衣原体图谱

ATLAS OF CHLAMYDIA

端青 李子华 著

Duan Qing Li Zihua

科学出版社

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衣 原 体 图 谱

衣原体典型形态及其某些特殊繁殖形式的观察和探讨

Atlas of Chlamydia

Observation and Exploration of the Typical and Some Special Multiplication Forms of Chlamydia

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内 容 简 介

本图谱是作者数十年的工作成果，共收集了300余幅图片资料。收录了不同衣原体种的主要的、常见的典型形态，使读者对衣原体形态学有全面而系统的认识，同时还收录了许多罕见的衣原体特殊繁殖形式，并阐明其原因。全书涉及的衣原体种类包括：沙眼衣原体、鹦鹉热衣原体和家畜衣原体、肺炎衣原体；其宿主细胞包括：鸡胚卵黄囊膜细胞、人羊膜FL细胞、McCoy、Hep-2、HL和鸡胚内胚层细胞等；染色方法包括：吉姆萨染色、吖啶橙染色、碘染色和免疫荧光抗体染色等；观察方法包括：光学显微镜、荧光显微镜观察和电子显微镜的投影、负染及超薄切片薄层扫描观察等。全书所展示的图片资料绝大部分为首次发表，其常见的衣原体典型形态可供初学者之用，其特殊的衣原体繁殖形式可供学术上探讨和商榷。

本书可供从事生物学、微生物学、医学、畜牧等学科的科研和教学人员参考，也可供临床检验和检疫工作人员参考。

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曾毅序

衣原体病（chlamydiosis）在人类医学方面向被忽视，但近年来所知衣原体的宿主范围正在不断扩大，且甚为多样，温血动物（homeothermal animal）、冷血动物（poikilothermal animal）甚至节肢动物（arthropod）中均有其宿主，其致病范围正快速延伸。就温血动物而言，呼吸系统、消化系统、泌尿生殖系统、神经系统无所不及，几乎涉及内、外、妇、儿、眼、耳、鼻、喉各科，近年特别引人关注的是衣原体能引起人类的一些严重甚至致命的疾病，如冠心病、动脉粥样硬化等心血管疾病，心肌炎、关节炎、自身免疫性疾病，甚至还涉及老年性痴呆（Alzheimer's disease）、多发性硬化（multiple sclerosis）、宫颈癌、肺癌等。

本图谱编写者积累了数十年的经验，在形态学观察上有所建树和创新，出版的300余幅照片中，除一般常见的典型形态外，还特别刊出了一些难得见到的特殊繁殖方式，并对其中的可能形成机制提出了独到的见解，尤其是细胞外增殖型（extracellular multiply form）的发现，首先提出了这是由EB→EB（elementary body）直接二分裂的结果，中间不需经过RB（reticulate body）重组的过程。作者们这一新的观点和见解，无疑是对衣原体原有的生物学定义“衣原体是严格的专性真核细胞内寄生的原核生物（rigorously obligate eukaryotic cell parasitical prokaryote）”提出质疑，亦为近年有人报道衣原体能在“无核细胞或细胞碎片（enuclated cells or subcellular cell）中培养成功”提供了有力的佐证。

即此，图谱的出版适应了客观现实的需要，我衷心祝贺该图谱的问世。

曾毅

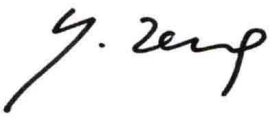
中国科学院院士
世界卫生组织全球卫生研究顾问委员会委员
2003年10月

Preface of Zeng Yi

The importance of chlamydiosis in human medicine was ignored in the past, but the host range of this disease was gradually expanded and even diverse, including the infections caused by this pathogen in homeothermal, poikilothermal animals or the arthropodes . Recent studies showed that the rang of pathogenicity was also rapidly extended to the respiratory,circulatory, digestive, urogenital and nervous systems in the homeothermal animals, and involved in the fields of medicine, surgery, gynecology, pediatrics and ENT. It is interesting to notice that some grave or even deadly diseases are caused by chlamydia, it is especially true for the cardiovascular diseases, including coronary heart disease, arteriosclerosis and myocarditis, as well as for arthritis, autoimmune diseases, Alzheimer's disease and multiple sclerosis or even carcinoma of cervix and lung, all of which are attached importance to these diseases.

