段を利用すればオフィスや自宅に居ながらにして入手できる．

革命と呼ばれるもうひとつの理由は，情報の量の飛躍的な増大で，医療情報の場合そのきっかけはMedlineの無償公開である．1997年6月米国政府は，それまでは有料で大学図書館など限られた場所でしかアクセスできなかったMedline（米国国立医学図書館がサービスしている世界で最も充実している医学関連文献データベース）を，インターネット上で誰でも無料でアクセス可能にすると宣言した．現在では**Pubmed**と呼ばれる，それだけで膨大な情報量を持つこのデータベースの無償公開は衝撃的であった．

近年これらのインターネットによる情報革命にもうひとつの革命が加わった．情報検索革命である．別名を**グーグル革命**という．容易に手に入れることができるようになった情報も，その量の膨大さゆえに，自分が求める情報が必ずしもすぐに見つかるわけではなく，大きな問題となっていた．これを解決してくれる決定打がグーグルである．

Google（グーグル）とはウェブブラウザ上ではたらく検索エンジンのひとつだが，その検索手法は評価型というまったく新しいコンセプトに基づいて開発されている．検索された情報はその時点での人気の高さでランク付けされる．人気の高さとはとりもなおさず多くの人が参照しているということであり，情報の質の高さが保証される．グーグルによる検索によって，情報の山に埋もれた中から欲しい情報を簡単確実にすぐ見つけることができるようになった．

こうして今や，ウェブブラウザにグーグルを導入すれば，wwwを利用してオフィスや自宅で自分の求める質の良い情報を，簡単に，瞬時に，大量に，しばしば無料で入手できる．寄生虫情報も例外ではなく，いまでは特定のwebpageのURLをあらかじめ知る必要はない．それでも寄生虫関連情報が豊富なwebpageに直接アクセスしたい読者のために，寄生虫に関する情報を掲載しているいくつかの名の通ったwebpageを**表1**で紹介する．

② メーリングリスト

ウェブブラウザにグーグルを組み合わせれば，情報収集の方法としては現在世界最強である．しかし世界最強というのも，世界のどこかに蓄積されている情報を受動的に入手する場合に限ってのことである．インターネットによる強力な情報入手手段にはより能動的な，電子メールによるメーリングリストと呼ばれる方法もある．メーリングリストとは，世界のどこかのコンピュータをベースに（どこにあろうと意識する必要はない），複数の人々がある共通の話題について電子メールで情報交換するシステムで，インターネットの妙味は実はこのメーリングリストにある．

メーリングリストは電子メールでつながった同好の士の集まりであると考えればよい．情報を受身で閲覧するだけのWWWとは異なり，その基本的な特徴は速報性と双方向性（対話型）にあり，意見や情報を多くの人々と自由に交換できる．参加者の誰かがメールを出せば，そのメールは参加者全員に配送される．メールの相手先はメーリングリスト参加者全員である．参加者は不特定多数の場合（オープン）もあれば，特定多数の場合（クローズド）もある．いわば**インターネット上の“討論会”“セミナー”あるいは“耳学問”の世界**といえよう．

実際には一方的に情報だけを送ってくるもの（一方向，狭義のメーリングリスト）と，誰でも自由に情報を発信できるもの（双方向，ディスカッションリスト）に分けることができる．ディスカッションリストで自分が発信しなければ狭義のメーリングリストと変わりはないし，それも許される．

表1　寄生虫関連の主要なWWWサイト（2004年8月）

URLと内容を簡単に紹介するが，数多くあるWWWのほんの一部にすぎない．
寄生虫に限らず感染症一般を扱うものも多い．

1）日本寄生虫学会
http://jsp.tm.nagasaki-u.ac.jp/welcome-2.html
日本寄生虫学会の公式ウェブページ．
Consultationとして医療従事者向けの寄生虫に関する相談窓口を設けているのがこのページである．
国内外の主要な寄生虫関連サイトはここからリンクされている．

2）「熱帯病・寄生虫症に対する稀少疾病治療薬の輸入・保管・治療体制の開発研究」班
http://www.ims.u-tokyo.ac.jp/didai/orphan/index.html
国内で発生する輸入熱帯病や寄生虫症の治療に必要な稀用薬を輸入・保管・供給している．薬剤保管機関・担当者一覧がある．

3）American Society of Parasitologist
http://asp.unl.edu/
日本寄生虫学会がやや医学に偏向した情報を提供するのに対して，米国寄生虫学会は医に止まらず，植物，魚類，野生生物など幅広い領域の情報を提供している．

4）CDC DPD Home Page
http://www.cdc.gov/ncidod/dpd/
米国伝染病対策予防センター，CDC（Center for Disease Control and Prevention, National Center for Infectious Diseases）の寄生虫疾患部門，DPD（Division of Parasitic Diseases）のホームページ．
DPDx（寄生虫疾患診断サポート）で寄生虫疾患の解説にとどまらず，寄生虫の診断法，検査材料のCDCへの送付法など多岐にわたって詳細に記しているのは秀逸．
CDC top pageはこの他にも海外旅行者向けに，海外旅行時の健康に関する諸注意，予防注射の必要性，地域別の疾病の危険度等，有用な情報を提供している．

5）Parasites and Parasitological Resources
http://www.biosci.ohio-state.edu/～parasite/home.html
オハイオ州立大学のDr. Peter W. Pappasが個人的に作った，寄生虫学関係の資料集．
写真がすばらしい．

6）Entomology Index of Internet Resources
http://www.ent.iastate.edu/List/
節足動物の情報の宝庫．衛星動物に関する情報も多い．

7）ACIPAC（Asian Center of International Parasite Control）およびESACIPAC（Eastern and Southern Africa Center of International Parasite Control）
http://www.tmd.ac.jp/med/mzoo/acipac/
http://www.esacipac.org/index.htm
外務省JICAによって設立された「国際寄生虫対策センター」のホームページ．ACIPAC（国際寄生虫対策・アジアセンター），ESACIPAC（国際寄生虫対策・東南部アフリカセンター）のほか，今年中にはWACIPAC（国際寄生虫対策・西部アフリカセンター）が稼働する．
いずれも日本寄生虫学会が総力を挙げてサポートしている．

8）World Health Organization WWW Web Page
http://www.who.int/en/
世界保健機構の公式ページ．
主要な寄生虫症の解説を見ることができる．
寄生虫症に限らず，世界の疫学情報WER（Weekly Epidemiological Report）が毎週公開されている．International Travel and Healthを購入し，それをベースに毎週WERに目を通していれば，感染症の世界的動向がわかる．

9）ProMED
http://www.promedmail.org
寄生虫症に限らず，最速の感染症アウトブレーク情報を得ることができる．
当時WHOに居たJack Woodallが組織の腰の重さに業を煮やし，NGOの支援を受けて1994年に立ち上げたメーリングリストが発展したもの．1999年からはInternational Society for Infectious Diseasesが公式に引き受けている．
日本語ページ（厚生労働省検疫所が運営する「海外渡航者のための感染症情報」http://www.forth.go.jp/）へもリンクされている．同時に運営されているメーリングリストへの参加申し込みもこれらのweb pageから可能である．

代表的なメーリングリストを**表2**で紹介するので，是非一度参加することをお勧めする．参加手続き完了直後から新鮮な情報が次々にあなたのメールボックスに放り込まれてくる．

Ⅲ　日本寄生虫学会コンサルテーションの仕組みと利用の薦め

さて，以上紹介してきたシステムで入手できる寄生虫情報を越える情報はあるか？　ある．日本寄生虫学会が用意した寄生虫情報システムがそれである．

これまで解説してきたシステムは，実は教科書的な情報を得るための手段である．実際の症例に具体的に役立つことは少ない．すでに述べたが，国内の寄生虫事情の変化に対応して，日本寄生虫学会は

表2　寄生虫関連の主要なメーリングリスト（2004年8月）

寄生虫に関連するもののすべてを把握できない．
主に感染症一般を扱うメーリングリストである．
参加の方法はそれぞれのメーリングリストで異なるが，いずれも無料でとくに義務は負わない．

1）MIM - Multilateral Initiative on Malaria
アフリカにおけるマラリア研究をサポートするために始まったイニシアティブ．
ホームページを見ても良いが，アフリカにおける研究の機会などのアナウンスをメールで受け取ることができる．
申し込み方法：mim@nih.gov にメールを送る．

