SPONDYLARTHROPATHIES

Edited by

ANDREI CALIN, M. D. M. R. C. P.

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GRUNE & STRATTON, INC.
(Harcourt Brace Jovanovich, Publishers)
Orlando San Diego San Francisco New York London
Toronto Montreal Sydney Tokyo São Paulo

Grune & Stratton, Inc.
Orlando, Florida 32887

Distributed in the United Kingdom by
Grune & Stratton, Ltd.
24/28 Oval Road, London NW 1

Library of Congress Catalog Number 83-49066
International Standard Book Number 0-8089-1613-0

Printed in the United States of America

PREFACE

Until five or ten years ago most interest in rheumatology focused on rheumatoid arthritis and systemic lupus erythematosus. Recently, however, there has been enormous growth in the clinical importance of the spondylarthropathies, in part because of their close association with HLA, and in part because of the recognition that a substantial number of patients suffer from different forms of these disorders.

Professionals in many branches of medicine have been fascinated by developments in this area. It is probable that no other field offers the same chance for unravelling the intricacies of the relationship between genetics and the environment in the pathogenesis of disease. For example, a specific infective agent (e.g., *Shigella*) has been found to precipitate a clearly defined clinical disorder (Reiter's syndrome) in a genetically susceptible individual (HLA B-27). Over the years, immunogeneticists, geneticists, epidemiologists, bacteriologists, membrane biologists, clinicians (both adult and pediatric), and other investigators have joined in the attempt to clarify our understanding of ankylosing spondylitis, Reiter's disease, psoriatic arthropathy, and other interrelated conditions. This multi-authored, internationally supported text is being presented now because we are experiencing a brief respite from the rapid advances of recent months and years, providing us with a chance to review the entire field.

The first chapter offers an overview of the spondylarthropathies and tells us something about the past, present, and (perhaps) the future, with a focus on terminology, criteria, and ethnic differences. The second chapter analyzes the criteria for the diagnosis of different entities. Subsequent chapters review epidemiology and pathology, Chapter 4 being a spectacular and painstaking study that is rarely available to readers because of the difficulty of obtaining sections of deep-seated tissue (for spondylarthropathies are rarely fatal). Chapters 5 through 12 deal with ankylosing spondylitis, Reiter's syndrome, psoriatic arthropathy, juvenile chronic arthropathy, the enteropathic arthropathies, and Behçet's syndrome. Undifferentiated spondylarthropathy is reviewed, and a discussion of spondylarthritis in non-Caucasians is presented. Chapters 13, 14, and 15 provide an up-to-date analysis of HLA and disease, HLA and the spondylarthropathies, and the use of HLA B-27 as a diagnostic tool. Radiology, scans, and their role in the analysis of these

disorders are discussed in Chapter 16. Chapter 17 covers the reactive arthritides. The book closes with a study of the measurements and definitions of rheumatic disease-related disabilities (Chapter 18).

The field of spondylarthritis transcends many of the boundaries of clinical and research medicine. For this reason the text will be of interest to professionals in many fields, including immunogeneticists, epidemiologists, pathologists, radiologists, and the many other individuals whose concerns lie within the pages of this volume.

Finally, it should be stated that there has been no attempt to define a concensus between the different authors. Where individual chapters overlap and opinions diverge, these very differences appear to this editor advantages rather than the reverse. To insist on or even to expect agreement where none exists (or where data are insufficient) would be anti-intellectual in the extreme. Only time will reveal who is nearer the truth. We accept that this editorial policy may invite the reviewers' criticism and in advance beg indulgence.

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CONTENTS

Chapter One

Spondylarthropathies: An Overview

Andrei Calin

Within the last 20 years ankylosing spondylitis and related disorders have been clearly demarcated from rheumatoid arthritis. The major forces leading to this separation have included careful clinical observation, painstaking epidemiologic work, attention to pathology, closer radiologic observation, and the development of immunogenetics. These different steps have been elegantly summarized in the monograph of Wright and Moll,[2] and the distinct pathology has been highlighted by Ball.[6] Major developments in our understanding of the various subsets of juvenile chronic arthropathy and the adult spondylarthritides will undoubtedly be realized in the future. The relationship between genetics and environment in the pathogenesis of the different disorders will almost certainly be elucidated. Meanwhile, this text will focus on our present understanding of the intriguing group of conditions known as the *seronegative spondylarthritides,* providing the reader with a global view of our present knowledge.