Editors of this collection of atlas, who have full experience in the field of chlamydiosis, have accumulated 300 copies of photos in the studies of chlamydia, in which, except the classical morphology of this pathogen illustrated, some of special forms of multiplication are shown. These special forms of multiplication are not easily discovered as usual, and the unique explanation for their formation is given in this collection of atlas. As regard to the discovery of the extracellular multiply form, the authors indicate that this is the result of recombination process by direct binary fission from elementary bodies to elementary bodies (EB→EB), excluding the requirement for the formation of reticulate bodies (RB). This new viewpoint question the original definition of chlamydia as "rigorously obligate eukaryotic cell parasitical prokaryotes " and strongly support the recent new findings that chlamydia was able to be incubated in "enucleated cells or subcellular cells" .

The practical requirement in this critical period induces the publication of this collection of atlas, and I heartfeltly congratulate its publication in the due time.



Academician of the Chinese Academy of Sciences
Member of WHO Global Advisory Committee on Health Research
October, 2003

范明远序

在分类学上衣原体属包括的种类愈来愈多，凡是分子生物学上其 16S 和 23S rRNA 基因同源性 50% 以上的细胞内寄生物可能都包括在内，其宿主范围愈来愈广，衣原体对人类的致病谱愈来愈扩充和延伸，不仅可引起常见的沙眼、肺炎和泌尿生殖道疾病（STD），还可通过胎盘屏障引起胎儿感染，通过血脑屏障引起神经系统疾病等，衣原体对人类致病范围已涉及到临床各个学科。

李子华和端青两位教授长期从事衣原体的科学研究，他们在已有的工作基础上，提供最新资料和精选 300 多幅图片，编著出版了我国第一部衣原体图谱。该图谱不仅收集了许多常见的典型形态，还展示了若干特殊繁殖型的形态。它的问世，将有助于生物医学工作者了解衣原体的形态、特性，并认识其本质，因此是一本有价值的参考书。

作者之一李子华教授早在 1983 年全国三体（立、衣、螺）学术讨论会上，就提出衣原体的生活周期可能有细胞内寄生和细胞外繁殖的观点，其进一步的研究结果发表于《中华医学杂志》英文版 1994 年第 9 期上。他们提出原体（EB）存在细胞外的增殖型，即 EB 在细胞外从 EB→EB 直接进行二分裂增殖，中间可能不需要经过网状体（RB）重组过程，这种探索性的观点，对衣原体原有的生物学定义“衣原体是严格的专性真核细胞内寄生的原核生物”提出了挑战，如在今后实验中进一步证实其规律性，将有助于阐明衣原体某些新的特性。

我国著名微生物学家汤非凡教授在沙眼衣原体研究方面，突破了 50 多年世界科学界的困扰，于 1955 年首先分离沙眼衣原体成功，1981 年国际防治沙眼组织对其杰出贡献予以追认，并授予他沙眼金质奖章。我国年轻一代科技工作者正以严谨的科学态度对衣原体进行基础研究和应用研究，以期达到国际先进水平。

我衷心祝贺该图谱的出版，它将对我国传染病防治事业做出应有的贡献。

范明远

中国微生物学会人兽共患病病原学专业委员会副主任委员
中国疾病预防控制中心传染病预防控制所研究员
2003 年 10 月

Peface of Fan Ming-yuan

Members of order of chlamydia increase and their host range broaded as time goes on. All the members intracellularly parasitized with more than 50% homogeneity in their ribosomal 16S and 23S rRNA genes are included in chlamydia. The pathogenicity spectrum of chlamydia to human expand and extend to induce not only the commonly encountered diseases, such as trachoma, pneumonia and the urogenital tract infection, but also the neonatal infection through placenta transfer or diseases of nervous system by passing the blood-brain barriers. So the range of pathogenicity of chlamydia involves in every aspects of medicine.

Prof. Li Tzy-hwa and Duan Qing engaged in the scientific studies in chlamydia for a long time and on the background of their works they have collected the modernest data and beautiful photos in the field of chlamydia. No doubt, publication of this collection would be very helpful for those biomedical workers to understand the morphological characteristics of chlamydia and to recognize the nature of this pathogen.