2）ProMED - PROgram for Monitoring Emerging Diseases
世界のあらゆる地域における Emerging Diseases の発生をいち早く知らせ，対策法，サーベイの方法などについても意見を交わす．
申込方法：http://www.promedmail.org/にアクセスし，subscribe のページから行う．
和訳版は http://square.umin.ac.jp/outbreak/autoregist.htm から．

3）EID - Emerging Infectious Diseases - a CDC monthly list
これに加入しておけば，CDC 発行の雑誌 Emerging Infectious Diseases（EID）が発行される度に，その目次を自動的に知らせてくれる．
申込方法：http://www.cdc.gov/ncidod/eid/subscrib.htm から．

4）MMWR - Morbidity and Mortality Weekly Report - a CDC list
これに加入しておけば，Morbidity and Mortality Weekly Report（MMWR）の発行をその目次とともに毎週知らせてくれる．
申込方法：http://www.cdc.gov/mmwr/にアクセスし，free subscription のページで申し込む．希望すれば，内容も同時に受け取ることができる．

5）WER - Weekly Epidemiological Records - a WHO list
Weekly Epidemiological Records（WER）の発行のお知らせの自動配信．
申込先メールアドレス：listserv@who.int
本文に書く内容（命令文）：subscribe wer-reh

早くから国内の医療関係者を支援する，日常診療で役に立つシステム，インターネットを介した寄生虫あるいは寄生虫疾患に関するコンサルテーション（寄生虫疾患診断システム）を計画した．1997年4月に運用を開始したこのシステムで得られる情報は，WWW やメーリングリストを凌駕する．

このコンサルテーションシステムは日本寄生虫学会会員で構成されるメーリングリストを利用しており，**図1**のような仕組みになっている．日本寄生虫学会のメーリングリストは不特定多数に開かれているわけではない．多くの学会でそうであるように，学会会員のみによって構成されているクローズドのメーリングリストである．したがって，学会会員以外の参加は認められないが，そのメーリングリストに第三者である相談者がいつでもコンサルテーションできる窓口を用意したところに工夫がある．

学会内に情報処理広報委員会が設けられている．この委員会が日本寄生虫学会 web page の表紙を介してメールで送られてきた寄生虫あるいは寄生虫疾患に関する質問や相談をまず受け付ける．質問や相談ができる第三者は医療関係者に限られているため，その資格やメールの内容を委員が簡単にチェックした後，学会会員メーリングリストへ送付される．受け取ったメールによるコンサルテーションに対し，意見，回答などを持つ会員は，メーリングリストを介してまたは直接相談者に回答をメールで送付する．最近はコンサルテーションに画像や動画などの追加情報が必要な場合が増えたが，その場合は相談者に対しその提供を求め，情報量の多いものは学会会員だけがアクセスできるウェブページ上で会員に公開し，意見を求めている．

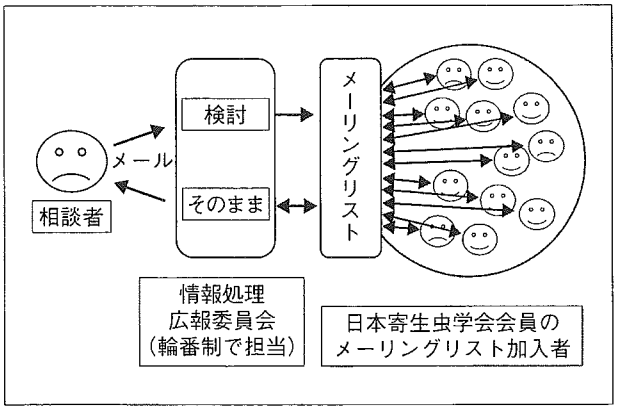

図1　コンサルテーションシステム内での情報の流れ

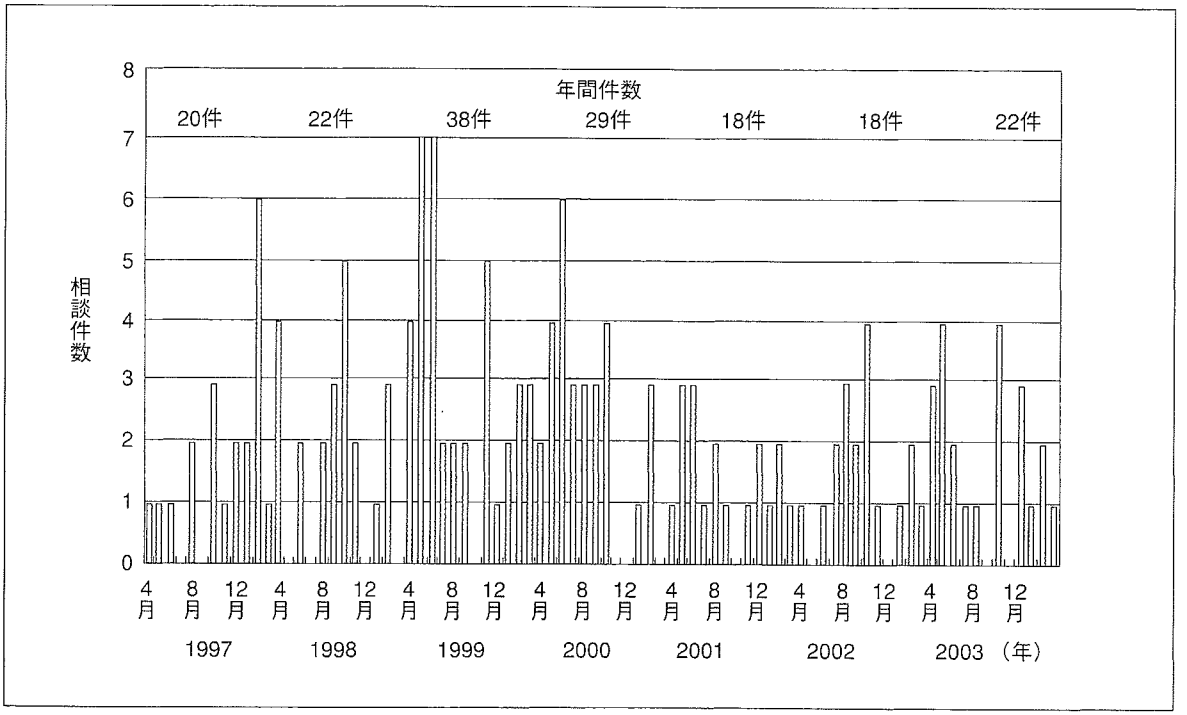

図2　コンサルテーション件数の推移

こうしてこれまでコンサルテーションシステムで解決してきた件数は**図2**の通りである．月間平均およそ3件の相談があり，少し古いが2000年に行ったアンケート調査では，依頼者の60％は医師，残りがコメディカルとなっている．相談の内容は診断・治療・寄生虫の同定をはじめ多岐にわたるが，回答までにかかった時間，回答の内容とも非常に高い満足度を得ている．**日本寄生虫学会のコンサルテーションシステムこそ最強の寄生虫情報システム**である．

おわりに

インターネットを介した寄生虫情報の強力な収集手段として，ウェブブラウザとグーグル，それにメーリングリストをはじめに紹介した．しかし日本寄生虫学会によるコンサルテーションはこれらにはるかに勝る寄生虫情報システムである．現在寄生虫学会会員でメーリングリストに参加している者は300名を越える．すなわち相談者はたった一本の電子メールによって同時に300名の寄生虫学専門家に相談したことになる．しかも疑問や追加情報の必要性があれば，学会会員から相談者にメールが返され，症例検討はさらに深まる．まさに対話型，双方向性の情報システムである．

WWWや狭義のメーリングリストなどではとても考えられない，寄生虫に関する贅沢かつ貴重な情報システムが**日本寄生虫学会会員のボランティア活動**として行われている．**是非利用していただきたい．**

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日本人に発症したビルハルツ住血吸虫症の1例

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赤　尾　信　明

A CASE BILHARZIASIS IN A JAPANESE MALE

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Bilharziasis is an endemic disease distributed mostly in African countries and the Middle East, and causes severe disturbances of urinary tract secondarily. Although it used to be a very rare disease in Japan, modern human mobility and jet travel have brought this tropical disease into our country far from endemic areas.

