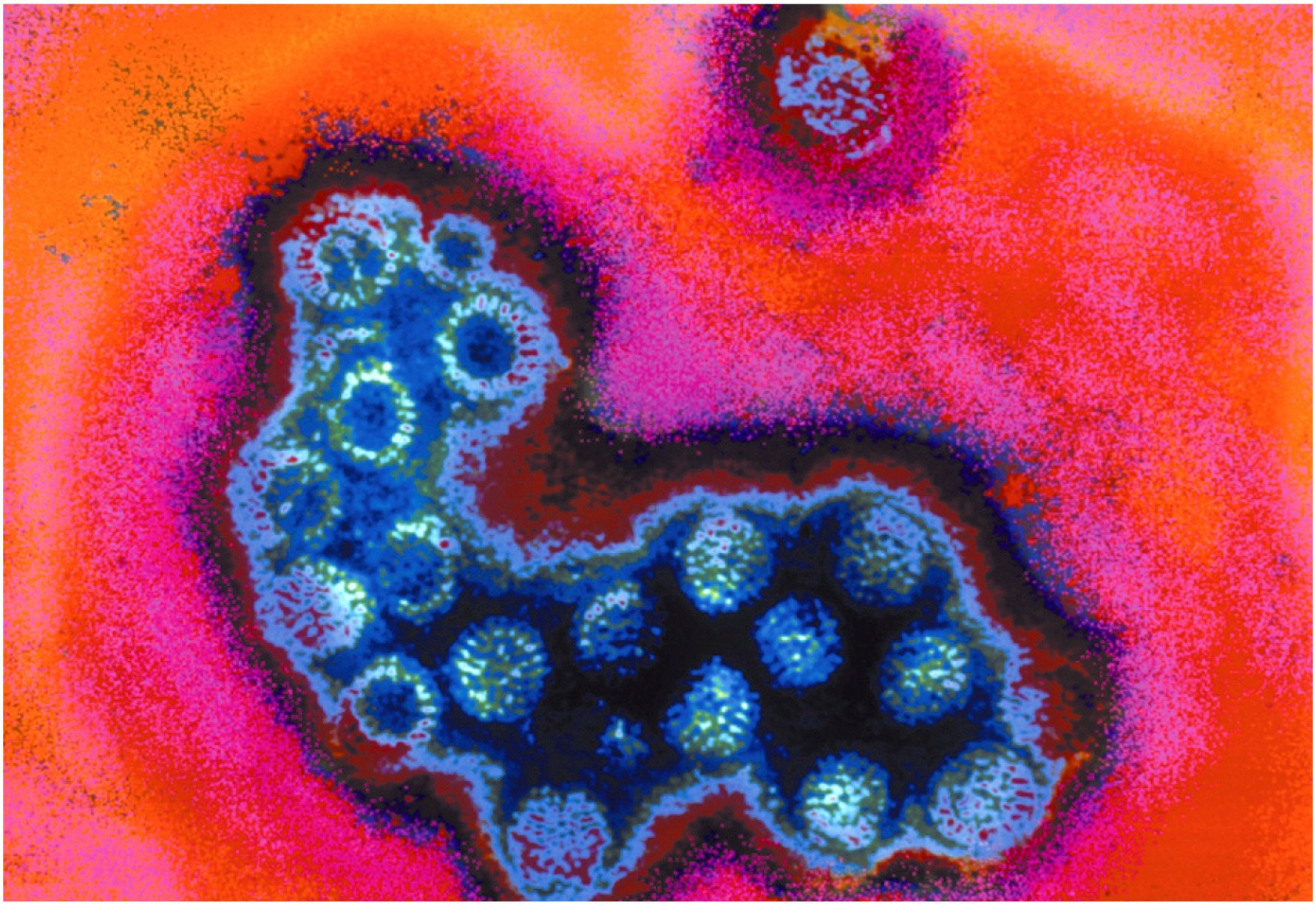

Figure 1-5a
