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LETTER OF AGREEMENT

Dated: October 29, 1984

Dr. Michael Gottlieb
Department of Medicine
UCLA School of Medicine
Center for the Health Sciences
Los Angeles, CA 90024

Dear Dr. Gottlieb:

We were pleased to learn from Drs. Robert Rubin and Lowell Young

Editor(s) of CLINICAL APPROACH TO INFECTION IN THE COMPROMISED HOST, 2nd Edition

which is to be published by Plenum Publishing Corporation, hereinafter called the "Publisher," that you are willing to contribute a chapter to this Work, entitled

THE ACQUIRED IMMUNODEFICIENCY SYNDROME

We trust that the following terms with regard to the publication of your chapter will be satisfactory to you:

1. You shall submit to the Editor by n/a a detailed outline of your chapter, and shall subsequently, by March 1, 1985, deliver to the Editor the original typescript and one copy of your completed manuscript, in the English language, consisting of approximately 30 double-spaced typed pages, together with black and white illustrations suitable for reproduction. You agree to make any changes which the Editor may request in the outline or manuscript to assure that your chapter conforms in size, content, and general plan with the requirements of the Work.

2. You agree that your contribution to the collective Work shall be considered a work for hire. This is a legal term which is defined in the new Copyright Act to include contributions to collective educational works, and the characterization of your contribution as a work for hire permits the Publisher to obtain copyright protection both for the collective Work and for your chapter.

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continued

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PLENUM PUBLISHING CORPORATION

By Janice Stern

Janice Stern
Senior Medical Editor

Consented and Agreed:

_____

Author

IMPORTANT!
Before you prepare your manuscript . . .

- remember that the final manuscript you submit will have to be the original ribbon copy of double-spaced typescript—*not* a Xerox or other copy.
- use *copies* of the manuscript for editorial review and revisions; then make all necessary changes in the original typescript just before you submit it.
- plan to have professionally executed illustrations suitable for direct reproduction ready to accompany the final manuscript.
- *read* our Author's or Contributor's Guide before you begin the preparation of either manuscript or illustrations. *Follow* the guidelines it presents, particularly those on reference style. Be sure that your *typist* has read the guide as well.

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THE LANGUAGE OF SCIENCE
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GUIDE FOR CONTRIBUTORS TO
CLINICAL APPROACH TO INFECTION IN
THE COMPROMISED HOST
(Second Edition)

These pages should be read very carefully by both the author and his typist. Meticulous attention to the instructions they contain will help not only the editor and the publisher but also the author, since careful preparation of manuscript is the most important single factor assuring error-free printed text that precisely reflects the author's intent.

X1 -1c
M2 -1c
M3 -1c
M4 -1c
GB4-2
GB4-3
MM5-1
X6 -1c
X6 -2

1. General Instructions

a. An outline or summary should be submitted to your editor well in advance of delivery of the manuscript.

b. If any of the material to be included (illustrations, tables, quotations of more than a few words) is taken from another publication, you must obtain permission to use this material from the copyright owner and insert acknowledgments in the form he prescribes into your manuscript.

c. The ribbon copy of the manuscript, together with all the necessary artwork, photographs, figure captions, tables, references, etc., must be submitted to the editor on or before the date specified in the agreement.

d. The manuscript must be typed double-spaced on one side of good-quality white or near-white paper, approximately 8-1/2x11 inches in size, with margins of at least one inch on all sides. (For detailed typing instructions, see Section 6.) Illustrations and tables must be prepared as specified in Sections 2 and 3. If your book contains unusual elements (illustrations, tables, or other material of unusual size, type, or conformation, unconventional symbols or arrangements, etc.), consult with your editor before such material is prepared in final form.

e. The first page of the manuscript should give the title of the chapter and the author's full name and affiliation. Do not use titles or degrees in the author's by-line, but do furnish the address to which proofs should be mailed.

f. The manuscript should be accompanied by a detailed table of contents.

