論文を書く「コツ」

OACIS臨床研究セミナー
2018年10月20日
沖縄県立中部病院　感染症内科
ICRT-Japan 2018 終了生
成田　雅

自己紹介

1994年　岩手医科大学医学部卒業

1994年　天理よろづ相談所病院　ジュニアレジデント

1995年　沖縄県立中部病院 内科研修医

1999年　沖縄県立八重山病院　内科医師

2001年　手稲渓仁会病院 臨床研修部

2004年　UPMC Shadyside Hospital　内科研修医

2006年　Pittsburgh VA Medical Center 感染症科　臨床研究員

2008年　太田西ノ内病院 総合診療科

2014年　沖縄県立中部病院　感染症内科

2018年　ICRT-Japan 2018終了

沖縄県立中部病院の理念と使命

私たちは、すべての県民がいつでも、どこでも安心して
満足できる医療を提供します

1. 患者中心主義：Patient Focused
2. 社会的貢献：Social Contribution
3. チームワーク：Fine Teamwork

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臨床研究の側面

1. 患者中心主義：Patient Focused　　研究倫理
2. 社会的貢献：Social Contribution　　真の「目的」
3. チームワーク：Fine Teamwork　　メンターシップ

中部病院医学雑誌　Vol.19 No.2 1993

原点とバランス
－リサーチ心と臨床心（こころ）－

内　科
喜舎場　朝　和

約10年前に、「リサーチVS臨床、ユニーク性VS普遍性」について小拙文を書かせてもらったことがある（沖縄県医師会報　昭和58年５月号）。また、折にふれて、私のところへ回ってくる研修医にボソボソとこの事について話してみたりもしてきた。やはり同じ内容めいた事を２度書くことには抵抗を感ずるが、10年前といえばそろそろ時効にしてもらってもよい頃だし、もともと目を止めて下さった方も多くはなかったはずである。一方、私などにこのような欄にふさわしい考えの持ち合わせがあれこれとあるはずもなく、またこの“問題”がそれにふさわしいと自負するものでもないが、浅はかながらも、ほぼ絶えず私の頭の中で気に掛けてきたこととはいえるので、前回の全くのコピーとはならぬように気を配りながら、この事について再び取り上げてみたいと思うのである。

浅学にして単純、独断にして偏見の可能性を私自身十分承知の上で言わせてもらうならば、医者や医

にある臨床心となれば、“普遍性の探究≒コンセンサス志向”となり、つまるところ“教科書志向”ということになるのではないか。それだから、リサーチにおけるユニーク性志向の議論の中から、ある方法や技術に対して、sensitivity と specificity、侵襲性とリスク、cost-effectiveness といった事柄に納得ができ、コンセンサスが得られたとき、初めて一般的臨床応用の実用性が承認されるに至るわけで、十分なコンセンサス作りの過程を経ずに、ユニーク的論文集がいきなり教科書となってしまってはいけない理屈である。

このように考えると、リサーチ心≒ユニーク性志向、臨床心≒コンセンサス志向は、全くといってよいほどに相対立する“性格”を帯びていることが分かる。ものは中庸で、私は何も両者の違いを必要以上に明確に区別したいと願っているわけではない。しかし、特に本邦における実状は、両者の共存両立がさもあたりまえに可能であるかのように“錯覚”

文献を書くために必要なこと

- 運命的な出会い　Encounter / Serendipity
- 綿密さ　Thoroughness
- 迅速さ　Rapidity
- 使命　　Mission
- 時間の確保
- 指導医をみつけること　Mentorship

運命的な出会い
Encounter / Serendipity

LEPTOSPIROSIS AFTER RECREATIONAL EXPOSURE TO WATER IN THE YAEYAMA ISLANDS, JAPAN

MASASHI NARITA,* SHIGEKI FUJITANI, DAVID A. HAAKE, AND DAVID L. PATERSON

University of Pittsburgh, Internal Medicine Department, Pittsburgh, Pennsylvania; University of Pittsburgh Medical Center, Presbyterian Shadyside, Pittsburgh, Pennsylvania; University of Pittsburgh, Critical Care Medicine Department, Pittsburgh, Pennsylvania; VA Greater Los Angeles Healthcare System, Infectious Diseases Section, Los Angeles, California; The David Geffen School of Medicine at UCLA, Los Angeles, California; University of Pittsburgh, Division of Infectious Diseases, Pittsburgh, Pennsylvania