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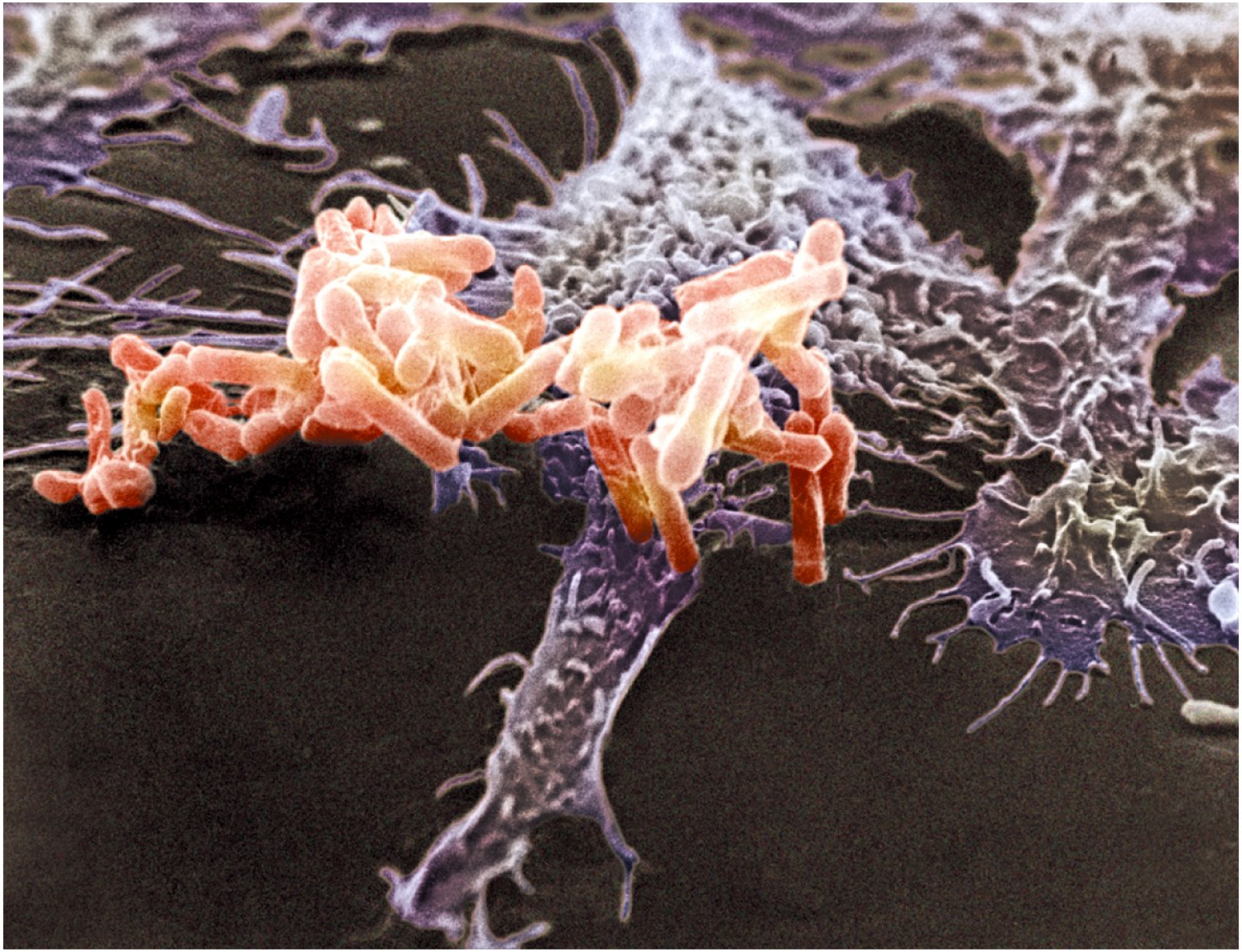