g. Current American spelling should be used. Webster's Third New International Dictionary may be used as final authority for spelling and hyphenation. Recent issues of the leading journals in the field may serve as a guide to preferred technical terminology and symbolic notation.

h. Footnotes should be used only if it is not possible to incorporate the thought into the text without disrupting the flow of the argument. The placement of footnotes is indicated in the text by asterisks (or daggers, double-daggers, etc., if there is more than one footnote on a page). The footnotes themselves are to be collected and typed double-spaced on a separate sheet at the end of the text, each footnote being identified in the left margin by the number of the manuscript page to which it belongs.

2. Illustrations

a. All illustrations submitted must be suitable for reproduction without further retouching or redrawing. Original inked drawings yield the best results and should be submitted with the manuscript if available. If not, prints made from the original drawing are generally acceptable. Xerox copies are not acceptable, and photostats frequently give poor results.

b. Drawings should be prepared at approximately twice the desired final size, keeping in mind that the type area in the printed book will be approximately 4-1/2 x 7 inches, and that no illustration can exceed these final dimensions. The drawings should be fully lettered, and the lettering must be large enough to remain legible after reduction.

c. Drawings should be free of unnecessary detail. If possible, graphs should be prepared with ticks on the axes rather than grid lines. If grid lines must be shown, the drawing may be prepared on light blue, nonreproducing graph paper and the major grid lines inked in.

d. Photographs should be used only if absolutely necessary. Large glossy prints made from the original negative must be furnished. If less than the entire area of the photographic print need or should be shown in the book, indicate the area to be included on a tracing paper overlay.

e. If the magnification of a photograph has to be indicated, this should be done, whenever possible, by means of a micron scale superimposed on the photograph rather than a numerical statement in the caption, since such a scale is not distorted by the reduction which the photograph may have to undergo to fit into the type area.

f. All illustrations should be numbered in a single sequence of arabic numerals in the order in which they are mentioned in the text. All text references should employ the word "figure" rather than such varied designations as "diagram," "chart," "photograph," etc.

g. Each drawing or photograph must be fully identified; the title of the book, the name of the author, and the number and/or title of the chapter must be given in addition to the figure number and (if necessary) an indication of which side of the figure should be toward the top of the page. This information should be written directly on the illustration or typed on strips of paper which are then glued (but not stapled or clipped) to the illustration. The information may be given in the margin of the illustration if it is sufficiently wide; otherwise it should appear on the back. In writing on the back of photographs, care must be taken not to make impressions that are visible on the face of the illustration.

h. Each figure must have a descriptive caption. The captions should be typed double-spaced in sequence on a separate sheet (or sheets) and should not be attached to the illustrations.

3. Tables

a. Each table should be typed double-spaced on a separate sheet or sheets and should be provided with a brief title. Descriptive material and lengthy explanations necessary to the understanding of the table should not be written into the title but typed as footnotes immediately below the table.

b. All tables should be numbered consecutively throughout the chapter, using roman numerals.

c. Each table should be mentioned in the text, the reference being made by number and not by such words as "above" or "below."

d. Tables that exceed the limitations of the type page in both width and length can as a rule only be printed on special foldout pages, which not only are expensive, but have a tendency to become detached and be lost, and therefore should be avoided. Frequently the problem can be solved by introducing arbitrary abbreviations in either the data columns or their headings. These abbreviations can be explained in footnotes to the table.

e. Superior lower-case letters should be used as footnote indices in tables to avoid confusion with the symbols used for text footnotes which may occur on the same page.