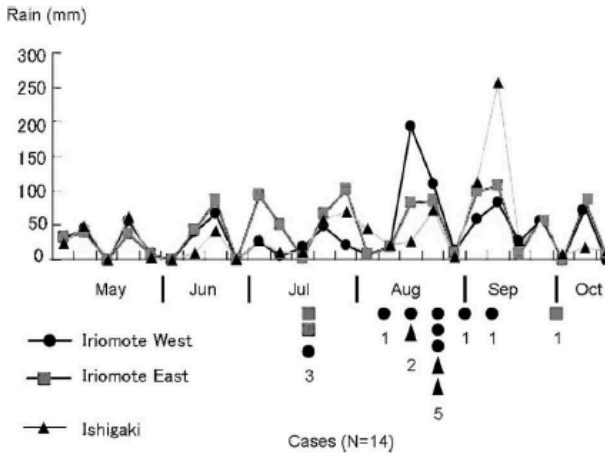

FIGURE 1. Relationship between rainfall and leptospirosis. Case of leptospirosis were clustered from July to September 1999, several days (latent period) after unusually heavy rainfall. According to the Ishigakijima Local Meteorological Observatory, most of this excess precipitation occurred over a relatively short period of a few days.

TABLE 2
Detailed clinical information of 14 cases of leptospirosis

Summary of leptospirosis (all cases)							
Case	Occupation	Water/soil exposure	Native vs. nonresident	Serovar(s)	Clinical course	JHR	IP (days)
61 yr M	Agriculture	Rice farming	Nonresident	Pyrogenes	Thrombocytopenia, renal failure	+	NA
22 yr M	Agriculture	Rice farming	Nonresident	Hebdomadis	Improved without antibiotics	–	NA
26 yr M	Tour guide	River	Nonresident	Hebdomadis	Thrombocytopenia	+	NA
49 yr M	Tour guide	River	Nonresident	Hebdomadis	Conjunctival hemorrhage, calf muscle pain	+	NA
13 yr M	Junion high student	Swimming	Native	Grippotyphosa	Vomiting, diarrhea, concerned HUS	–	6
28 yr M	Tour guide	River	Nonresident	Grippotyphosa	Headache without meningismus	+	NA
54 yr M	Tour guide	River	Native	Hebdomadis	Arthralgia, myalgia	–	NA
22 yr M	Agriculture	Swimming	Nonresident	Hebdomadis	General joint pain	–	NA
22 yr M	Tour guide	River	Nonresident	Hebdomadis	Doxycycline, switched to ampicillin	–	NA
48 yr M	Tour guide	River	Nonresident	Hebdomadis	Headache and lower back pain	–	NA
31 yr M	Doctor	Canoeing	Nonresident	Grippotyphosa	Biphasic clinical course with aseptic meningitis	–	10
30 yr M	Laborer	River	Native	Kremastos	Severe JHR	+	NA
25 yr F	Office worker	Swimming	Native	Grippotyphosa	Well clinical course	–	14
60 yr F	Agriculture	Rice farming	Native	Grippotyphosa	General fatigue, joint pain	+	7

HUS, hemolytic uremic syndrome; JHR, Jarisch-Herixheimer reaction; IP, incubational period; NA, not assessed.

Am. J. Trop. Med. Hyg., 73(4), 2005, pp. 652–656

綿密さ　Thoroughness

Linezolid-Associated Peripheral and Optic Neuropathy, Lactic Acidosis, and Serotonin Syndrome

Masashi Narita, M.D., Brian T. Tsuji, Pharm.D., and Victor L. Yu, M.D.

Table 2. Summary of Seven Patients with Linezolid-Induced Lactic Acidosis

Age(yrs)/ Sex	Underlying Disease	Pathogens	Infection Site	Duration to Initial Signs (wks)[a]	Duration from Initial Signs to Discontinuation (days)[b]	Lactate Level (mmol/L)
52/F[16, 21]	Unknown	*Nocardia otitidiscaviarum*	Disseminated	11	0[d]	11.0
81/M[22]	Unknown	MRSA	Osteomyelitis	1	Unknown	17.5
49/F[16]	AML, BMT	*Mycobacterium abscessus*, vancomycin-resistant *Enterococcus*	Sepsis (source unknown)	8	1	13.3
74/F[16]	Biliary cirrhosis	Coagulase-negative *Staphylococcus*	Prosthetic joint	6	4	18.4
70/M[8]	Cutaneous T-lymphoma	MRSA	Bacteremia	1	0	12.5
Unknown[4]	Cirrhosis	Unknown	Unknown	2	Unknown	10.0
63/F[15]	Hypertension	MRSA	Prosthetic joint	16	2	24.5

MRSA = methicillin-resistant *Staphylococcus aureus*; AML = acute myeloblastic leukemia; BMT = bone marrow transplant.
[a]Duration from linezolid initiation to first signs of lactic acidosis.
[b]Duration from initial signs to discontinuation is the duration from appearance of lactic acidosis to discontinuation of linezolid; 0 indicates immediate discontinuation.
[c]Survived indicates alive beyond 4 weeks after lactic acidosis.
[d]Linezolid was restarted after discontinuation.