Figure 1-5b
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Figure 1-5c
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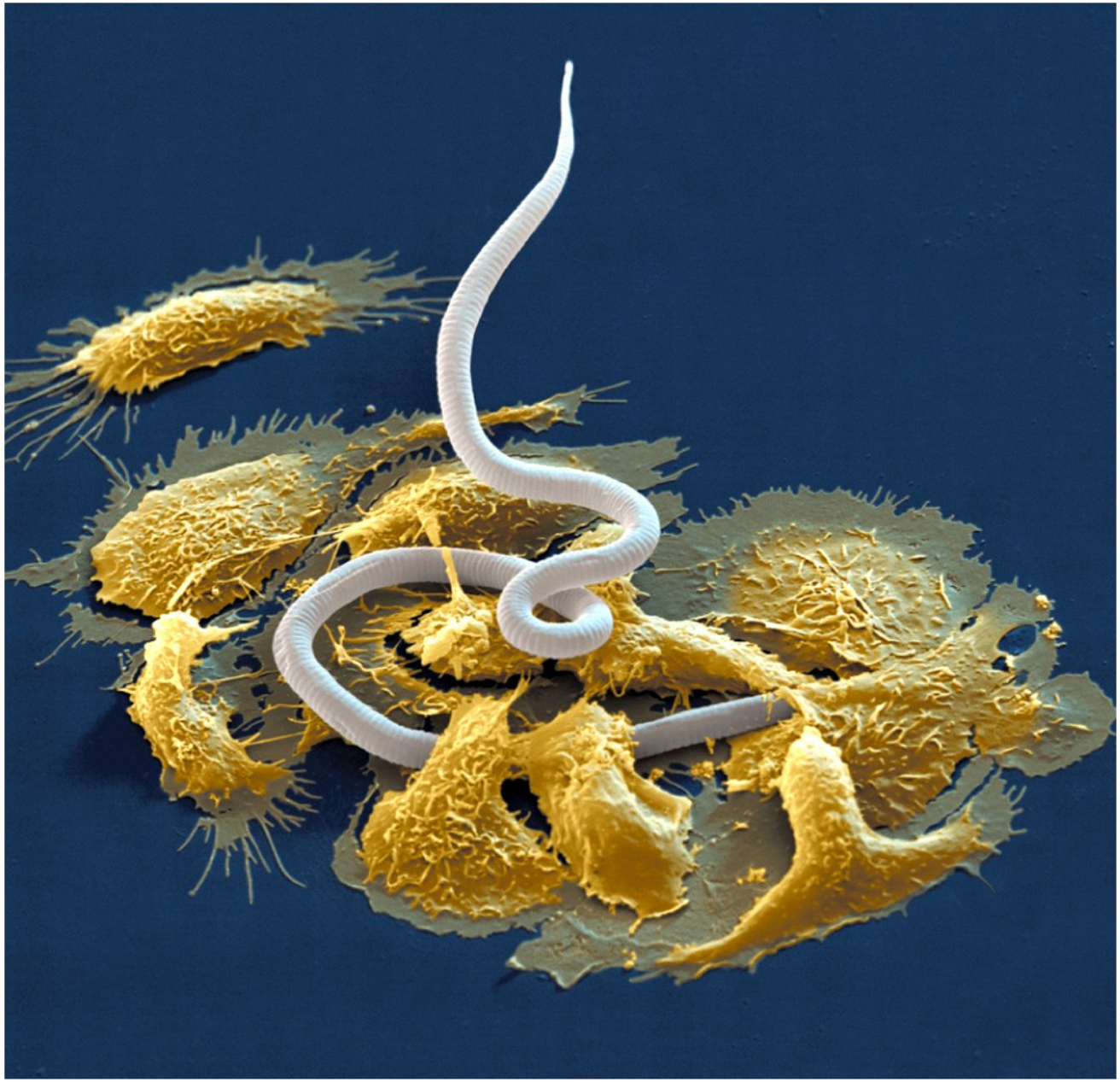

Figure 1-5d
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Immune System Must:

- Deal with pathogens and tumors
- Distinguish self from non-self
  - React to non-self
  - Not react to self
  - Reject tumors, but not reject the fetus
- Distinguish “danger” vs. “non-danger”
  - e.g. clear dead cells that aren’t dangerous without responding with inflammation but also appropriately respond to infection/infected cells

To do this, the immune system:

- Uses a variety of cells and soluble molecules
- Exhibits redundancy and alternatives
- Generates memory

- Exceptions to almost every “rule”!!