4. Numbers, Units, Symbols, and Equations

a. Numbers up to ten should generally be spelled out, but numerals should be used for numbers from 11 up, except that numerals are always used in conjunction with symbols and units of measurement. Commas should separate groups of three digits in numbers of five or more digits (12,583), but no commas should be used in numbers of four digits (5837) unless they are aligned in a column with numbers that do contain commas:

1,356,778
78,562
5,283

Numbers between zero and one should be written with a cipher in front of the decimal point (0.5 — never .5).

b. Units of measurement should be abbreviated when used with numerals but written out when they occur in the text without numerals. The abbreviations listed below should be employed. Note that these abbreviations are used without periods:

ampere	A	microgram	µg (not γ)
angstrom unit (avoid -- give dimensions in nanometers)	Å	microliter	µl (not λ)
		micrometer	µm
		micromole	µmole
atmosphere	atm	micron (micrometer)	µm
calorie, gram	cal	milliampere	mA
calorie, kilogram	kcal	milliequivalent	meq
centimeter	cm	milligram	mg
counts per minute	cpm	milliliter	ml
cubic centimeter	cm^3	millimeter	mm
cubic meter	m^3	millimeter of mercury	mm Hg
cubic millimeter	mm^3		
curie	Ci	millimicromole (nanomole)	nmole
cycle per minute	cycle/min	millimicron (nanometer)	nm
cycle per second (hertz)	Hz	millimole	mmole
degree Centigrade	°C	millivolt	mV
degree Fahrenheit	°F	minute (time)	min
degree Kelvin	°K	minute (angle)	'
degree (angle)	°	mole	spell out
disintegrations per minute	dpm	nanometer	nm
		ohm	Ω
electron volt	eV	parts per million	ppm
farad	F	percent	%
foot	ft	pound	lb
gallon	gal	revolutions per minute	rpm
gram	g		
gram-atom	g-atom	roentgen	R
gram-molecule	mole	second (time)	sec
hour	hr	second (angle)	"
inch	spell out	square centimeter	cm^2
international unit	IU	square meter	m^2
joule	J	Svedberg unit	S
kilogram	kg	volt	V
liter	spell out	watt	W
meter	m	wave number (unit)	cm^{-1}

c. The unit abbreviations listed above stand for the plural as well as the singular. Write 5 lb, not 5 lbs.

d. The following prefixes may be combined with the basic unit abbreviations:

d	deci	($=10^{-1}$)	p	pico	($=10^{-12}$)
c	centi	($=10^{-2}$)	k	kilo	($=10^{3}$)
m	milli	($=10^{-3}$)	M	mega	($=10^{6}$)
μ	micro	($=10^{-6}$)	G	giga	($=10^{9}$)
n	nano	($=10^{-9}$)	T	tera	($=10^{12}$)

e. The following standard abbreviations should be employed in the form shown:

aqueous	aq.	minimum	min.
atomic weight	at.wt.	molar (concentration)	M
calculated	calc.	molecule, molecular	mol.
compare	cf.	molecular weight	mol.wt.
concentrated	conc.	normal (concentration)	N
concentration	concn.	number (in enumeration)	No.; plural Nos.
crystalline, crystallized	cryst.	observed	obs.
dilute	dil.	page, pages	p., pp.
Experiment (with reference numeral)	Expt.; plural Expts.	precipitate	ppt.
Figure (with reference numeral)	Fig.; plural Figs.	preparation	prep.
infrared	IR	recrystallized	recryst.
insoluble	insol.	soluble	sol.
logarithm (base 10)	log	solution	soln.
logarithm (base e)	ln	species (singl. and pl.)	sp., spp.
maximum	max.	temperature	temp.
millimolar (concentration)	mM	ultraviolet	UV
		variety	var.
		versus	vs.
		weight	wt.

f. The following abbreviations may be used without definition (abbreviations may also be used for other terms if they occur very frequently, but should be defined in a footnote at their first occurrence).