"Spondarthritis" was a term introduced by Moll and colleagues in 1974 in a major pre-HLA-B27 publication. The concept was developed further in 1976 by Wright and Moll in their book entitled "Seronegative Polyarthritis."[2] As pointed out by Wright[3] (in Moll's 1980 text on ankylosing spondylitis[4]) in a chapter entitled "Relationships between ankylosing spondylitis and other spondylarthritides," we misquoted their term as "spondylarthritis" in our 1978 monograph on the subject.[5] Since then, common usage has resulted in the widespread acceptance of the terms "spondylarthritis," "spondylarthropathy," and even "spondyloarthropathy." We will continue to use the best-known and most commonly applied term, "spondylarthritis," with respect and apologies to Moll, Wright, and colleagues.

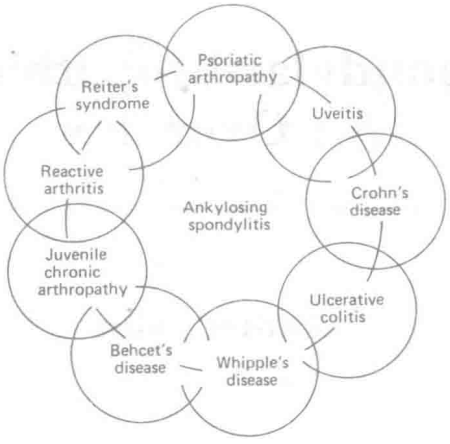

Fig. 1-1 Interrelationship between the spondylarthropathies with ankylosing spondylitis as prototype.

The interrelated conditions, discussed in this text, are summarized in Figure 1-1. The common features shared by the spondylarthrides are (1) negative tests for rheumatoid factor, (2) absence of rheumatoid nodules, (3) inflammatory peripheral arthritis, (4) radiologic sacroiliitis, (5) clinical overlap, and (6) tendency to familial aggregation. That ankylosing spondylitis is distinct from rheumatoid arthritis may be demonstrated in tabular form (Table 1-1).[7] The similarities and differences between the different members of the seronegative spondylarthropathies are summarized in Tables 1-2 and 1-3. Actual figures derived during a retrospective study of a cooperative approach that attempted to define criteria for Reiter's syndrome are shown in Table 1-4.[8] This highlights the intriguing relationship between seronegative "rheumatoid arthritis" and the spondylarthritides. The former may be differentiated from seropositive disease on clinical, epidemiologic, immunogenetic, and radiologic grounds.[9] Where seronegative polyarthritis of adulthood fits into the spectrum of rheumatic disease remains unclear, and its link with seronegative-polyarthritis of childhood can be defined only by ongoing immunogenetic and other studies.

McEwen and colleagues have defined radiologic differences between primary ankylosing spondylitis, ankylosing spondylitis associated with inflammatory bowel disease, and the spinal arthropathy associated with Reiter's syndrome and psoriasis (Table 1-5).[10] The explanation for these intriguing differences remains unknown.

The reader will note from the chapter titles that a practical overview of the spondylarthropathies has been attempted. Possible additional

Table 1-1

Ankylosing Spondylitis and Rheumatoid Arthritis Compared and Contrasted

	Ankylosing Spondylitis	Rheumatoid Arthritis
History	~5000 Years	~200 Years
Distribution	Racial	Worldwide
Prevalence	~1%	~1%
Etiology	Unknown	Unknown
Family history	+++	+ (Seropositive)
Sex distribution	M > F	F > M
Age group	Peak at 20–30 Years of Age	All Ages; Peak at 30–50 Years of Age
Joint involvement	Oligoarthropathy; asymmetric; large joints; lower limbs more than upper limbs	Polyarthropathy; symmetric; small and large joints; upper and lower limbs
Sacroiliac involvement	Yes	No
Spine involvement	Total (Ascending)	Cervical only
Nodules	No	Yes
Aortic regurgitation	Yes	No
Eyes	Conjunctivitis, uveitis	Sicca syndrome, scleritis, scleromalacia perforans
Lungs	Upper lobe pulmonary fibrosis	Caplan's syndrome, effusions
Rheumatoid factor	5% (normal)	~90%
HLA B27	~90%	~8% (normal)
HLA-DR4	~20% (normal)	~60% (seropositive only)
Pathology	Enthesopathy	Inflammatory synovitis
Radiology	Asymmetric erosive arthropathy, new bone formation, ankylosis, sacroiliitis	Symmetric erosive arthropathy
Therapy	Indomethacin, phenylbutazone	Aspirin, gold, penicillamine