Pharmacotherapy. 2007 Aug;27(8):1189-97.

Stenotrophomonas maltophilia: an emerging opportunist human pathogen

W John Looney, Masashi Narita, Kathrin Mühlemann

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Clinical presentation

The most common clinical manifestation of *S maltophilia* infection is pneumonia, followed by blood-stream infection and, less frequently, wound and urinary tract infection.[5,66–68] Rare cases of an expanding array of other clinical entities have been reported, including meningitis (mostly postsurgery), endocarditis (mainly postsurgery in prosthetic valves or intravenous drug users), sinusitis (which may mimic fungal infection), mastoiditis, cholangitis and peritonitis, eye infections, epididymitis, bursitis, arthritis, and osteochondritis.[66,69–71]

Respiratory tract infection

Isolation of *S maltophilia* from the respiratory tract represents colonisation in most cases, and suggests an

Blood-stream infection

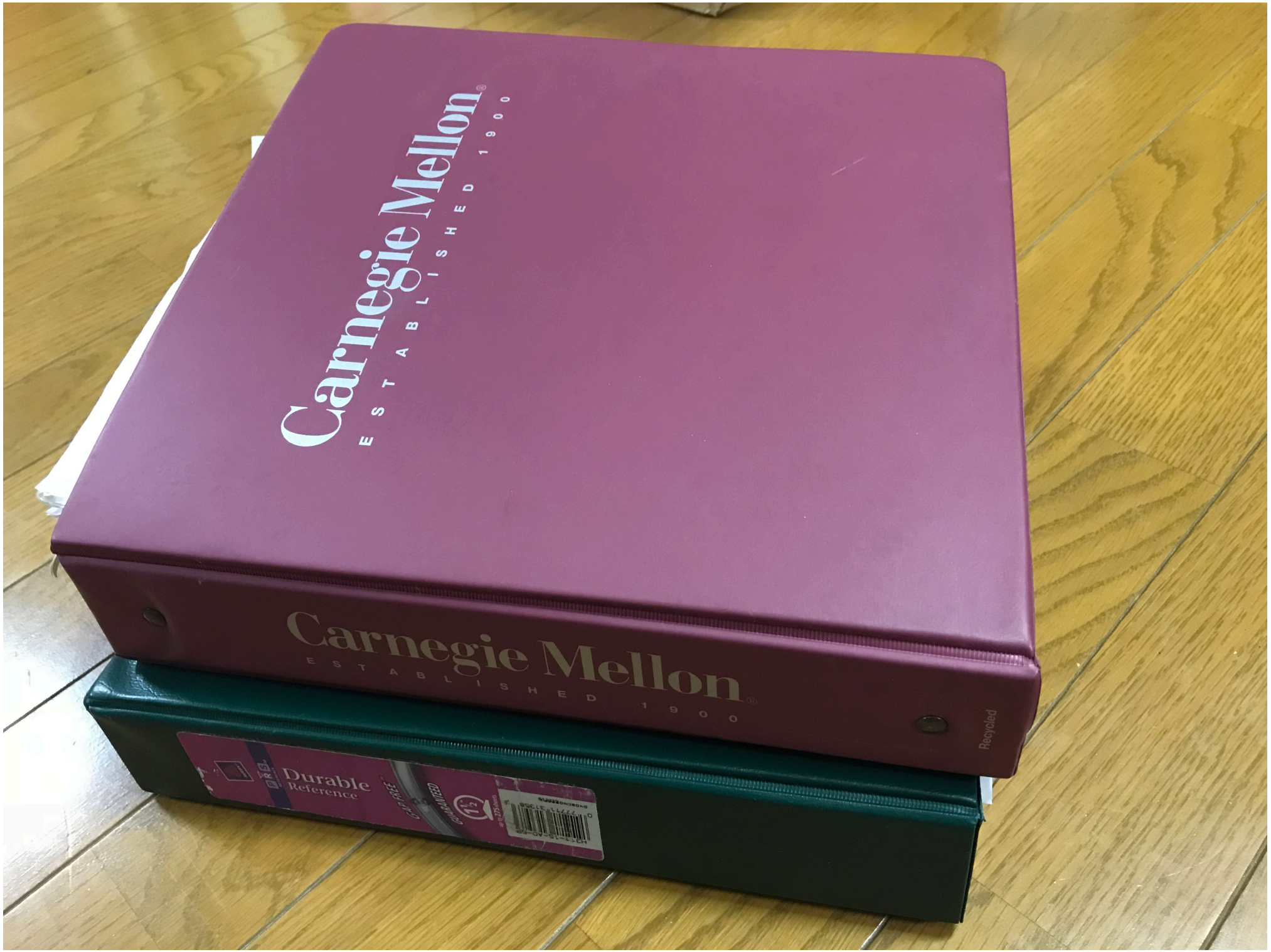
Isolation of *S maltophilia* from a blood culture should prompt a careful evaluation of the patient to differentiate between contamination, colonisation, and true blood-stream infection. Central-venous lines are the most common source of *S maltophilia* bacteraemia.[11,13,56,57–59,61] Blood-stream infections and catheter-related blood-stream infections (CR-BSIs) are often (20–40%) polymicrobial.[11,13,53,56,58,59,61,62,79] The prognosis for CR-BSIs is good upon prompt removal of the infected catheter.[53,57,59,61] In patients with haematological malignancies, *S maltophilia* has been associated with breakthrough bacteraemia.[62] Senol and colleagues[80] estimated a 27% attributable mortality for *S maltophilia* blood-stream infection, which is similar to that for

