Exposure

A GUIDE TO SOURCES OF INFECTIONS
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Preface

*All interest in disease and death is only another expression of interest in life.*

T. Mann (1875-1955), *The Magic Mountain*

What do a tick in the scalp of a child, a man with a boil after an adventure trip to Kenya, and a febrile elderly person reporting the death of her pet bird have in common? The answer is exposure: the critical first step in infection. Like light impacts on a film, exposure impacts on hosts.

Exposure embraces all agents (prions to parasites), ages (embryo to elderly), and habitats (city to coast). Exposure is the key to directed search for causative agents, characterization of infection severity and stage, interpretation of laboratory test results, and preventive and public health action. Determining the exposure history should be a part of any patient evaluation. You might take the table of contents or the checklist in the appendix as a starting point. By generating a reduced list of agents to consider for priority laboratory work up, treatment, and prevention, the exposure history can curb health care costs. I grouped the diverse methods of exposure into chapters and sections in a way that I felt would be useful for clinicians, public health officers, and microbiologists.

Infections are still with us. Worldwide in 2002, infectious diseases accounted for nearly 25% of disability-adjusted life years (DALYs) (350 of 1,490 million) and nearly 20% (11 of 57 million) of deaths. Impact is considerably greater in low-income than high-income countries (causing 2% of DALYS and 4% of deaths in high-income countries versus 10 and 50% in low-income countries). Despite these gradients, infections remain significant in high-income countries. In the United States in 2001, about 3% of outpatients (23.8 million of 880.5 million) were diagnosed infectious diseases, and about 9% of all prescriptions were antimicrobials (114 million of 1,314 million). Exposure helps a physician decide whether a patient’s illness is likely to be infectious. Further evidence comes from symptoms and signs. Infectious diseases cause localized (organ-related, calor, rubor, dolor, or tumor), regional (migrating lesions or adenopathy), or systemic (fever, rash, somnolence, or shock) signs.

The scope of the book is epidemiologic rather than clinical. For reasons of space, I had to omit many details and simplify a number of complex issues. I regret any oversimplifications, inconsistencies, or errors. Please contact me through ASM Press for your comments or suggestions (books@asmusa.org).
Nonetheless I hope that practitioners, infectious disease specialists, travel clinic managers, clinical and environmental microbiologists, and public health promoters will benefit from working with the book, without the feeling “I understand it, so it must be wrong.”

Dieter Sturchler
Büren, Switzerland
2 December 2005

As the epidemiologic situation, recommended treatments, and preventive measures can change rapidly, readers are urged to consult national guidelines and formularies before administering any vaccines or medications.
I am deeply grateful to my wife Tjoek and to our three children who supported me in the 5 years I was laboring on this book. All gave valuable input to make the book practical.

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Introduction

Better to be approximately right than exactly wrong.
Attributed to J. W. Tukey (1915–2000)

CONVENTIONS AND METHODS

ACRONYMS
Acronyms are introduced in chapters and listed in the appendix.

TERMS
Terms are explained in the glossary and in chapters. I aimed to distinguish colonization and infection from disease and to avoid ambiguous terms, e.g., “ascariasis,” which could mean infection or disease. Country names are for geographic reference only and do not imply political or legal status. For brevity, prefixes such as “Republic” are omitted. For practical purposes, high-income (industrial) countries here include those in North America and Europe and Australia, Japan, and New Zealand, while low-income (developing) countries are all remaining countries of Africa, Latin America, Asia, and the Pacific. A “tree of life” is presented in Table 20.1.

NUMBERS
Numbers are generally rounded to a full digit. I aimed to provide magnitude and range rather than precision. For the same reason, confidence limits are preferred over significances. Attack rates are per 100 exposed persons, and infection and disease rates are per 1,000 person-years or 10^5 population. In general, “infrequent” refers to a prevalence <1–5% or a rate <100/10^5 and year. International units are used, including meter and centigrade. Season is a diagnostically useful, perhaps underrated variable that I have emphasized whenever possible.

EVIDENCE
This book is based on evidence and my own clinical and epidemiological experience. For years, I have watched journals (e.g., American Journal of Tropical
INTRODUCTION


REFERENCES

I reviewed >13,000 publications. Only a fraction could be cited (using EndNote version 7.0), however. I selected only the most recent publications in a series, although I aimed to represent a mix of review and original work from all continents.

EXPOSURE HISTORY

Goal: To efficiently recognize and manage infectious agents and diseases.

INTERVIEW

An exposure interview should be part of the medical history. At least the following topics should be covered: susceptibility (past infectious diseases, vaccines, and immune impairments), time and place of exposure (home, work, leisure, and travel), possible sources (humans, animals, foods, and environment), and preventive measures.