A 25-year-old Japanese male presented to our hospital with macroscopic hematuria. He had an experience of traveling to Malawi two years before. Cystourethroscopy demonstrated so-called 'bilharzial tubercles', many yellowish specks of mucosa at the posterior wall and dome of the bladder. The diagnosis of bilharziasis was made by detection of *Schistosoma haematobium* eggs in urine and histological specimen obtained by transurethral biopsy. In this case, radiographic and pathological examinations revealed neither obstructive uropathy nor urothelial malignancy. He was treated with praziquantel, and the disease is under good control.

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Key words: Bilharziasis, Urinary tract infection, Parasitic infection

緒　　言

海外旅行者が増加し国際協力も盛んとなって，いわゆる輸入感染症が臨床上また社会的にも問題となっている．ビルハルツ住血吸虫症は主にアフリカが流行地で泌尿生殖器に特異的に発症する寄生虫感染症であるが，調べえたかぎり日本人感染者の報告は17例と比較的稀である．今回われわれはアフリカのマラウィー湖で感染したと考えられるビルハルツ住血吸虫症の日本人症例を経験したので報告する．

症　　例

患者：25歳，男性

主訴：肉眼的血尿

既往歴：22歳時アメーバ赤痢，マラリア

家族歴：特記すべきことなし

現病歴：患者は1999年から2001年の約2年間にアフリカ・中南米・東アジアを旅行し，アフリカ滞在中の1999年10月にはマラウィー湖でダイビングを行った経験がある．2000年秋から肉眼的血尿が出現し，2001年にはメキシコシティーの病院を受診した．検査の結果，ビルハルツ住血吸虫症の診断で praziquantel を1回投与された．その後血尿は消失するが，2002年10月になって再び肉眼的血尿が出現したため，近医を受診した．血中好酸球増多を認め，活動性の寄生虫感染症を疑われ当科紹介受診となった．

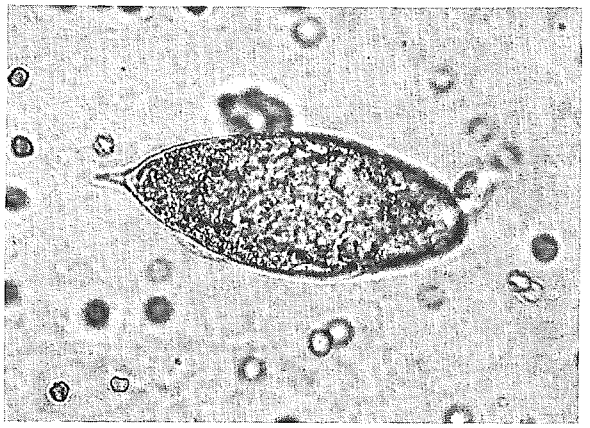

Fig. 1. An egg of *Schistosoma haematobium* in urine sediment. Diameter is 250 μm. This is a viable egg with moving cell for excretion (×40).

初診時現象：身長 166 cm，体重 53 kg，胸腹部に理学的異常所見はなかった．表在リンパ節を触知せず，皮膚・四肢・外陰部に異常はなかった．直腸診でも異常所見を認めなかった．

初診時検査所見：検尿にて軽度の血膿尿があり，1回排尿量全量の沈渣ではビルハルツ住血吸虫に特有な突起（terminal spine）を持つ虫卵を認めた（Fig. 1）．尿細胞診は class IIであり，尿中に好酸球を多数認めた．血液学的には好酸球が22.4%と高値，Hb 12.9 g/dl とやや貧血を呈した以外，異常値を認めなかった．また，血中抗マンソン住血吸虫虫卵抗体価は0.6（正常値；0.2以下）であり，これはビルハルツ住血吸虫症として矛盾しない値だった．尿流測定の結果は最大尿流率 30.4 ml/sec，平均尿流率 20.6 ml/sec，排尿量 334 ml と正常パターンを示し，残尿はなかった．

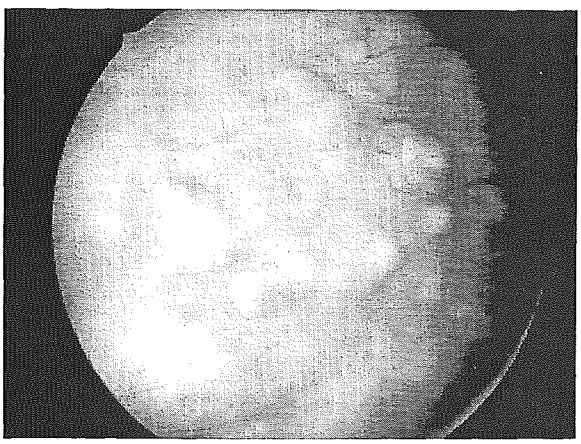

Fig. 2. Endoscopic finding. Many yellow tubercles (so-called 'bilharzial tubercles') are seen in the bladder. This nodule contains calcified eggs and living eggs. The area around the tubercles mucosa is reddish and edematous. Bladder mucosa in other regions seemed normal, and bilateral ureteric orifices are intact.

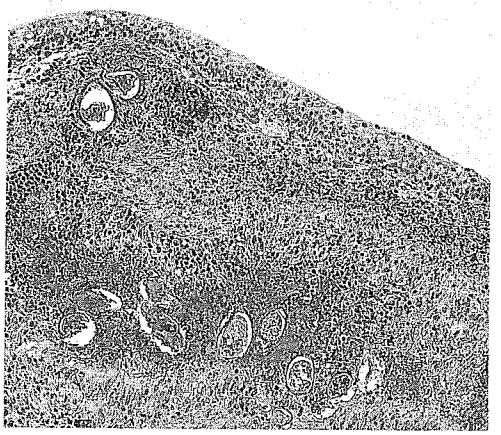

Fig. 3. Mucosal biopsy of the bladder. Bladder mucosa contains many calcified eggs. There are many granulomas and eosinophils in the storoma. There is neither atypia nor hyperplasia of the bladder epithelium (Hematoxylin-eosin stain, ×400).

画像所見：腹部超音波検査，KUB にて腎・膀胱に石灰化はなく，異常所見を認めなかった．

内視鏡所見：三角部から後壁にかけて黄白色の結節（bilharzial tubercle）を多数認め（Fig. 2），同部を生検した．尿道および膀胱頸部に異常を認めず，左右尿管口は正常であった．

病理組織学的所見：膀胱粘膜下に一部石灰化を伴う虫卵を多数認めた．虫卵の周囲には著明な好酸球浸潤，肉芽腫の形成を認めた．上皮の異型はみられなかった（Fig. 3）．

診断後経過：診断後，praziquantel 40 mg/kg/day を 2 日間投与した．投与後 1 カ月を経たが，尿中より虫卵が検出されているため再び同量の praziquantel を投与した．その後尿中虫卵は陰性化しており，外来での follow up を継続している．Praziquantel 投与後半年を経過するが，血尿や膀胱刺激症状を認めず経過は良好である．

考　　察

ビルハルツ住血吸虫症は，住血吸虫の 1 種である *Schistosoma haematobium* が骨盤静脈叢に寄生して発症する疾患である．ヒトへの感染は流行地域の淡水に接触して経皮的に幼虫が侵入することによって起こる[1,2]．幼虫は皮下でリンパ管あるいは静脈内に侵入し他動的に肺・門脈へ到達するが，その後直腸静脈叢・膀胱静脈叢・Santorini 静脈叢へ移動して約 3 カ月で成虫となる．成虫は，膀胱粘膜下に 1 日200～500個ほどの虫卵を産み，虫卵は尿とともに体外へ排出され，水中で孵化して幼虫になる．幼虫は中間宿主である，ある種のサカマキガイへ寄生したのち，終宿主で

あるヒトへ感染する．流行地はこのサカマキガイが生息するアフリカ西・南部，ナイル川流域で，上下水道の普及が遅れる発展途上地域である．この地域では，日常生活で幼虫に汚染された淡水と接触する機会が多いため幼少期から感染率が高く，アフリカでは現在も約1億人が感染していると推定されている[2]．