AMP, CMP, GMP, IMP, UMP	5'-Phosphates of adenosine, cytidine, guanosine, inosine, and uridine
ADP, etc.	5'-(Pyro-)diphosphates of adenosine, etc.
ATP, etc.	5'-(Pyro-)triphosphates of adenosine, etc.
CoA and acyl-CoA	Coenzyme A and its acyl derivatives
DNA	Deoxyribonucleic acid
RNA	Ribonucleic acid
DNP	2,4-Dinitrophenol
EDTA	Ethylenediaminetetraacetate
FAD, $FADH_2$	Flavin-adenine dinucleotide and its reduced form
FMN	Flavin mononucleotide
GSH, GSSG	Glutathione and its oxidized form
NAD, $NADH_2$ or NAD^+, NADH	Oxidized and reduced forms of nicotinamide-adenine dinucleotide
NADP, $NADPH_2$ or $NADP^+$, NADPH	Oxidized and reduced forms of nicotinamide-adenine dinucleotide phosphate
NMN	Nicotinamide mononucleotide

tris	2-Amino-2-hydroxymethylpropane-1,3-diol
ATPase	Adenosine triphosphatase
5-HT	5-Hydroxytryptamine (serotonin)
GABA	γ-Aminobutyric acid
ACh	Acetylcholine
Pi	Orthophosphate
PPi	Pyrophosphate
S.D.	Standard deviation
CNS	Central nervous system
CSF	Cerebrospinal fluid
EEG	Electroencephalogram

Amino Acids*

Ala	Alanine	Ile	Isoleucine
Arg	Arginine	Leu	Leucine
Asn	Asparagine	Lys	Lysine
Asp	Aspartic acid	Met	Methionine
Cys	Cysteine	Orn	Ornithine
CyS	Cystine (half)	Phe	Phenylalanine
Gln	Glutamine	Pro	Proline
Glu	Glutamic acid	Ser	Serine
Gly	Glycine	Thr	Threonine
His	Histidine	Trp	Tryptophan
Hyl	Hydroxylysine	Tyr	Tyrosine
Hyp	Hydroxyproline	Val	Valine

*Single letter code may be more appropriate in complex peptide sequences (see IUPAC - IUB, Biochem. J. 113, 1-4, 1969).

Sugars

Ara	Arabinose	Glc	Glucose
dRib*	Deoxyribose	Man	Mannose
Fru	Fructose	Rib	Ribose
Gal	Galactose	Xyl	Xylose

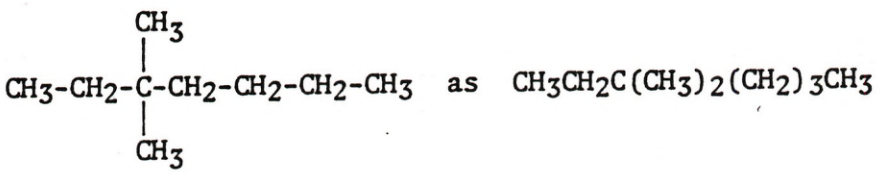
*Similarly for other deoxy sugars (Biochem. J. 101, 1, 1966).

g. Steroids. See IUPAC-IUB tentative rules; Biochem. J., 113, 5-28, 1969.

h. Lipids. For nomenclature see Biochem. J. 105, 897, 1967, and 112, 17, 1969.

i. Nucleotides. See Biochem. J. 101, 1, 1966; 116, 1, 1970.

j. The chemical notation selected should avoid ring structures and vertical side chains whenever possible. Cl—⬡—OH may without loss of clarity be written as p-ClC_6H_4OH or



as $CH_3CH_2C(CH_3)_2(CH_2)_3CH_3$

5. References (Text citation by number)

a. Each author is responsible for the accuracy of the references in his chapter. All names, dates, and volume and page numbers should be double-checked before the manuscript is submitted.

b. References should be numbered in the order of their first mention in the chapter. Text citations should take the form of raised numerals. The citation may be used with or without the author's name: "...it has been shown by Johnson[17] that..." or "...experiments with calcium,[6] potassium,[7] and strontium[8] have shown...." Several references may be cited together, the numbers being separated by commas: "several recent investigations[6,7,9,15] indicate...." If three or more consecutive references are cited together, a dash should be used between the lowest and highest reference numbers: "...while others[10-14] show that...."