Early in 1983, in the symposium on rickettsia, chlamydia and spirochaetes, Prof. Li had proposed a new concept on the life cycle of chlamydia with possible existence of intracellular and extracellular stages of multiplication, the results of further studies were published in *Chinese Medical Journal,* 1994, 107 (9): 658-663. In this paper, he proposed the existence of the extracellular multiply form of elementary bodies (EB) and the extracellular EB →EB transformation without the formation of reticulate bodies (RB). This pioneer idea would be a challenge to the original definition for " chlamydia as a rigorously obligate parasitized prokaryote in eukaryotic cells". This new idea would advance the research of chlamydia if it could be definitely proven to be so after further experimentations.

Our outstanding microbiologist Prof. F. F. Tang succeeded at first time to isolate *C. trachomatis* in 1955 after breaching the difficulties existing for more than 50 years. In 1981 he was awarded with the Gold Prize on the study of trachoma by International Organization for Trachoma Prevention and Treatment on account of his great

contribution in this field. At present, our young generation of researchers is working with the rigorous scientific approach to investigate the fundamental as well as the practical problems in order to elevate the level of scientific research up to the international standard.

I heartfeltly congratulate publication of this collection of atlas because it might contribute to our works in the prevention of infectious diseases.

Ming-Yuan Jan

Vice Director of Committee on Agents of Zoonoses,
Chinese Society for Microbiology, IUMS.
Prof. of Institute of Epidemiology and Microbiology,
Chinese Academy of Preventive Medicine
October, 2 0 0 3

前　言

衣原体是人兽共患病病原体，可引起人类许多疾病，如沙眼、结膜炎、泌尿生殖系统感染、肺炎和心血管疾病，也是养殖、畜牧业的大敌。衣原体病的诊断依赖于实验室，衣原体形态学是衣原体鉴定的重要内容之一。当前，越来越多的实验室欲开展衣原体研究工作，但无论国内还是国外均没有一本较全面系统的衣原体图谱，使研究者尤其是初学者对衣原体形态学的了解感到困难。为此，我们将自己积累数十年衣原体研究工作的经验，精选、编辑出版这本图谱，以飨读者。

本图谱所涉及到的衣原体种类包括：沙眼衣原体、鹦鹉热衣原体（包括家畜衣原体）、肺炎衣原体；宿主细胞包括：鸡胚卵黄囊膜细胞、人羊膜 FL 细胞、McCoy、Hep-2、HL 和鸡胚内胚层细胞等；染色方法包括：吉姆萨、吖啶橙、碘染色和免疫荧光抗体染色等；观察方法包括：光学显微镜、荧光显微镜观察和电子显微镜的投影、负染以及超薄切片薄层扫描观察等。

本图谱共收集 300 余幅图片资料，其中绝大部分为首次发表，图片资料主要来自军事医学科学院微生物流行病研究所端青研究员和上海医科大学李子华教授，此外，上海医科大学中山医院内科免疫室项俊庆、兰州畜牧兽医研究所李英才、上海医科大学眼耳鼻喉科医院眼科研究所周忆萍等提供了部分图片；图片资料除署名外，均由端青提供。图谱中除收录了各种衣原体主要的、常见的典型形态外，还收录了一些罕见的衣原体特殊繁殖方式，并对其成因进行了一一阐述，使读者对衣原体形态学有一个较全面和系统的了解。值得一提的是，上海医科大学李子华教授首先发现和提出衣原体细胞外繁殖方式〔见 *Chinese Medical Journal*，1994,107(9):658-663〕，这一新发现和新理论的提出，是对“衣原体是严格专性真核细胞内寄生的原核生物”这一定义的质疑，将会对衣原体研究工作产生深远影响。

在这里，我们向对衣原体研究做出过杰出贡献的汤飞凡教授等我国老一辈科学家致以崇高敬意，并衷心希望本图谱能对读者有所帮助，成为衣原体研究成果百花园中又一朵绚丽的奇葩。

端　青

2003 年 10 月

Foreword

Chlamydia is the causative agent of an expanding spectrum of human and animal diseases, such as trachoma, conjunctivitis, genitourinary infections, pneumonia and cardio-vascular diseases, and also the grave obstacle for breeding of animals and rearing of livestock. The diagnosis of chlamydia infections depends upon the laboratory examinations of the suspected speciemens, of which the morphological examinations of chlamydia is one of the most important criterion for diagnosis. Although an increasing number of laboratories attempts to do some works in the chlamydia research, at present time, it is not available for the researchers, especially for the beginners, to have a complete and comprehensive atlas of chlamydia, thus making them very difficult to grasp the general characteristics of chlamydia. For this purpose, we have strictly selected, edited and published this collection of chlamydia atlas under the base of our several decades of experience on chlamydia researches.