本邦での感染者の報告は少なく，調べえたかぎり日本人の感染者としては本例が17例目の報告である[3~9]．日本人の感染者の報告17例のうち，本症を含めた3例はアフリカマラウィー湖での水泳が原因で感染したと考えられる[3,4]．現在の日本では寄生虫感染症は稀となっており，特に若い世代では寄生虫感染症に対する予防意識が低く，流行地における淡水との接触は危険であるという認識は薄いと考えられる．今後も，旅行や海外協力などで流行地へ渡航者が増加することが予想され，本症を含めた寄生虫感染症に関して十分な啓蒙が必要と考えられる．

本症の初期症状は，ほとんどは肉眼的血尿，排尿障害などの尿路症状である．流行地への渡航歴があり，水と接触歴がある血尿患者では本症を積極的に疑うべきである．尿中から虫卵が検出されるのは感染後80日ほどたってからであり，感染から血尿などの初期症状出現までには数カ月以上を要することもある[1]ため，病歴聴取時には注意を払う必要がある．本症は，尿中に terminal spine と呼ばれる特有の突起をもつ虫卵を検出することで確定診断される（Fig. 1）．虫卵の検出には24時間蓄尿，もしくは9～14時に採取された尿（1回排尿量全量）が望ましいとされている．また，虫卵の長径は 100～200 μm と血球成分と比べると大きいため，40倍程度の弱拡大での検鏡が有用である．血中の住血吸虫虫卵抗体価の測定などの血清検査も間接的診断法として有用であるが，日本ではかぎられた施設でしか行われておらず，寄生虫病学の専門家との協力が必要である．膀胱鏡所見では粘膜浮腫，充血などの非特異的な所見に加え，本例に見られたような bilharzial tubercles と呼ばれる結節性病変（Fig. 2）が見られることが多く，この結節1つには無数の石灰化した虫卵が含まれると言われている[1]．

治療は praziquantel が第一選択薬である．本症例は praziquantel 投与後の再発例であるが，再発の原因としては初期投与量が不十分であったことが考えられる．一般に，40～60 mg/kg/day の2日間経口投与が推奨されており，根治率は60～90％であるとされる．しかし，praziquantel は成熟虫体にしか効果がなく，投与時に未成熟の虫体が体内にいる場合，それらは駆虫されない可能性が指摘されている[10]．また，虫卵は数週間排泄されるので，初期投与1カ月後に検尿を行い，尿中から生きた虫卵が検出された場合は，再投与が必要である．

本症では，2次的に尿路閉塞や膀胱癌が発生する事が重大な問題である．膀胱壁内に残った虫卵の石灰化，虫卵周囲の肉芽腫形成や繊維化による膀胱壁の肥厚だけでなく，尿管蠕動障害や，膀胱尿管逆流も併発し，慢性期には水尿管・水腎症に至る．慢性期のビルハルツ住血吸虫症患者の膀胱では，尿流測定により明らかな異常が認められなくとも，多くの平滑筋は虫卵の存在による線維化を起こして，潜在的に排尿筋収縮力が低下しているという報告もある[11]．膀胱癌の発生も多く，特に扁平上皮癌が多いと言われている[12]．ビルハルツ住血吸虫症の好発地域では，全膀胱癌のうち扁平上皮癌は6～9割とされる[1]．発癌に至る機序は未だ不明な点が多いが，虫卵自体による慢性の刺激，二次性に合併する細菌感染症および細菌感染によるニトロソアミンなどの発癌性物質の増加など，いくつかの原因が想定されている[1]．これらの2次病変が発生すると，駆虫では病状の改善はみこめないため，早期の診断・治療が大切であると考えられる．本症例は，現時点においては2次病変はみられないが，潜在的な膀胱粘膜の線維化の可能性，2次病変が発生する可能性は高く，今後も定期的な経過観察を行う予定である．

結　　語

ビルハルツ住血吸虫症の日本人感染者の1例を報告した．

本論文の要旨は，第557回日本泌尿器科学会東京地方会にて報告した．

また，血中抗マンソン住血吸虫虫卵抗体価の測定にご協力いただいた獨協医科大学熱帯病寄生虫病学教室の先生方にこの場をかりて御礼申し上げます．

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10. Human Dirofilariasis in Japan

Nobuaki Akao

10.1 Introduction

Human filariasis is mainly caused by the parasites, *Wuchereria bancrofti* and *Brugia malayi*, whose adults live in the lymphatic vessels of humans. In Japan, bancroftian filariasis was once endemic, but has been completely eradicated from the country. Although imported cases of filariasis are occasionally reported [1,2,3], no autochthonous case has been identified in recent years. By contrast, more than 10 cases of filariasis of animal origin are diagnosed annually in Japan. The most important parasite responsible for zoonotic filariasis in Japan is *Dirofilaria immitis*, the canine heartworm. The adult worms reside in the pulmonary arteries and the right ventricle, resulting in severe heart failure, which may cause sudden death of the affected dog. Humans can also be infected with *D. immitis* by a mosquito bite, but the larvae are unable to reach maturity in humans or primates, which are unsuitable hosts. Infected people present either pulmonary infarct or a subcutaneous nodule. The parasite is also occasionally observed in a deep inner organ. Hence, it is frequently confused with malignant tumor.

Human dirofilariasis, therefore, can be categorized into two groups: pulmonary and extra-pulmonary dirofilariasis. Extra-pulmonary dirofilariasis is classified further into four groups: cardiovascular, subcutaneous, visceral, and ophthalmic dirofilariasis. In this article, we focus on the studies of zoonotic filariasis that have been carried out by Japanese researchers in Japan.

10.2 Case reports of dirofilariasis since 1964 in Japan

10.2.1 Cardiovascular dirofilariasis

The filarial parasite of animal origin was first found in the left ventricle of a Brazilian boy (Magelhaes, 1887). Later, the worms were identified as adult male and female worms of *D. immitis* by Faust *et al.* [4]. This was a very unusual case in which the invading worm survived and grew into maturity in a human, just as it would do in the definitive host, Canidae. To date, only four cases of cardiovascular dirofilariasis have been reported worldwide; one of these was in Japan. Takeuchi *et al.* [5] found two slender nematodes in the heart and inferior vena cava of a 36-year-old Japanese male who died of liver cirrhosis. The worms were incidentally found through an administrative autopsy, and there was no evidence that the worms were involved as a cause of death. Both worms were identified as non-gravid adults females of *D. immitis*. The other two cases, a 73- and a 40-year-old women, were reported in New Orleans in the United States.

10.2.2 Pulmonary dirofilariasis

In Japan, pulmonary dirofilariasis, the most common type of human dirofilariasis, was first found in Kanazawa city in 1968 [6]. The patient was a 42-year-old male high school teacher. He was admitted to the hospital because of loss of consciousness for 20 minutes following his morning stretching routine. Chest X-ray examination revealed a coin lesion in his left lower lobe. Under the diagnosis of tuberculosis or lung cancer, a thoracotomy was carried out. Histopathological examination showed a pulmonary infarction caused by a premature female of *D. immitis*. Six years later, two additional cases of pulmonary dirofilariasis were independently reported by Fuse *et al.* [7] and Otsuru *et al.* [8].

Thereafter, many clinical cases were noticed every year. Makiya *et al.* [9] reviewed the clinical cases published from 1964 to 1986. A total of 41