c. The reference list should be typed triple-spaced on a separate sheet or sheets, in the style indicated by the following examples:

1. Wood JH, Ziegler MG, Lake CR, et al: How to clean the air we breathe, J Neurosurg 45:54-67, 1978

2. Wynn RM (ed): Biology of the Uterus, New York, Plenum Press, 1977

3. Zangger J, Taufer M: Chronic gastritis, atypical epithelia in biopsies, and therapeutic consequences, in Hellmann K, Connors TA (eds): Chemotherapy, Vol. 8, Cancer Chemotherapy II, New York, Plenum Press, 1976, pp 265-268

4. Zopf CW: Criteria for the Screening of Food Additives, Report No. 37X-2A, U.S. Department of Agriculture, 1972

The examples illustrate the following characteristic cases:

1. A journal article. Note that the full title of the article is given. The abbreviated journal names should employ the forms used in Index Medicus. The number preceding the colon is the volume number, the number following the colon is the page number. For journals with unnumbered volumes, the year takes the place of the volume number: J Chem Soc 1965:3896. For journals that start the pagination of each issue with 1, the issue number must be given in parentheses following the volume number: Prib Tekh Eksp 7(3):53.

2. A simple book reference.

3. A paper in a multiauthor book. Note that the title of the paper is given as well as the book title.

4. For pamphlets, bulletins, or any publications other than "regular" books or journals, give all the information available and avoid any but the most common abbreviations.

6. Typing Instructions

a. Paper: Use opaque white or near-white paper of good quality, approximately 8-1/2x11 inches in size. Do not use tissue or other lightweight papers, nor easy-erasing papers on which it is difficult to write.

b. Typewriter: Use an elite or pica typewriter in good condition. Make sure the keys are clean and the ribbon is not excessively worn. Do not use a typewriter with a face smaller than elite or larger than pica, nor one with a script typeface or a typeface in which the lower-case letters are merely smaller versions of the capital letters.

c. Margins: Leave one-inch margins on all four sides of the page.

d. Spacing: All the material without exception is to be at least double-spaced. The 1-1/2 spacing that some machines can provide is not sufficient. If it is necessary to set off material in the text (e.g., quotations or lists), this should be done by indentation, i.e., changing the margins, and not by single-spacing.

e. Paragraphing: Indent the first line of each paragraph five spaces. The "blocked" style that looks so good in letters can lead to confusion in a manuscript.

f. Headings: Number the major subdivisions of the chapter consecutively, using arabic numerals. Type subheadings of the same value in the same manner throughout the manuscript. The following style is suggested:

1. FIRST-VALUE SUBHEADING

1.1. Second-Value Subheading

1.1.1. Third-Value Subheading

1.1.1a. Fourth-Value Subheading. The first three values are typed on separate lines; the fourth is typed as the beginning of a paragraph. Except for first-value headings, all digits except the last are exactly those of the preceding subheading of next higher rank.

g. Numbering: Arrange the material in the following sequence, and number the sheets consecutively:

Title page
Table of contents
Text
Footnotes
References
Tables
Figure Captions

Note that each item in this list is to start on a new page and that, moreover, each chapter and each individual table is to start on a new page. Remember that the references are to be triple-spaced, all other material double-spaced, and that no part of any of these items is to be single-spaced.

h. Punctuation: Observe the following typing rules with respect to punctuation marks.

1. The comma and period are always typed before rather than after the closing quotation marks. Other punctuation marks are typed before the closing quotation marks if they are part of the quoted material and after the quotation marks if they are not.

2. If parentheses enclose one or more complete sentences, a period is used just inside the closing parenthesis. If parentheses at the end of a sentence enclose less than a full sentence, the period follows the closing parenthesis.

3. Superscript numerals (for literature references) and asterisks (for footnotes) should be typed after a comma or period but before any other punctuation mark.