TABLE 1-3 Comparison of innate and adaptive immunity

	Innate	Adaptive
Response time	Hours	Days
Specificity	Limited and fixed	Highly diverse; improves during the course of immune response
Response to repeat infection	Identical to primary response	Much more rapid than primary response
Major components	Barriers (e.g., skin); phagocytes; pattern recognition molecules	Lymphocytes; antigen-specific receptors; antibodies

Table 1-3
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Course Housekeeping

- Course will meet mostly in C-555 (exceptions will be emailed)
- Text: Kuby Immunology 6e
  - Online access www.whfreeman.com/immunology6e
  - Book has questions at the end of the chapters. At least one question from the book will be used on each exam
- Lecture notes will be posted on course website: http://www.umdnj.edu/gsbsnweb/olc/mci/index.htm
  - Login: immunology2009
  - Password: lymphocyte

Course Grading

- Midterm exam: 30%
- Paper: 25%
- Final Exam: 45%

Course Written Assignment:

- Immunology:
  - Nobel Prize report: pick a Nobel laureate and write about why this prize was awarded and how it is still important to immunology today
- Molecular/Cellular Immunology:
  - Write a nominating letter for the 2009 Nobel Prize in Medicine for an immunology breakthrough

TABLE 1-2 Nobel prizes for immunologic research

Year	Recipient	Country	Research
1901	Emil von Behring	Germany	Serum antitoxins
1905	Robert Koch	Germany	Cellular immunity to tuberculosis
1908	Elie Metchnikoff Paul Ehrlich	Russia Germany	Role of phagocytosis (Metchnikoff) and antitoxins (Ehrlich) in immunity
1913	Charles Richet	France	Anaphylaxis
1919	Jules Bordet	Belgium	Complement-mediated bacteriolysis
1930	Karl Landsteiner	United States	Discovery of human blood groups
1951	Max Theiler	South Africa	Development of yellow fever vaccine
1957	Daniel Bovet	Switzerland	Antihistamines
1960	F. Macfarlane Burnet Peter Medawar	Australia Great Britain	Discovery of acquired immunological tolerance
1972	Rodney R. Porter Gerald M. Edelman	Great Britain United States	Chemical structure of antibodies
1977	Rosalyn R. Yalow	United States	Development of radioimmunoassay
1980	George Snell Jean Dausset Baruj Benacerraf	United States France United States	Major histocompatibility complex
1984	Cesar Milstein Georges E. Köhler Niels K. Jerne	Great Britain Germany Denmark	Monoclonal antibodies Immune regulatory theories
1987	Susumu Tonegawa	Japan	Gene rearrangement in antibody production
1991	E. Donnall Thomas Joseph Murray	United States United States	Transplantation immunology
1996	Peter C. Doherty Rolf M. Zinkernagel	Australia Switzerland	Role of major histocompatibility complex in antigen recognition by T cells
2002	Sydney Brenner H. Robert Horvitz J. E. Sulston	S. Africa United States Great Britain	Genetic regulation of organ development and cell death (apoptosis)

Table 1-2
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Recent prizes - not quite immunology but relevant

- 2006: RNA interference
- 2007: Knock-out and knock-in mice
- 2008: Discovery of HPV, HIV

2009: Immunology Nobel Prizes?

- Therapeutic approaches: transplantation, autoimmunity
- Fundamental processes: what do we now understand (e.g. MHC restriction fits this category)
- Immunotherapies: immunomodulatory drugs (e.g. interferon and other cytokines or inhibitors of these); immunotoxins; immunodepletion
- Novel cells
- Vaccines: recombinant, DNA, cell-based
- Immunodiagnostics
- New technologies?
- Animal models: knock-in/knock-out mice - too late; awarded 2007!