This chlamydia atlas includes *C.trachomatis, C.psittaci* (including chlamydia of pecorum), *C.pneumoniae*. The cell lines used in the cell cultures are yolk sac membrane cells of chicken embryo, FL cells of human amnion, McCoy cells, Hep-2 cells, HL cells and endoderm cells of chicken embryo, etc. The staining methods used are Giemsa, Acridine orange, Iodine stain and immunofluorescence staining. Methods of examinations include observations under light microscopy, fluorescence microscopy and electron microscopy with shadow-casting, negative staining and ultra-thin layer scanning observations.

All together, this atlas consists of 300 pictures which are mainly published at the first time and are collected by Prof. Duan Qing of Military Medical Institute and Prof. Li Tzy-hwa of Shanghai Medical University. In addition, Xiang Jun-qing of Shanghai Zhong Shan Hospital, Li Ying-cai of Lan Zhou Veterinary Medical Institute, Zhou Yi-ping of Shanghai Ophthalmology and ENT Hospital have also supplied some pictures. In this collection of pictures the principal and commonly observed morphology as well as some special multiplication forms of rarely discovered chlamydia are

collected and the causes of formation of these special forms are discussed. In this way, the readers can get a complete and systematic understanding with regard to the morphology of chlamydia. It should be emphasized that the idea of extra-cellular multiplication form of *Chlamydia trachomatis* in tissue cultures was firstly introduced and discovered by Prof. Li Tzy-hwa of Shanghai Medical University. This new idea might be a great challenge for the primary theory, i.e. " chlamydia are the obligate intracellular prokaryotic microorganism " and would give a great impact on the chlamydia research work〔see *Chinese Medical Journal,* 1994,107(9):658-663〕.

Primary acknowledgment must go to Prof. Tang Fei-fan who had made great contributions on the chlamydia research work. It is our hope that this collection of atlas would be helpful to the readers and become one of the beautiful flowers in the field of chlamydia research work.

Duan Qing

October, 2003

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1. 概　　述
Introduction

衣原体是一类细胞内寄生的原核生物，需要宿主细胞为其提供代谢所需的能量物质（如ATP），人工培养基条件下不能生长，具有独特的繁殖周期，原体（elementary body EB）和始体（initial body，或称网状体 reticulate body RB）均为圆形，EB 大小约为 0.3 μm，RB 可比 EB 大 3~5 倍，由于其可滤过性，曾被称之为“大病毒”，目前归于细菌的范畴，具有类似于革兰氏阴性菌的细胞壁，含有两种核酸，其双链 DNA 约有 1.45Mb，为目前所知具有最小基因组的微生物，其 RNA 主要为 21S、16S tRNA，对四环素类及大环内酯类抗生素敏感。

衣原体与细菌和病毒的主要区别见表 1 。

表 1. 衣原体与细菌和病毒的主要区别

	衣　原　体	细　菌	病　毒
大　小	0.3 μm	>0.3 μm	<0.3 μm
形　状	圆　形	球形、杆形、弧形	多　样
细 胞 壁	有	有	无
核酸类型	DNA 和 RNA	DNA 和 RNA	DNA 或 RNA
繁殖方式	复杂的发育周期	二分裂	复　制
培养方式	组织或细胞培养	人工培养	细胞培养
抗生素敏感性	敏　感	敏　感	不敏感

人们对于衣原体的认识最早是从沙眼衣原体引起的一种疾病——沙眼开始的，公元前 27 世纪和公元前 19 世纪中国和埃及都描述了沙眼及其治疗方法和并发症，但是这种微生物在生殖道感染中所起的作用直到 20 世纪初才被人们了解。在分娩过程中对新生儿眼睛采取淋球菌感染的预防措施后，新生儿结膜炎仍然发生，1909 年从患结膜炎的新生儿结膜刮物中发现带有胞质内涵物的细胞，这些细胞与沙眼患者中看到的相同。后来从感染婴儿母亲的子宫颈、父亲尿道上皮细胞及非淋菌性尿道炎男性患者尿道上皮中均发现这种带有包涵体的细胞，从而证实了衣原体引起人泌尿生殖系统感染。

最早记载鹦鹉热的文章发表于 1880 年 ，文章用德文详细描述了一次疾病流行，其中包括 7 个病例，最终死亡 3 人。作者认为鸟是传染源，不会产生人 → 人传播，并将之命名为