MASSACHUSETTS GENERAL HOSPITAL ◆ HARVARD MEDICAL SCHOOL

ROBERT H. RUBIN, M. D., F.A.C.P.
Associate Professor of Medicine
Chief of Infectious Disease
for Transplantation

Please Address Replies To:
MASSACHUSETTS GENERAL HOSPITAL
BOSTON, MASSACHUSETTS 02114

March 4, 1985

Michael S. Gottlieb, M.D.
Acting Chief
Division of Clinical Immunology/Allergy
Department of Medicine
UCLA School of Medicine
Center for the Health Sciences
Los Angles, California 90024

Dear Mike:

Thank you for your note. I understand completely and look forward to seeing your chapter next month. I must confess that it is a big switch for me to be on the receiving end of such a letter, as opposed to writing one. I am sure in your case that the wait will be more than worthwhile.

Best personal regards,

Robert H. Rubin, M.D.

RHR/wld

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UCLA SCHOOL OF MEDICINE
CENTER FOR THE HEALTH SCIENCES
LOS ANGELES, CALIFORNIA 90024

February 23, 1985

Robert Rubin, M.D.
Professor of Medicine
Massachusetts General Hospital

Dear Bob:

I regret that I will need an additional month beyond March 1 to complete my chapter on AIDS for Infections in the Compromised Host. This new year has been very hectic for reasons that I need not detail. I very much appreciate the opportunity to do the chapter, and promise that the delay will not be excessive. I will keep both you and Lowell advised of my progress with the manuscript.

With warm regards,

Mike

Michael S. Gottlieb, M.D.

Acting Chief
Division of Clinical Immunology/Allergy

cc: Lowell S. Young, M.D.

MASSACHUSETTS GENERAL HOSPITAL ◆ HARVARD MEDICAL SCHOOL

ROBERT H. RUBIN, M. D., F.A.C.P.
Associate Professor of Medicine
Infectious Disease Unit
and
Transplantation Unit

Please Address Replies To:
MASSACHUSETTS GENERAL HOSPITAL
BOSTON, MASSACHUSETTS 02114

July 30, 1984

Dr. Michael Gottlieb
Department of Medicine
UCLA School of Medicine
Center for the Health Sciences
Los Angeles, California 90024

Dear Mike:

We are delighted that you will be contributing to the second edition of Clinical Approach to Infection in the Compromised Host. The response to the first edition has been most gratifying, in terms of sales, acceptance by the medical community, and critical review in scholarly journals. We hope to build upon this success with this next edition, with the addition of five new chapters, ten new authors and much new material.

Again, the emphasis in the book will be on clinically useful information based upon the most up-to-date scientific data. We hope that practical approaches for the clinician to important decision-making will be clearly outlined. Short case reports, with appropriate illustrative material, should be utilized to emphasize important clinical points. Where areas of controversy exist, they should be defined, with the author's view and the reasons for this view emphasized. Under separate cover, you will receive specific instructions from the publisher, Plenum Medical Book Company.

Enclosed with this note is an outline of the 2nd edition and the contributors. We believe that this is the most distinguished group of international experts in this field ever to be gathered for such an endeavor. We are deeply grateful for your contribution to an effort that can only improve the care we deliver to the patients with compromised host defenses.

Sincerely,

Bob

Robert H. Rubin, M.D.