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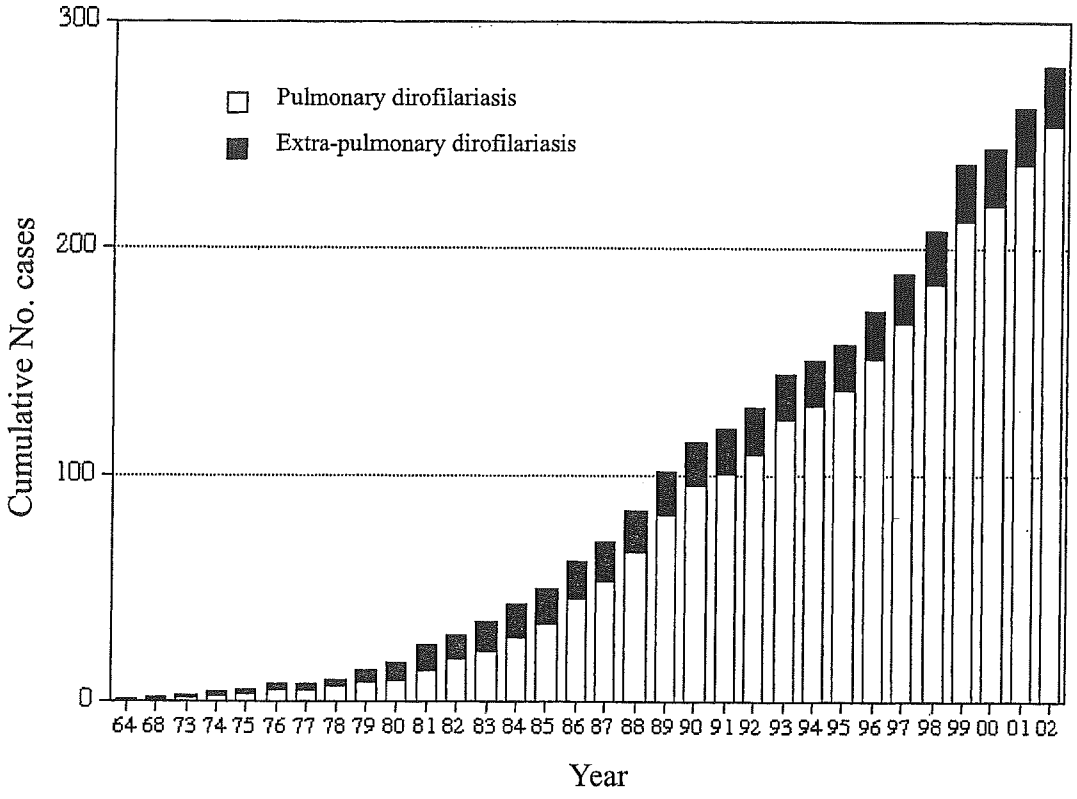

Fig. 1 Cumulative number of cases of human dirofilariasis in Japan from 1964 to 2002.

cases of pulmonary dirofilariasis were reported in this period. The coin lesions were mostly located in the right lower lobe of the affected lungs. They also observed that the most of the patients resided in the southwestern part of Japan but a few were in the northern part of Japan. They suggested that the geographical difference was attributable to the lower prevalence of microfilaremia in dogs with *D. immitis* infection in the northeastern part of Japan relative to the southwestern part, since the cumulative temperature in the northeastern part was insufficient to develop the same number of vector mosquitoes. For this reason, no cases have been reported in Hokkaido thus far, which is located in the northernmost part of Japan and has a far-colder climate than Tokyo.

The overall incidence as compiled from published cases from 1964 to 1995 was recorded by Kagei [10]. According to his report, 103 additional cases of pulmonary dirofilariasis were counted from 1986 to 1995 in Japan. These figures indicated that the patients drastically increased in number, more than doubled in 10 years. Figure 1 shows the cumulative cases of pulmonary dirofilariasis as of the end of 2002, in which the data from 1964 to 1986 and from 1986 to 1995 were quoted from Makiya *et al.* [9] and Kagei [10], respectively. The number of cases continues to increase, and since the study by Kagei [10], a total of 117 cases of pulmonary dirofilariasis have been cited in the database of Japana Centra Revuo Medicina over the last 7 years. In addition, three cases appeared in the Japanese Journal of Clinical Parasitology [11,12] and four more cases were referred to us (Dr. I. Sato, Department of Pathology, Miyagi Prefectural Hospital, personal communication). Consequently, 254 cases of pulmonary dirofilariasis have been recorded as of the end of 2002 (Fig. 1).

Kobayashi *et al.* [13] noted that the maximum diameter of the pulmonary lesions induced by the infarct of the worm was less than 3 cm. Therefore, a coin lesion of more than 3 cm in diameter on a chest X-ray examination should be excluded from the diagnosis of pulmonary dirofilariasis (Fig. 2). Thoracotomy, which is a high-risk procedure, used to be the only option for making a clear diagnosis prior to the 1990's. Fortunately, thoracoscopic

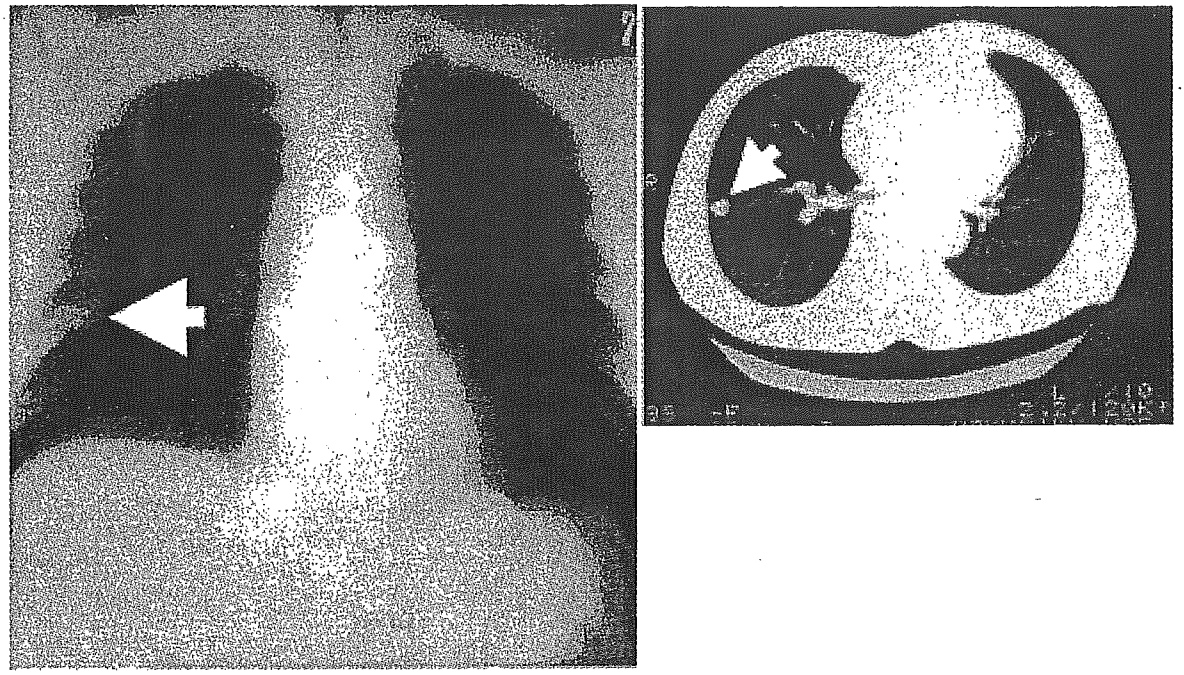

Fig. 2 Chest X-ray (left) and CT (right) appearance of a patient with pulmonary dirofilariasis. A solitary nodule called "coin lesion" is adjacent to the pleural membrane (arrow).

surgery introduced in the early 1990's has been adapted to resect the parasitic nodule provoked by *Dirofilaria* infection. Miura *et al.* [14] performed a thoracoscopic lung biopsy and observed an immature worm of *D. immitis* in the necrotic tissue of a peripheral pulmonary artery of a removed nodule. The patient, a 50-year-old male, was discharged 7 days after the medical treatment from Oita Medical University Hospital without any complications. This technique is now widely accepted as a less-invasive medical procedure and for diagnosing pulmonary dirofilariasis.

10.2.3 Cutaneous dirofilariasis

Nishimura *et al.* [15] reported the first case of cutaneous dirofilariasis in Japan. The patient, a 52-year-old female living in Ibaragi city of Osaka prefecture, was admitted to a hospital with a chief complaint of a left breast nodule of 4 days' duration. A surgical resection of the nodule was performed on 19 January 1961. A thread-like nematode of 50 mm in length and 0.21 mm in width was found in the removed tissue. From the morphological characteristics, they concluded that the worm was identical to a male *D. immitis*. Ten years later, an additional case of cutaneous dirofilariasis was reported by Otsuru *et al.* [8]. The patient, a 68-year-old male, was admitted to the Hospital of Okayama University because of a subcutaneous nodule on his right abdominal wall. Pathological specimens revealed several transverse sections of an immature female worm of *D. immitis*. Since then, 12 cases of cutaneous dirofilariasis have been reported between 1964 and 1986 [9], and nine additional cases were published between 1987 and 2002.

The parasites responsible for cutaneous nodules are thought to be *D. immitis*, except for the case described by MacLean *et al.* [16]. The patient, a 67-year-old male, living in Okinawa prefecture, which is in the southernmost part of Japan, presented with 2 cm (diameter) subcutaneous nodule which had appeared on his left anterior chest wall. The nodule was surgically removed, and pathological examination revealed several transverse sections of a worm, which was identified as *Dirofilaria repens* based on its morphological characteristics.