Lancet Infect Dis 2009;9: 312–23

With Dr.McConnell, the editor –in-chief of The Lancet Infectious Diseases Oct 6, 2018

Dr. Victor Yu

“The road to hell is paved with good intentions”
Oct 2, 2018


Carnegie Mellon
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Reference

Drug Interactions Between Linezolid and Selective Serotonin Reuptake Inhibitors: Case Report Involving Sertraline and Review of the Literature

Deidre B. Clark, Pharm.D., Miranda R. Andrus, Pharm.D., and Debbie C. Byrd, Pharm.D.

A 47-year-old woman developed confusion, incoordination, and hypertension after she was given linezolid in addition to sertraline for 5 days. Her symptoms resolved within 4 days of discontinuing linezolid. One and a half months later, she received a second course of linezolid; sertraline was discontinued on day 1 of linezolid therapy. On day 9 of therapy, the patient developed confusion, myoclonus, and incoordination, and cardiopulmonary arrest occurred, leaving the patient in a coma. Diarrhea, hypertension, and tachycardia developed after cardiopulmonary arrest. Linezolid was discontinued on day 10, and cyproheptadine was given. Linezolid is a weak monoamine oxidase inhibitor and has been reported to interact with selective serotonin reuptake inhibitors (SSRIs). Several cases of serotonin syndrome in patients taking linezolid and SSRIs have been reported, including two reports with sertraline, one with paroxetine, four with citalopram, and two with fluoxetine. One abstract of a retrospective analysis reported that serotonin syndrome did not occur in patients who received linezolid and fluoxetine, paroxetine, or sertraline. Because of several limitations, however, no conclusions can be drawn from that retrospective analysis. A drug interaction involving escitalopram and linezolid has not been documented. Caution should be used when linezolid is used in patients receiving an SSRI. Other antibiotic options should be considered first, and linezolid should be reserved as the last resort if possible. If the infection requires linezolid, the SSRI should be discontinued, and the patient should be monitored closely for serotonin syndrome.

Key Words: *linezolid, selective serotonin reuptake inhibitor, SSRI, drug interaction, serotonin syndrome, sertraline.*

(Pharmacotherapy 2006;26(2):269–276)

Patients receiving a selective serotonin reuptake inhibitor (SSRI) are at an increased risk for drug interactions because SSRIs are metabolized by the cytochrome P450 (CYP) system and increase the amount of serotonin in the body.[1–5] When SSRIs are used with agents that inhibit their metabolism or those that result in elevated serotonin levels, serotonin syndrome can occur. Serotonin syndrome is a very serious condition that can result in death.[6] It can occur within hours of administration of the precipitating agent(s), and mild cases usually resolve spontaneously within 24 hours after discontinuation of the precipitating agent(s).