Sincerely,

Lowell

Lowell S. Young

Chapter Outline for the Second Edition of
Clinical Approach to Infection in the Compromised Host

Section I: Basic Principles

Introduction - Dr. Jean Klastersky, Brussels, Belgium*

Chapter 1 - An overview of Infection in the Compromised Host
- Lowell S. Young, Los Angeles, California and
Robert H. Rubin, Boston, Massachusetts

Chapter 2 - Epidemiology and Prevention of Infection in the Compromised Host
- Stephen C. Schimpff, Baltimore, Maryland

Chapter 3 - Defects in Host Defense Mechanisms in Compromised Patients
- Jos W. M. van der Meer, Leiden, The Netherlands*

Section II: Clinical Problems in the Compromised Host

Chapter 4 - Fever and Septicemia
- Lowell S. Young, Los Angeles, California

Chapter 5 - Dermatologic Manifestations of Infection in the Compromised Host
- John S. Wolfson, Boston, Massachusetts,* and
Arthur J. Sober, Boston, Massachusetts*

Chapter 6 - Etiology and Management of Pulmonary Infiltrates in the
Compromised Host
- Robert H. Rubin, Boston, Massachusetts

Chapter 7 - Central Nervous System Infections in the Compromised Host
- Donald Armstrong, New York City, New York

Section III: Special Microbial Problems in the Compromised Host

Chapter 8 - Fungal Infections in the Compromised Host
- Francoise Muenier-Carpentier, Brussels, Belgium*

Chapter 9 - Mycobacterial and Nocardial Infections in the Compromised Host
- Harvey B. Simon, Boston, Massachusetts

Chapter 10 - Parasitic Diseases in the Compromised Host
- Joel Ruskin, Los Angeles, California

Chapter 11 - Legionellosis in the Compromised Host*
- Edward Wing, Pittsburgh, Pennsylvania*

Section III: Special Microbial Problems in the Compromised Host (continued)

Chapter 12 - Hepatitis in the Compromised Host
- Jules Dienstag, Boston, Massachusetts*

Chapter 13 - Herpes Group Virus Infections in the Compromised Host
- Martin S. Hirsch, Boston, Massachusetts

Chapter 14 - Retroviruses, Papovaviruses, and other Viral Infections in the Compromised Host
- Robert T. Schooley, Boston, Massachusetts*

Section IV: Infections in Different Clinical Forms of Host Defense Compromise

Chapter 15 - The Acquired Immunodeficiency Syndrome
- Michael Gottlieb, Los Angeles, California*

Chapter 16 - Infections Complicating Congenital Immunodeficiency Syndromes
- Harry R. Hill, Salt Lake City, Utah

Chapter 17 - Diagnosis and Management of Infectious Disease Problems in the Child with Malignant Disease
- Dr. Phillip Pizzo, Bethesda, Maryland*

Chapter 18 - Management of Infection in the Adult Patient with Leukemia and Lymphoma
- Lowell S. Young, Los Angeles, California

Chapter 19 - Infection in the Patient with Collogen-Vascular Disease
- Donald Payan, San Francisco, California*

Chapter 20 - Infection Complicating Bone Marrow Transplantation
- Joel D. Meyers, Seattle, Washington

Chapter 21 - Infection in the Renal and Liver Transplant Patient
- Robert H. Rubin, Boston, Massachusetts

Chapter 22 - Infection in the Cardiac Transplant Patient
- Lane Gentry, Houston, Texas*

Chapter 23 - Surgical Aspects of Infection in the Compromised Host
- A. Benedict Cosimi, Boston, Massachusetts

*New contributors to Clinical Approach to Infection in the Compromised Host.

bill – canned prepared texts

magnitude of problem.

1st item of business is to define ARC which is no simple task. The original working definition was made before HTLV-III and LAV and was patterned after the Jones criteria for RF, a combination of symptoms, signs, and surrogate lab tests. It was never official and was never uniformly accepted. LAV HTLV-III & ARV and antibody testing have added a new dimension.

From the standpoint of pathophysiology it makes sense to speak of the spectrum of HTLV-III-related conditions ranging from the asymptomatic HTLV-III antibody positive state through PGL to AIDS.

In our practices it still may be useful to advise patients that they have: HTLV-III related PGL or ITP rather than ARC with its more ominous connotations.

Once the name of the virus is finally settled on we could craft psuch a terminology. ~~my own pdp~~

It does however seem likely that the term ARC will continue to be used for the near future. As evidence recall how difficult it has been to eradicate its predecessor pre-AIDS.