10.2.4 Visceral dirofilariasis

A developing immature *D. immitis* worm is occasionally found in deep inner organs, such as

the liver, uterus, and abdominal cavity. Tada *et al.* [17] reported a case of visceral dirofilariasis following a death due to bleeding in the abdominal cavity resulting from liver cirrhosis. A tumor-like mass was found embedded in the adipose tissue of the mesentery. At the central region of the nodule, they found several fragments of a female worm of *Dirofilaria* sp., probably *D. immitis*. In 1980, an additional case of extra-pulmonary dirofilariasis was found in a 74-year-old female, residing in Toyama city, in Toyama prefecture [18]. She was admitted to the Toyama Medical and Pharmaceutical University Hospital because of uterine bleeding over the past 1 year. A hysterectomy was performed and an endometrial polyp measuring 2.0 x 1.5 x 1.0 cm was seen in the rear right wall of her uterus, in which a nematode parasite was revealed by a histopathological examination. The parasite, measuring 150 to 160 μm in diameter, showed the typical appearance of a male *D. immitis*. Miyakawa *et al.* [19] reported a case of accidental identification of several transverse or oblique sections of *Dirofilaria* sp. in the liver of a 58-year-old female with colon cancer.

10.2.5 Ophthalmic dirofilariasis

The *Dirofilaria* worm has also been implicated in certain ophthalmic infections. According to the review of Kagei [10], six cases of ophthalmic dirofilariasis have been reported so far: two cases of orbital tumor, two of neuroretinitis, one of peripheral proliferative vasculitis of the fundus, and one of an eyelid legion. However, the last case did not precisely constitute ophthalmic dirofilariasis since the parasite was recovered from subcutaneous tissue from the eyelid. Moreover, there

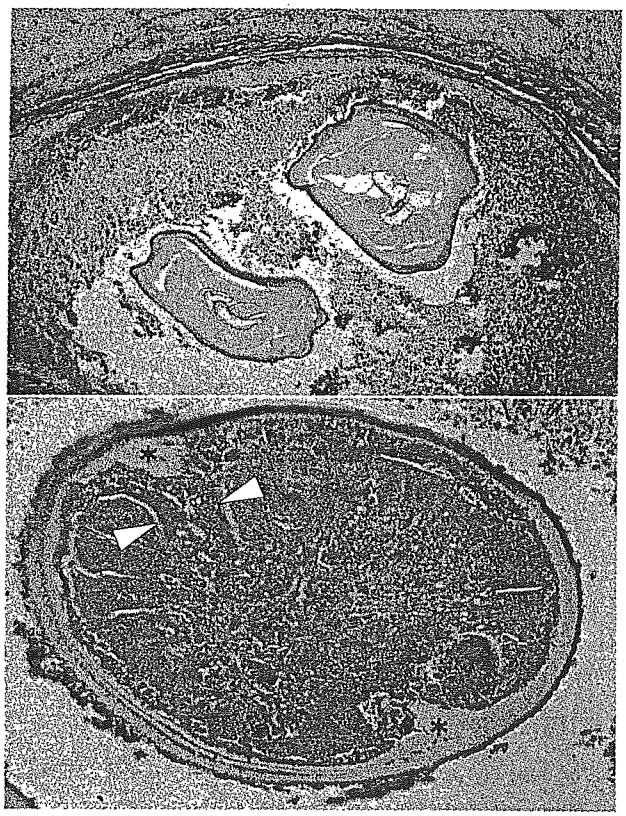

Fig. 3 Histopathologic findings of the nodule. Two transverse sections of an immature worm of *D. immtis* are seen in a small pulmonary artery (upper, Elastica van Gieson stain), and a transverse section of an immature adult worm showing large lateral chords (arrow head) with internal longitudinal ridges (*) and multilayered cuticle (bottom, HE stain).

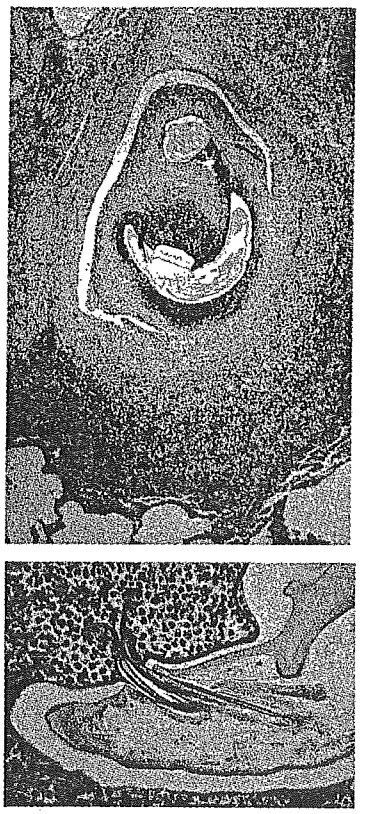

Fig. 4 Low-power view of a pulmonary infarct containing a transverse section and a longitudinal section of a mature male *D. immitis* (upper). Two spicules are clearly observable (bottom).

is no apparent evidence that the *Dirofilaria* worm is responsible for the eye pathologies in the remaining cases. The patients were suspected of having the parasitic infection based not on the pathological findings but on the clinical and serological examinations; otherwise, the authors only stated that the patient had a parasite without any evidential presentation of photographs. Therefore, it is uncertain whether these patients were frank cases of ophthalmic dirofilariasis in Japan, despite a number of cases that have appeared in the foreign literature [20,21]. In conclusion, the number of extra-pulmonary dirofilariasis cases in Japan was estimated to be 26 as of the end of 2002 (Fig. 1).

10.3 Diagnostics

10.3.1 Diagnostic morphology of zoonotic filariasis

Gutierrez [22] described the diagnostic features of zoonotic filariae in tissue sections. A review article written by Chitwood and Lichtenfels [23] also mentioned the morphological characteristics of Filaridae. Both reviews are useful for pathologists to distinguish each filarial worm from the others in pathological specimens. In Japan, Uni *et al.* [24] studied the comparative morphology of *D. urusi* and *D. immitis* in cross-sections. Yoshimura and Akao [25] investigated the cross-sectional morphology of human and zoonotic filarial worms that were found in human tissues (Figs. 3 and 4). These studies have contributed to the identification of filarial infections, including an imported case of onchocerciasis and a case of zoonotic onchocerciasis, among the Japanese [1,26].

Nagano *et al.* [27] attempted to detect the genomic DNA of *D. immitis* by polymerase chain reaction (PCR). This is a promising tool for identifying necrotizing parasites that do not show normal structures.

10.3.2 Serological investigations

Serology is an alternative method of diagnosing parasitic infections because the invading parasite cannot always be identified by pathological examination of resected tissues. Therefore, many attempts have been made to detect a specific antibody against filarial proteins. At first, filarial antigen derived from *D. immitis* was studied to diagnose bancroftian filariasis in Japan. Ishizaki *et al.* [28] prepared a defatted somatic antigen of adult *D. immitis* and adapted it to the epidemiological survey of bancroftian filariasis in an endemic area of Ehime prefecture as an intradermal test. Of 54 patients with microfilaremia, 44 showed a positive reaction and the remainder were negative, indicating that the sensitivity was unsatisfactory for a field survey. Tada and Kawashima [29] demonstrated the usefulness of a purified antigen derived from adult *D. immitis* for an intradermal skin test against bancroftian filariasis. This antigen showed extremely low cross-reactivity against the sera from eight other parasitic infections and did not show nonspecific reaction in patients with allergic diseases. Sawada and his colleagues studied the antigenic nature of a purified *D. immitis* antigen, FST, and its derivatives [30-32]. Although all these antigens were prepared for use in an intradermal test of bancroftian filariasis, they had a potential diagnostic benefit for human dirofilariasis.