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III. Lactic acidosis

A. Overview

Lactic acidosis is a toxic effect of linezolid whose mechanism is unknown. It is thought that linezolid interferes with mitochondrial protein synthesis, probably owing to similarities between bacterial and mitochondrial ribosomes[1].

Seven cases of linezolid-induced lactic acidosis were reported in five case reports and one clinical trial[2-7]. As described in table 1, resistant organisms such as methicillin-resistant Staphylococcus aureus (MRSA), vancomycin resistant enterococcus(VRE) and others were targeted by linezolid for prosthetic ~~devices~~ joint infection, osteomyelitis, bacteremia and disseminated nocardiosis. The range of treatment period varies from 1 to 16 weeks. Patient's serum lactate levels were found to be 9.9mmol/L or more ~~on the diagnosis of lactic acidosis~~. Elevated lactate levels in these cases were resolved after discontinuation of linezolid, except two of grave cases. Underlying diseases of these cases disclosed ~~hematological malignancy, cirrhosis and others~~ immunosuppressive conditions in 3 cases.

Complications with linezolid-indiced lactic acidosis ~~are serious~~ with organ failure, ~~stroke, thrombocytopenia~~ and serotonin syndrome. ~~Prognosis is poor, followed by~~ death occured in three cases out of seven. Other case left serious neurological complications of blindness and disorientation. In the ~~grave cases~~, serum lactate levels were increased

MN see me

- Infections which typically require prolonged therapy

The infections included

two patients who died acutely.

NP

NP

NP

NP

One had

the 2 patients who died acutely included loss of vision, thrombocytopenia and serotonin syndrome in 3 patients.

61歳男性　肝移植後の敗血症

C型肝炎・肝硬変にて肝移植後　糖尿病（＋）
術前：食道静脈瘤、肝腎症候群、透析6ヶ月
術前感染症:　UTI: ESBL K.pneumoniae
MRSA, VRE carrier
術後の免疫抑制剤(tacrolims, mycophonolate mofetil, prednisone)
予防投与:　TMP/SMX, Micafungin
術後敗血症（VRE, CMV, E.coli)
治療：Daptomycin, Gancyclovir, Meropenem, Cefepime

移植後30日目、抗菌薬、抗真菌薬の投与中
septic shockを呈した。

考えられる病原体は？

ST合剤(バクタ)で予防できる感染症

“2L TPN”