TIME AND DOSE

Exposure can be instantaneous (e.g., a date marked by a meal, injection, or a flight), seasonal (e.g., tick emergence in spring or swimming in summer), continuous (e.g., hours spent in a closed room or days on assisted ventilation), or intermittent (e.g., frequent drinks of raw milk or drug injections). The infective dose can be estimated from microbiological (e.g., from leftover foods) or entomological (e.g., from vectors) data, experimental studies (animal or human volunteer), or epidemiologic data (e.g., number of cups of tap water consumed per day). Intensity is a measure of exposure that aggregates dose over time. Intensity helps to interpret laboratory findings (e.g., a single water contact is incompatible with a heavy Schistosoma mansoni egg output) and to assess causality.

RECALL

Memory of many exposing events is lost within days. A few measures may assist recall. Ask your patient for vaccination, travel, and other records. Recounting life around the clock (“from breakfast to bed”) in the last 24 h before the visit may bring back memories of routine activities, meals, drinks, and exposures from work or leisure. Habitat photos could also enhance recall. Alternatively, you may obtain a structured exposure interview (appendix 1).

Some events are remembered for life, typically deliveries, abortions, owned pet animals, continents visited, past and current sex partners, some diagnoses and treatments (e.g., tuberculosis, AIDS, and sexually transmitted infections [STI]), injection drug use, general anesthesia for major surgery, stays in an intensive care unit, organ transplants, and implants.

MODES OF SPREAD AND AGENT CLUSTERS

Humans acquire agents from animals, from the environment, from foods or objects, from other humans (including by droplets, by close and sexual contact, and transplacentally), and nosocomially, including by injection drug use and invasive health procedures. Agents may use several modes. Direction of spread can be opposite, from humans to animals (e.g., Mycobacterium tuberculosis from caretaker to captive primate), to the environment (e.g., Giardia from hiker to mountain creek), or to foods (e.g., Salmonella enterica serovar Typhi from carrier to food). Agents can be taken up from ingestion, inhalation, inoculation, or contact. These portals can be difficult to identify clinically. Fecally polluted foods and hands could result in uptake by ingestion. Skin contact could result from touching water, soil, or other skin and from human or animal droplets settling on hands or conjunctiva.

About 300 agents commonly infect humans. For convenience, this list is broken down into five arbitrary “ecotransmission” clusters and further into seven agent classes (prions, viruses, bacteria, fungi, protozoa, helminths, ectoparasites). For acronyms of viruses, see appendix 2, and for agent taxonomy, see Table 21.1.

DROPLET-AIR CLUSTER (~40 agents or 13%)

Viruses. Vaccine-preventable viruses include Influenzavirus; mumps, measles, and rubella viruses; poliovirus; and varicella-zoster virus. Others include adenovirus, Epstein-Barr virus, Enterovirus, parainfluenza virus, parovirus B19, Rhinovirus, and respiratory syncytial virus.
Bacteria. Vaccine-preventable bacteria include Bordetella pertussis, Corynebacterium diphtheriae, Haemophilus influenzae b (Hib), Mycobacterium tuberculosis, Neisseria meningitidis, Streptococcus pneumoniae, and the “four pneumos” (Chlamydia pneumoniae, Klebsiella pneumoniae, Legionella pneumophila, and Mycoplasma pneumoniae).

Fungi. Fungi from air include, e.g., Aspergillus, Blastomyces, Cryptococcus, Histoplasma, and Pneumocystis.

FECES-FOOD CLUSTER (~70 agents or 24%)
Agents in this cluster are found in foods, beverages, and drinking water and on objects.

Prions. Prions from foods are those associated with variant Creutzfeldt-Jakob disease.

Viruses. Viruses include astrovirus, hepatitis viruses A and E, Norovirus, and Rotavirus.

Bacteria. Bacteria include all Enterobacteriaceae (e.g., Escherichia, Salmonella, and Shigella), Bacteroides, Clostridium (C. botulinum, C. difficile, and C. perfringens), Helicobacter, Listeria, and Vibrio (V. cholerae and V. parahaemolyticus).

Fungi. Fungi from foods include Microsporidia, e.g., Encephalitozoon and Enterocytozoon.

Protozoa. Protozoa include Cryptosporidium, Cyclospora, Entamoeba, Giardia, Sarcocystis, and Toxoplasma.

Helminths. Helminths from foods include Anisakis, Ascaris, Fasciola, Paragonimus, Taenia, Trichinella, and Trichuris.

ZOOONOTIC CLUSTER (~100 agents or 34%)
Viruses. Viruses from mammals include Lyssavirus and Hantavirus. Many zoonotic viruses are vectorborne, including, for example, dengue virus.

Bacteria. Bacteria include Bacillus anthracis, Borrelia, Brucella, Coxiella, Francisella, Rickettsia, and Yersinia pestis.