I will ~~therefore against my better instincts put forward~~ a definition of ARC which may have practical use in the clinic.

people mean by ARC

ARC is a spectrum of symptoms and signs persisting for several months which cannot be explained by diagnoses other than HTLV-III infection.

Frequent clinical features include PGL, oral thrush, zoster, fungal infections of skin and nails, fatigue, low grade fevers, sweats, non-specific diarrhea.

CDC defined AIDS is obviously excluded.

We are aware that apparently healthy seronegative carriers exist, and therefore must be open to the possibility that there are seronegative individuals with ARC-like syndromes. At this time I do not think it would be advisable to apply the term ARC to illness in HTLV-III seronegative individuals.

Let me make it very clear that there is potential to overdiagnose ARC and we should be careful with its use. Let's not overlook the fact that the A in ARC is AIDS. Thus the very term ARC inevitably produces psychological distress. On the medical record ARC can impact on insurance and employment.

We must be very careful not to fall into the trap of concluding that any illness in antibody positive individuals is related to that exposure. And we must continue to warn health providers who are less aware of this problem. As we all know the advent of HTLV-III infection did not eliminate syphilis, various bowel syndromes, and TB.

Let me also make it clear that I do not think that an antibody test is necessary to make the diagnosis of ARC in a clearcut case, e.g. the gay man with 18 months of PGL amd thrush. I think it will be useful for differential diagnosis in less clearcut instances.

When I feel that the test is indicated for clinical decision making I will advise my patients of the advantages of getting it done at one of the alternate testing sites soon to be established. I will ask the patient to share me the result which will help me choose further diagnostic studies.

A few points on other laboratory studies in patients with suspected ARC.

Our ordering of studies should as usual be directed by signs signs and symptoms. Stool cultures and O's and P's for diarrhea, chest xray for dyspnea or persistent cough, blood cultures for fevers.

A number of studies have indicated that T cell subset tests can be valuable in assessing the severity of immunologic defect and prognosis for developing AIDS. The key test is the absolute # of helper cells (ie. OKT-4 or Leu 3). Ratio is less useful so insist that your lab provide absolute T helper #. If they won't change labs.

In our experience with 101 PGL patients a % of the group with Th# less than 200 at entry developed @ over 3 yrs, compared to

All labs are not proficient in these tests. My advice is to choose a consistent one and stick with them. If the test result is surprising (much better or worse than expected on clinical grounds) repeat it.

One of the most frequently asked ?'s dermatology is when to obtain a LN bx?

In my practice the indications for lymph node biopsy in ARC patients with lymphadenopathy are:

associated weight loss
any major change in clinical status
systemic symptoms
marked increase in node size

Otherwise I observe.

Other serologies notably EBV and CMV are rarely helpful since these antibodies are almost invariably present. High titer IgM to CMV may be helpful as an indicator of recent infection.

The marketing of expensive and unncessary so called AIDS panels by many commercial labs is repulsive. The inclusion of such tests as HLA-typing , bet-2, thymosin alpha one, alpha fetoprotein and others can best be described as a ripoff.

Management

Honest but reassuring
Further medical evaluations for sicker patients
Quarterly followup for stable patients
Counseling on suspected co-factors and protective measures
Counseling on potential to transmit sexually and through blood

Team approach/physicians, social worker, psychologist/ groups/community resources
Maintainance of insurance

Therapy

Antivirals. Immunomodulators may have a role in combination with antivirals.
Testing suramin in PGL-too soon to tell if benefit.
Other candidiate drugs are in trials- ribavirin, others.
I personally do not advise self-administration of ribavirin or isoprinosine, nor do I condemn it.

So to sum up: The spectrum of HTLV-III induced illness is extensive, and likely to remain part of our practices for at least a few years. The approach will undoubtedly change as we learn more. I have offered you my own approach to this problem, and look forward to your comments or questions. TY