TPN: Total Parenteral Nutrition

Legionella　レジオネラ

Listeria　　リステリア

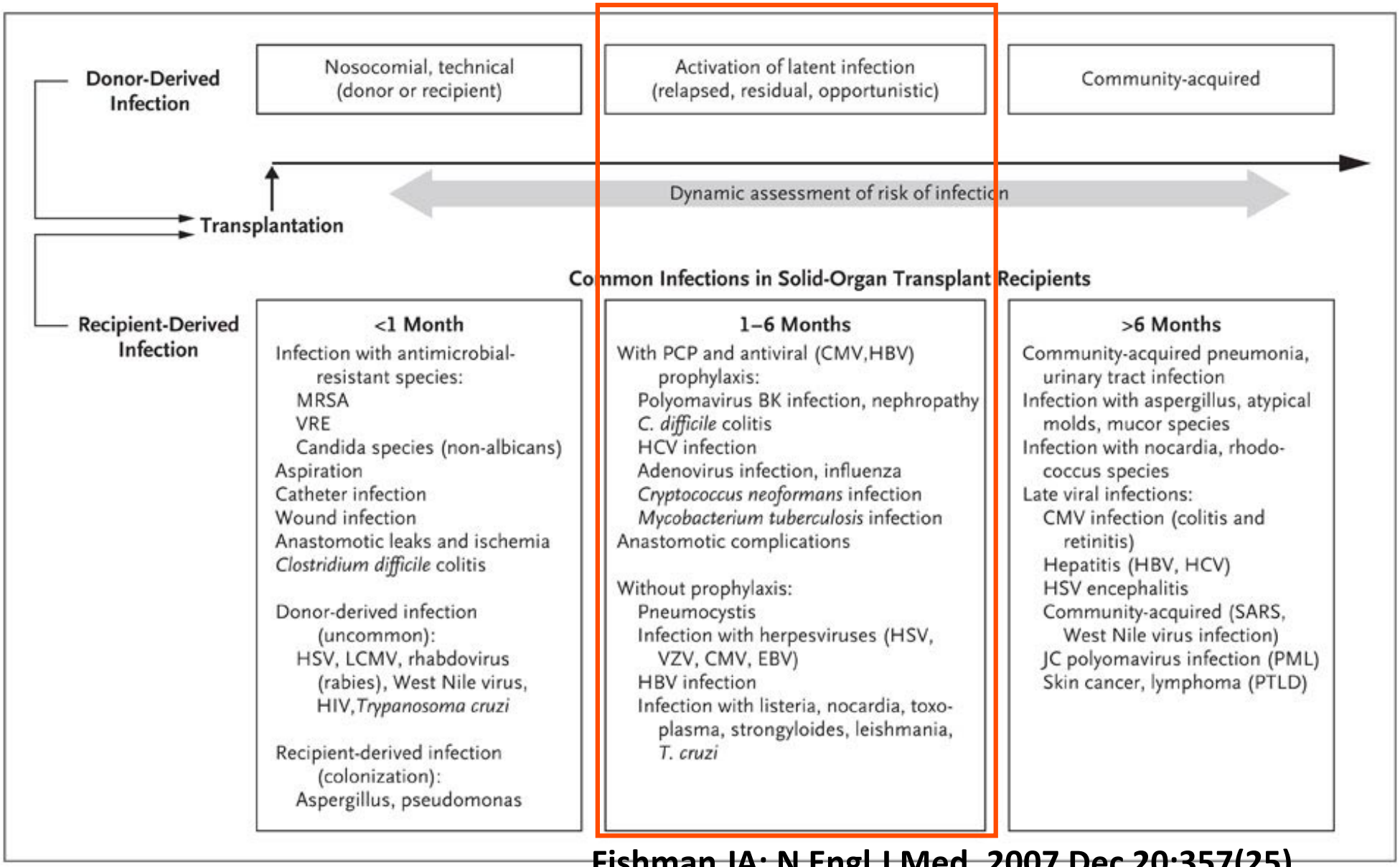
Toxoplasma トキソプラズマ

Pneumocystis jirovecii

　　ニューモシスチス肺炎

Nocardia　ノカルジア

Changing Timeline of Infection after Organ Transplantation



Fishman JA; N Engl J Med. 2007 Dec 20;357(25)

Prototheca wickerhamii）


Department of
Veterans Affairs
Property
Not For Sale

迅速さ Rapidity

Protothecosis After Liver Transplantation

Masashi Narita, Robert R. Muder, Thomas V. Cacciarelli, and Nina Singh
VA Medical Center and University of Pittsburgh, Pittsburgh, PA

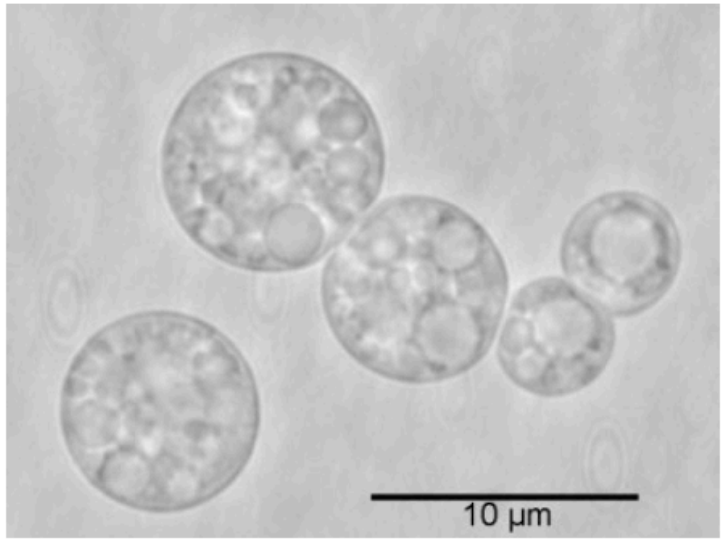


Figure 1. Wet mount of growth from a blood culture on a chocolate agar plate showing round, symmetrical sporangia (4-8 μm in diameter) containing endospores or sporangiospores (1-3 μm in diameter; magnification, ×1000).