The first step in making a serodiagnosis of human dirofilariasis in Japan was achieved by Tamaoki *et al.* [33], who performed several immunological tests, intradermal skin test, agar-gel diffusion, and immunoelectrophoretic analysis, that lead to a preoperative diagnosis. Sato *et al.* [34] introduced an enzyme-linked immunosorbent assay (ELISA) for the diagnosis and follow-up study of dirofilariasis. The antigen they used included a veronal-buffered saline extract of adult worms of *D. immitis* to detect specific IgG antibody. The antibody was demonstrated in the patient's serum preoperatively, but the serum also reacted with the antigen derived from adult worms of *Ascaris suum*. After operation, the IgG responses to both antigens decreased gradually, with more prominent reduction of *Ascaris* antibody. The ELISA could be useful for the post-operative follow-up in human dirofilariasis. Around the same time in the United States, Glickman *et al.* [35] demonstrated that an antibody to somatic antigen of adult *D. immitis* was detectable by indirect hemagglutination test and ELISA in eight patients with radiologically evident pulmonary nodules in whom the final diagnosis was confirmed pathologically as *Dirofilaria* sp. infection. A mixed passive hemagglutination test was also attempted to detect the IgG antibody [36].

Akao *et al.* [37] demonstrated that the

excretory-secretory (ES) products of female worms of *D. immitis* provided a more sensitive antigen than the adult somatic antigen by using an immunoblot analysis. They also suggested that a low molecular component of ES products strongly cross-reacted with the sera from non-filarial patients, and that adult somatic antigen shared this antigenic component. Nakagaki *et al.* [38] observed that, using an ELISA, the sensitivity of ES antigen was less than 50%, but periodate-treated ES (PI) antigen was superior to that of ES antigen. They also noted that not only phosphate buffer extracted antigen but also ES and PI antigens highly cross-reacted to the sera of patients with loasis, tropical eosinophila, and gnathostomiasis, suggesting that it was extremely difficult to diagnose human pulmonary dirofilariasis by ELISA. Sun and Sugane [39] isolated an immunodominant antigen of *D. immitis* from genomic DNA and established a recombinant DNA-derived fusion protein for ELISA. However, there is no report on the practical application of this antigen for human dirofilariasis to date. In conclusion, the reliability of serological tests is still questionable and further investigations are needed to identify a more specific antigen suitable for immunodiagnostics.

10.4 Animal models for human dirofilariasis

To understand the pathophysiology and to improve the serodiagnosis of dirofilariasis in humans, several animal models have been investigated. Experimental infections with fifth-stage larvae molting in the dog were successful in rabbits, rats, and guinea pigs, while infections with third-stage larvae molting in vector mosquitoes were only successful in dogs and ferrets [40,41]. Nakagaki *et al.* [42] observed that the subcutaneous transplantation of these juvenile *D. immitis* migrated into lung arteries, resulting in pulmonary hemorrhagic infarction. They noticed that the pathological findings of the lung closely resembled the lesions of human pulmonary dirofilariasis. They are also studying the immune response of experimentally infected rabbits to develop a more precise diagnosis of human dirofilariasis (Dr. K. Nakagaki, personal communication).

10.5 Investigations of vector mosquitoes

In Japan, at least 16 species of mosquitoes are thought to play a role as a vector of *D. immitis*. Of these, *Culex pipiens pallens* and *Cx. tritaeniorhynchus* are the major species and are distributed nationwide. A detailed distribution of these vector mosquitoes and the prevalence of the infection in dogs have been described in a review article by Kagei [10].

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6 Critical Assessment of Existing and Novel Model Systems of Toxocariasis

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Introduction

Toxocariasis is a disease caused by the larval stage of *Toxocara* sp., and predominantly involves *Toxocara canis* and *T. cati*. The infectious stage larvae, which develop in the egg within 2 weeks after their excretion to the surrounding environment and mature 4 weeks after excretion, can migrate through the entire body of either a definitive or paratenic host. In paratenic hosts including human beings, the larvae cause tissue damage as either a direct or indirect effect of their presence. For example, some level of visual impairment may occur when larvae in the retina pass over the macular region, and neurologic disturbance may appear when larvae reside in the brain for a long period of time. In addition, larvae in the retina may elicit an inflammatory response resulting in serious ocular disease such as chorioretinitis or uvitis. These medical problems have been well known since 1952, when Beaver *et al.* (1952) proposed a disease syndrome characterized by chronic eosinophilia with granulomatous lesions in the liver, as reported in three young children. Since then, much effort has been invested in understanding the pathogenesis of this parasite using animal models.

Toxocariasis in Humans

Toxocariasis is clinically divided into four types of diseases: visceral, ocular, neurologic and covert types (Taylor *et al.*, 1987; Glickman and Magnaval, 1993). Visceral toxocariasis is associated with the migratory behaviour of the larvae in the early stage, in which they penetrate the intestinal wall, reach the liver, and then the lung, from where they are then distributed throughout the entire body of the host. Ocular toxocariasis is a specific form of the visceral type. This syndrome is not always accompanied by a systemic disorder, but is the type in which the disseminated larvae emerge in the retina. In some patients, a full-body or a part of a larva has been recovered from the vitreous fluid after vitrectomy (Maguire *et al.*, 1990). However, it is still unclear just how the larvae enter or the time course for this invasion after infection. Regarding neurological involvement, some previous studies have shown that neurological defects or epilepsy may be associated with *Toxocara* infection. Children who have a history of epilepsy showed a statistically significant increase in antibody against *Toxocara* antigens. Additionally, meningoencephalitis with eosinophilia and increased antibody in the cerebrospinal

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fluid is another clinical manifestation of the disease. These findings are common in neurologic toxocariasis. In contrast, the concept of covert toxocariasis is less well established. In the Midi-Pyrenees of France and Ireland, patients who had relatively non-specific symptomatology including fatigue, abdominal pain, nausea, fever, lymphoadenopathy, etc., with or without accompanying moderate eosinophilia, showed positive results for an anti-*Toxocara* antibody test (Glickman *et al.*, 1987; Taylor *et al.*, 1988). It is increasingly accepted that *Toxocara* infection could account for this syndrome. Although the variety of symptoms in human cases is a characteristic feature of the infection, our knowledge about *Toxocara* pathogenesis is fairly limited. For this reason, *Toxocara* infection has long held the attention of both parasitologists and immunologists.

Experimental toxocariasis: Existing animal models

Mice

Both inbred and outbred strains of mice are commonly used in studies of infectious disease. An outbred strain was first used in a study of the migratory behaviour of *Toxocara* larvae in 1952 (Sprent, 1952), soon after Beaver *et al.* (1952) introduced the notion of 'visceral larva migrans' by *T. canis*. Since then, many attempts were made to clarify the distribution pattern after oral administration of embryonated eggs. Embryonated eggs hatch in the upper gastrointestinal tract and then the infectious stage larvae penetrate the enteric mucosal membrane. Most of the larvae remain there until 6 h after infection, and migrate to the liver by way of the portal vein. They then remain in the liver for some time before migrating to the lung. Typically, the larvae migrate to the lung and heart; however, with repeated infection or presensitization treatment with *Toxocara* antigen, the larvae accumulate in the liver in both outbred and inbred mice. These findings, along with the fact that trapping of the larvae in the liver does not occur in congenitally athymic mice, suggest that the host immune response plays an important role in this phenomenon (Sugane and Oshima, 1983; Concepcion and Barriga, 1985; Parsons and Grieve, 1990). Thus, the mouse is a useful model for determining why the parasite is so often found in biopsy specimens of the human liver.

In general, different strains of mice show different larval distribution patterns and pathophysiological courses (Koizumi and Hayakawa, 1984). Among the inbred mice strains, BALB/c mice, but not C57BL/6 mice, are the best suited for investigations of a possible connection between allergic asthma and *Toxocara* infection (Pinelli *et al.*, 2001).

When they leave the lung, the larvae enter the systemic circulation, from which they reach the skeletal muscles and central nerve system. Interestingly, *Toxocara* larvae tend to accumulate in brain tissue and can remain alive and motile for years, resulting in behavioural changes in affected mice (Summers *et al.*, 1983; Holland and Cox, 2001). These mice also show a reduced ability in maze learning. However, little information is available on the relationship between the site of the larvae in the brain and behavioural changes in the host (Donovick and Burright, 1987; Cox and Holland, 1998). Additionally, there is no correlative evidence regarding the site where the larva was detected and a possible clinical syndrome in these mice. In fact, these findings suggest that mice are not a suitable model for neurologic toxocariasis. In spite of having the same MHC haplotype background, BALB/c and DBA mice reacted quite differently in terms of their allergic inflammation in the brain, indicating that the host response to an infection is not dictated by MHC haplotype alone (Epe *et al.*, 1994).