Table 1-2
Similarities Between the Seronegative Spondylarthritides

	Ankylosing Spondylitis	Reiter's Disease	Psoriatic Arthropathy	Intestinal Arthropathy	Juvenile Chronic† Arthropathy	Reactive† Arthropathy*
Sex	M ≥ F	M ≥ F	F ≥ M	F = M	M ≥ F	M = F
Age	20+	20+	Any age	Any age	<25	Any age
Uveitis	+	++	+	+	++	+
Prostatitis	+	+	−	−	−	±
Peripheral Joints	Lower Limb: Often	Lower Limb: Usually	Upper > Lower	Lower > Upper	Upper = Lower	Lower > Upper
Rheumatoid Nodules	<1%	<1%	<1%	<1%	<1%	<1%
Sacroiliitis	Always	Often	Often	Often	Often	Often
Plantar Spurs	?Common	Common	?Common	?	?	?
Rheumatoid Factor	<5%	<5%	<5%	<5%	<10%	<5%
HILA B27	90%	90%	20%	5% (±50% With Sacroiliitis)	20%	90%
Enthesopathy	+	+	+	?+	+	?
Aortic Regurgitation	+	+	?+	?	?	+
Familial Aggregation	+	+	+	+	+	+
R_x NSAIDs Better Than Aspirin	+++	+	++	+	+	+
Risk for HLA B27+ Individual	?20%	20%	?	?	?	20%

* Particularly seronegative enthesopathic-arthropathy syndrome
† Salmonella, Shigella, and Yersinia

Table 1-3
Differences Between the Seronegative Spondylarthritides

	Ankylosing Spondylitis	Reiter's Disease	Psoriatic Arthropathy	Intestinal Arthropathy	Juvenile Chronic Arthropathy	Reactive Arthropathy*
Onset	Gradual	Sudden	Variable	Peripheral joint: sudden Sacroiliac joint: gradual	Variable	Sudden
Urethritis	−	+	−	−	−	+
Conjunctivitis/Uveitis	+	+++	+	+	+	+
Skin involvement	−	+	+++	−	−	+
Mucous membranes	−	+	−	(+)	−	−
Peripheral joints	25%	90%	90%	±	90%	90%
Hips, shoulders	+++	+	++	±	++	Rare
Spine	+++	+	+	+	±	+
Symmetry	+	−	−	+	±	±
Self-limiting	−	+	±	±	±	±
Remissions, relapses	−	+	+	±	±	±

* Salmonella, Shigella, and Yersinia.

Table 1-4
Comparison of Symptoms of the Seronegative Spondylarthropathies*

	RS	AS	RA (−)	PsA	GcA
$n =$	75	53	33	53	27
Arthritis†	100	100	100	100	100
Tendinitis	30	12	7	6	23
Heel pain	40	12	0	4	8
Back pain	46	87	0	28	4
Polyarthritis	84	29	68	84	54
Dactylitis	19	6	0	52	0
Urethritis	84	4	0	0	38
Diarrhea	12	4	0	0	4
Cervicitis (♀)	71	0	0	0	33
Conjunctivitis	53	20	0	4	0
Mucous membrane	27	0	0	2	12
Skin	49	2	0	96	54
Nail	9	0	0	67	0
Balanitis	38	0	0	2	0
Fever	31	2	6	4	50
Weight loss	34	4	9	12	0
Duration					
< 1 Week	0	0	0	0	42
1–4 Weeks	2	0	0	0	46
> 4 Weeks	98	100	100	100	12

* Reiter's Syndrome (RS), Ankylosing Spondylitis (AS), Seronegative Rheumatoid Arthritis [RA (−)], Psoriatic Arthropathy (PsA), and Gonococcal Arthropathy. Data from the American Rheumatism Association (ARA) Committee on Preliminary Reiter's Syndrome Criteria[8]/†Numbers refer to percentages.

entities such as pustulotic arthroosteitis[11] have not been included because there is no consensus as yet that such conditions are indeed spondylarthropathies. Chapter 2 reviews the criteria of the various conditions, while another (Chapter 11) on undifferentiated spondylarthropathy, highlights the fact that we still have patients who fulfill none of the generally accepted definitions for specific disease entities.

Despite our ever-increasing knowledge of pathology, genetics, and clinical variables, we still know too little about long-term outcome and