Fungi. Fungi include zoophilic dermatophytes, e.g., Microsporum canis.

Protozoa. Protozoa include Babesia, Leishmania, Plasmodium, and Trypanosoma.

Helminths. Helminths from animals include Echinococcus granulosus, E. multilocularis, and filariae (e.g., Onchocerca, Wuchereria).

ENVIRONMENTAL CLUSTER (~45 agents or 15%)
Bacteria. Bacteria from water and soil include Acinetobacter, Burkholderia cepacia, Clostridium tetani, mycobacteria, Leprosy, and Pseudomonas aeruginosa.

Fungi. Fungi from soil and plants include Acremonium, Fonsecaea, Fusarium, Penicillium marneffei, Sporothrix, and Trichosporon.

Protozoa. Protozoa include Rhinosporidium seeberi and free-living amebas (e.g., Acanthamoeba and Naegleria).

Helminths. Helminths from water and soil include hookworms (Ancylostoma and Necator), Schistosoma, Strongyloides, and Toxocara.

Ectoparasites. Ectoparasites from soil include Tunga penetrans.

SKIN-BLOOD CLUSTER (~40 agents or ~14%)
Prions. Prions from blood include those causing sporadic Creutzfeldt-Jakob disease.

Viruses. Viruses from skin, sexual transmission (STI), or blood include cytomegalovirus, hepatitis viruses B and C, herpes simplex virus, human immunodeficiency virus, human papillomavirus, human T-lymphotropic virus, molluscum contagiosum, and vaccinia virus.

Bacteria. Bacteria from skin, or STI, include Chlamydia trachomatis (ocular and genital), Mycobacterium leprae, Neisseria gonorrhoeae, Staphylococcus aureus, Streptococcus pyogenes, and Treponema pallidum pallidum.

Fungi. Fungi include anthropophilic dermatophytes, e.g., Candida, Epidermophyton, Malassezia, and Trichophyton.

Protozoa. Protozoa include Trichomonas vaginalis.

Helminths. Helminths from contact include Enterobius vermicularis and Hymenolepis nana.

Ectoparasites. Ectoparasites from contact include Pediculus humanus (var. capitis, var. corporis) and Sarcoptes scabiei.

DIAGNOSTIC WORKUP
Probable impossibilities are to be preferred to improbable possibilities.

Aristotle of Stagira (384–322 BC)

A targeted microbiologic workup should be attempted from the exposure history and clinical examination. If
more than a dozen agents are tentatively included in the differential diagnosis, priority should be given to infections with high lethality (e.g., >5%), high potential for spread (e.g., 2\textsuperscript{nd} attack rates >5% or $R_0 > 2$), or rapid response to locally available, presumptive antimicrobials (e.g., antimalarials). In the chapter on agents (see chapter 21), impact variables are summarized by agent genus. Taxonomy (Table 20.1) helps to explain serologic cross-reactivities.

Clinical materials for laboratory workup should be commensurate with the natural history of the disease concerned (prepatent and incubation periods, time to appearance of immunoglobulins M and G). At an early disease stage, immunoglobulin M may not yet be detectable. A “null” serum sample can then be stored for antibody determination with a second sample obtained 2–3 weeks later (“paired” sera). Tests with high (>95%) sensitivity, specificity, and predictive values are ideal, because they substantially increase the pretest to posttest disease certainty. In general, the preferred test is culture. If clinical material cannot be obtained, consider surrogates such as leftover foods, tap or recreational water, removed ectoparasites, samples from pet or domestic animals, soil from flower arrangements or gardens, or home or office dust. Archived specimens may still be available (e.g., null sera at work places or aliquots at diagnostic laboratories).

A colonized, infected, or ill person points to agents that circulate in the source community. Clinicians and microbiologists should therefore always keep in mind the “three I’s” of information: inform yourself (epidemic situation, test methods), inform the patient (what to expect and do), and inform health authorities (reporting).

### Box I.1 Suggested vertebrate animal exposure history

**Right now,** name all pet animals that you own, including dogs, cats, birds, reptiles, and fish.

**In the past week:**
- Have you touched a farm, pet, sick, or dead animal, including bird, reptile, fish, or rodent?
- Have you been near a sick or parturient animal, including a sneezing cat or a dog with diarrhea?

**In the past 3–12 months:**
- Have you sustained bites or scratches by animals, including pets, livestock, bats, mosquitoes, or ticks?
- Have you seen rats, foxes, bugs, or other animals in or on your premises, or seen birds, horses, or rats die?
- Have you cleaned animals, handled manure, removed bugs from an animal, or worked with bones or wool?

**In your lifetime:**
- Has any of your jobs involved contact with animals, including at zoos, research facilities, or abattoirs?
- Name all the kinds of animals that you have ever kept at home.
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