Studies of ocular toxocariasis have also been conducted with outbred mice (Olson, 1976; Rockey *et al.*, 1979; Ghafoor *et al.*, 1984). After oral administration of eggs, mouse eyeballs were crushed and observed microscopically. *Toxocara* larvae were observed and inflammatory changes were confirmed histologically, but the incidence was very low. Thus, the use of a mouse model for ocular toxocariasis is not recommended, since it is time-consuming to determine the migration route of the larvae to the retina and the pathogenesis of the larvae, even though useful information has been obtained from some experiments using mice.

The influence of maternal infection on offspring has been the subject of study with murine toxocariasis. In mice infected during pregnancy, larvae were found in the uterus, placenta and foetus (Lee *et al.*, 1976), and there was a predictable decrease in litter size in female mice with

Toxocara infection (Akao *et al.*, 1990; Reiterova *et al.*, 2003).

Numerous immunological and immunopathological studies of *Toxocara* infection in mice have also been performed in the last two decades. Among them, larval trapping in the liver of presensitized hosts is an interesting phenomenon (Sugane and Oshima, 1983; Concepcion and Barriga, 1985; Kayes, 1997). This event might remind us why *Toxocara* larvae are frequently observed in the liver of human visceral toxocariasis. Eosinophilic granuloma formation in the liver was found to be regulated by the host TH1/TH2 response, and eosinophils play an essential role in the pathology of infected C57BL/6 mice (Takamoto *et al.*, 1997). However, eosinophils do not play a significant role in the expulsion and killing of *T. canis* larvae in infected mice (Sugane *et al.*, 1996). Furthermore, the presence of IgE antibody to excretory-secretory products of *T. canis* has been monitored during infection, and allergic asthma in murine models has been studied (Buijs *et al.*, 1994; Dent *et al.*, 1997).

To interpret the findings from these experimental studies, it is very important to know the precise count and administration method of the eggs in each experiment. In this context, the work done by Oshima (1961), was an important advance in this field. Oshima described a standard method for the oral inoculation of eggs and specified that all equipment used in their preparation should be siliconized and that the albuminoid coat of the egg should be removed. It is also important that the number of eggs be counted in a statistically valid manner so that this and other techniques, taken together, will ensure reproducible results.

In conclusion, while mice provide a very informative model for studying the contribution of genetic diversity to *Toxocara* infection and the distribution of larvae after infection, the mouse model cannot provide a complete understanding of all aspects of *Toxocara* infection.

Rats

The utility of the rat model is similar to that of the mouse model; however, the reports on experimental toxocariasis of rats are limited. The pattern of migration of larvae in rats is similar to that in mice (Lescano *et al.*, 2004) and in one study, rats infected with *T. canis* showed a decline in learning ability of maze (Olson and Rose, 1966). Rats infected with *Toxocara* have also been used to demonstrate eosinophilic chemotactic activity in bronchoalveolar lavage fluid and eosinophils-mediated cardiomyopathy (Fujimoto *et al.*, 1990; Schaffer *et al.*, 1992; Okada *et al.*, 1996). Ocular infections have also been reported in infected rats (Burren, 1972), but occurred less commonly than in mice.

Guinea pigs

In allergic asthmatic children, a high prevalence of antibody to *Toxocara* antigens has been reported worldwide (Oteifa *et al.*, 1998). To better understand the factors involving the onset of this disease, guinea pigs are frequently used due to their high responsiveness of bronchial refraction to antigen (Buijs *et al.*, 1995). Collins and Ivey (1975) reported that IgE antibody in infected guinea pigs was evident using homologous passive cutaneous anaphylaxis tests. Ocular inflammation was induced by intravitreal infection (Rockey *et al.*, 1979); however, guinea pigs are considered to be an inappropriate model for the study of ocular toxocariasis due to their atypical immune response (Ghafoor *et al.*, 1984; Fenoy *et al.*, 2001).

Hamsters

Very little information is available on toxocariasis in the hamster (Burren, 1972). Since hamsters are frequently used to investigate airway hyper responsiveness or inflammation to foreign materials, it would be helpful to understand their possible allergic response to *Toxocara* infection.

Rabbits

Since, with rabbits, blood samples can easily be taken once or twice a week, they have frequently been used to investigate the time course of antibody production during infection. Specific IgG antibody against excretory-secretory antigens of *T. canis* was first detected in the serum after the

5th day of infection and reached its peak at 2 weeks post-infection. Thereafter, the level of antibodies remained high for a long period of time (Fernando, 1968; Kondo *et al.*, 1981; Smith *et al.*, 1982). By contrast, eosinophil counts in the peripheral blood reached their peak at 4 weeks after infection, and decreased gradually to the normal level after 10 weeks of infection. Immunoblot analysis has also been performed in rabbits to examine changes in the antigen recognition in infected rabbits and to identify the specific antigen moieties in larval excretory-secretory products (Akao *et al.*, 1982).

Primates

The genetic homology between human beings and primates has made the primate model of toxocariasis an attractive option for studies of the pathogenesis of toxocariasis (Fernando *et al.*, 1970; Fernando and Soulsby, 1974; Tomimura *et al.*, 1976; van Knapen *et al.*, 1982). In the cynomolgus macaque, *Macaca fascicularis*, the haematologic and serologic changes were similar to those observed in children with VLM, and some individuals (three out of 16 macaques) developed neurologic signs such as ataxia and nystagmus (Glickman and Summers, 1983). Despite intensive studies using oral inoculation of eggs, intraocular lesions associated with larval migration have not been observed, although intraocular inoculation with larvae did cause inflammatory changes. Histopathologically, *Toxocara* larvae can survive for at least 10 years after infection in rhesus monkeys (Beaver, 1969).

Despite these advantages over other animals, primates tend to be nervous and difficult to handle for experimental purposes. Moreover, studies using primates are much more expensive and controversial than those using other animals.

Chickens, Pigs and other mammals

Visceral toxocariasis was thought to be a disease affecting younger children who accidentally ingested *Toxocara* eggs, even though ocular toxocariasis can occur in older children or in individuals of any age (Glickman and Magnaval, 1993). In 1989, a new infection route of toxocariasis was reported (Nagakura *et al.*, 1989). Twin brothers, aged 21 years, were admitted to the hospital due to fever, nausea and myalgia with urticaria of both lower legs. They had eaten raw chicken liver and meat 12 days before admission. Eosinophilia, elevation of total IgE and *T. canis* specific IgG antibodies were confirmed by a laboratory examination. In another case, a 26-year-old woman presented to the hospital complaining of fever, headache and a dry cough. Laboratory examination revealed eosinophilia, elevated concentration of IgE and positive for *T. canis* specific IgG. A *Toxocara* larva was detected in a small brown itchy nodule on her left ankle (Aragane *et al.*, 1999). Before the onset, the patient had a history of eating raw beef liver. Similar cases have been reported from Switzerland (Sturchler *et al.*, 1990), North America (Salem and Schantz, 1992) and Spain (Espana *et al.*, 1993). In addition, experimental studies revealed that *Toxocara* larvae tend to accumulate in the liver of chicken (Taira *et al.*, 2003) and quail (Pahari and Sasmal, 1990; Maruyama *et al.*, 1994). We assure, therefore, that table fowls play an important role in the transmission of toxocariasis.

In a pig model, Taira *et al.* (2003, 2004) demonstrated that no clinical signs developed in infected pigs, although most of the larvae were recovered from the lungs and there were numerous white spots in the liver due to the continuous migration of the larvae. Although few in number, the larvae were detected in various organs and tissue. Therefore, they suggested that the experimental infection of pigs may be a useful model of covert toxocariasis in humans (Taira *et al.*, 2004). Furthermore, Helwigh *et al.* (1999) stated that the pig was a useful non-primate model for human visceral larva migrans, since *T. canis* larvae migrated well and induced a strong immunological response in the pig.

New Model for Human Toxocariasis: Mongolian gerbils, *Meriones unguiculatus*

Mongolian gerbils are known to be susceptible to a variety of parasites, including *Brugia pahangi*, *Strongylus stercoralis*, *Nippostorongylus brasiliensis* and *Entamoeba hystolytica* (Horii *et al.*, 1993; Nolan *et al.*, 1993; Campbell and Chadee, 1997). However,