TABLE 1: *Prototheca* Infection in Transplant Recipients

Reference Number	Age, sex	Underlying disease/ comorbidity	Immuno-suppression	Type of transplant	Type of infection	Co-infection	Time to onset after transplant	Treatment	Diagnosis, Outcome
21	58M	GVHD	Prednisone, cyclosporine A, mycophenolate mofetil	Stem cell transplant	Disseminated, algaemia, skin (*P.wickerhamii*)	*K.pneumoniae* bacteremia	562 days	Liposomal Amp B iv	Antemortem, recurrent algaemia, died
22	58M	Acute leukemia, pancytopenia	Cyclosporine, fludarabine, cytarabine, G-CSF, gemtuzumab ozogamicin	Bone marrow	Disseminated, algaemia, Lung, kidney, heart, liver (*P.zopfii*)	Pulmonary aspergillosis	3 months	Amp B iv, liposomal Amp B iv	Antemortem, died
23	59F	ESRD, COPD, CAD	Unknown	Lung	Disseminated, algaemia (*P.zopfii*)	Cytomegalovirus viremia, *Serratia marcesens* pneumonia	Unknown	Unknown	Antemortem, died
24	44M	ESRD	Azathioprine, corticosteroids	Kidney	Local, skin (*P.wickerhamii*)	Unknown	Unknown	Local excision, tetracycline po	Antemortem, improved, died of MI, SCC, pancreatitis
25	45M	Diabetes	Unknown	Kidney	Local, skin (*P.wickerhamii*)	Unknown	8 months	Amputation of finger, local debridement	Antemortem, cured
26	45F	ESRD	Steroids, cyclophosphamide	Kidney	Local, cellulitis (*P.wickerhamii*)	Unknown	Unknown	Unknown	Unknown
27	50M	ESRD	Azathioprine, prednisone, Horse antilymphocyte globulin	Kidney	Local, skin abscess (*P.wickerhamii*)	Skin infection: *Candica albicans*, *Proteus mirabilis*, *Klebsiella spp* Bacteremia: *K.pneumoniae*, *P.aeruginosa*	2 years	Open drainage, topical gentamicin sulfate	Antemortem, died
28	50M	ESRD, DM	Azathioprine, prednisone, cyclophosphamide	Kidney	Local, Skin abscesses (*P.wickerhamii*)	Skin infection: *Candida albicans*, bacteremia: *Proteus spp.*, *Klebsiella spp*	2 years	Tetracycline po, topical Gentamicin sulfate	Antemortem, died
Present case	61M	ESLD, DM	Tacrolimus, prednisone, Mycophenolate mofetil,	Liver	Disseminated, algaemia (*P.wickerhamii*)	Bacteremia: *E.coli*; VRE Cytomegalovirus viremia	40 days	Amp B iv	Antemortem, Died

Abbreviations: GVHD, graft-versus-host disease; G-CSF, granulocyte colony-stimulating factor; MI, myocardial infarction; SCC, squamous cell carcinoma; CAD, coronary artery disease; ESRD, end stage renal disease; ESLD, end stage liver disease; COPD, chronic obstructive pulmonary disease; AmB, amphotericin B; HSV, herpes simplex virus; VRE, vancomycin resistant enterococcus; PO, orally; IV, intravenously; DM, diabetes mellitus.

LIVER TRANSPLANTATION 14:1211-1215, 2008

2011.3.11. 14:46


ERの様子

	原発事故	病院の対応・出来事	感染症関連	指導医業務	指導医個人
3/11（金）	津波襲来 全交流電源喪失 1号機炉心溶融開始	旧館機能不全（水道管破裂） 入院患者新館へ 外来診療中止　トリアージ開始 エレベータ停止 倒壊した市内の病院からの患者受入 外傷患者受入（藤沼湖ダム決壊）	破傷風トキソイドの確保	ER対応 志願当直	病院泊
3/12（土）	1号機爆発	原発近くの病院から来院（10名）	津波肺患者3名搬送	ER.外来対応	一時帰宅　断水 部屋カオス
3/13（日）		原発近くの病院から来院（7名）		病棟対応	午後自宅片付け
3/14（月）	3号機爆発	原発近くの病院から来院（5名）		ER当番	実家で風呂と 温かい夕食
3/15（火）	2号機・4号機 爆発	研修医一部離れる 職員の家族避難		外来 患者少ない 午後コンサルテーション 患者他院搬送の準備開始	家族会津に避難 病院泊
3/16（水）		薬品在庫あり 吸引チューブ、輸液ラインは複数回使用	感染症注意事項の伝達確認	患者退院	自宅泊
3/17（木） 降雪				避難してきた職員家族の受け入れ	病院泊
3/18（金）				入院乳び胸	
3/19（土）				当直	昼実家に戻り食事 夜当直
3/20（日）					帰宅 部屋の整理
3/21（月）				病棟 受け持ち患者死亡	家族避難
3/22（火）				入院 DKA血糖500	
3/23（水）		研修医一部帰る 医局会		入院2名	

「あり得ないはず」の原子炉爆発が次々と起こった！

- 風評被害も加わって、当院への原油供給が途絶えた。
- 医療品、食料品も底を尽いてきた。手術着も枯渇。
- 燃料不足で出勤できないスタッフが増えてきた。
- 自主的に病院を離れて避難する職員も続出。
- しかし入院を要する患者は日々増加（震災後1週間で41名の避難入院を収容）、病院はパンク状態。

↓

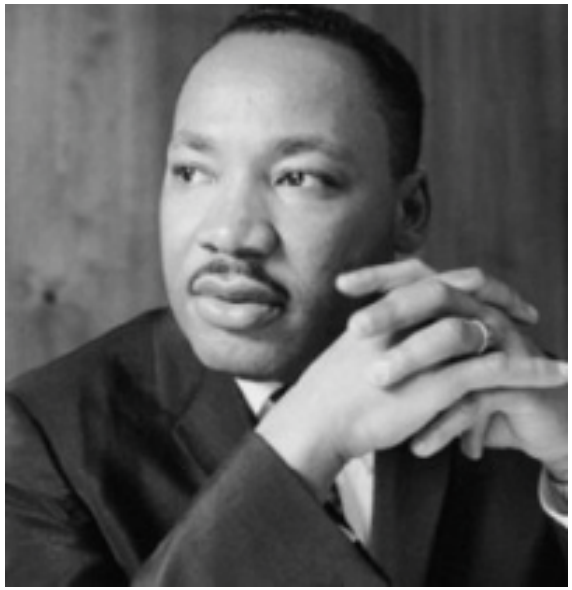
- せめて**1.移動できる患者を安全な地域に転院させ、**
  2.若い職員には避難を提案した。

研修医に「主治医感」を要求するのは酷か？
震災下におけるプロフェッショナリズムとは？

The ultimate measure of a man is not where he stands in moments of comfort and convenience, but where he stands at times of challenge and controversy.

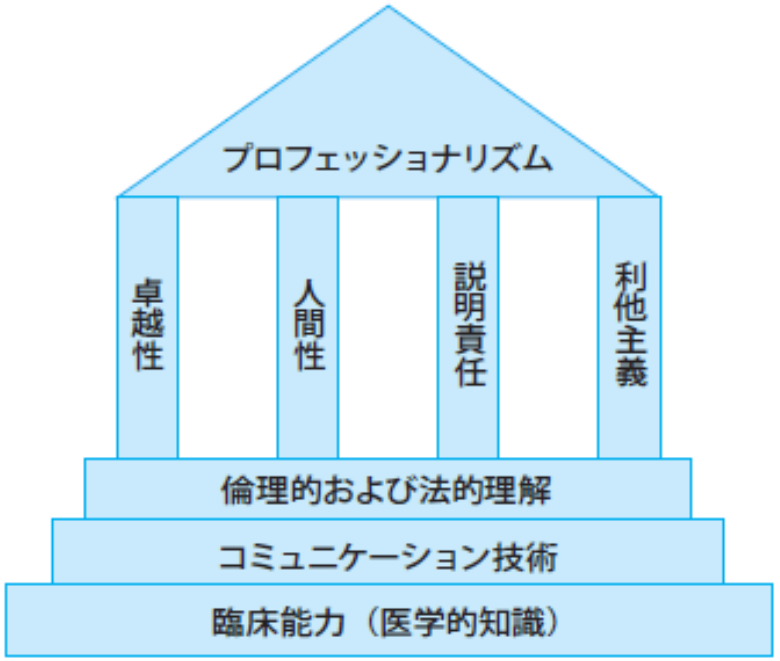
人の真価がわかるのは喜びに包まれている瞬間ではなく、試練や論争に立ち向かうときに示す態度である

Martin Luther King Jr. *Strength to Love, 1963*



プロフェッショナリズム
共通する要素

- Excellence　卓越性
- Humanism　人間性
- Accountability　説明責任
- Altruism　利他主義



Stern DT. Measuring medical professionalism. Oxford University Press, 2006, p19）

震災下でのAltruism「利他主義」

一医師個人の利益より、患者の利益を尊重する

「患者のshakingを見たら、まず主治医がshakingしろ!」

No stain No life 喜舎場の感染症語録

ある種の極限状態で、医療者が被災地を離れることに対するある指導医の視点

沈みゆく船の「船長判断」 若い医療者を守る視点

患者のみならず、他の医療者への「利他主義」

2015年6月27日　臨床研修指導医講習会　セッション３資料より

使命　Mission

Professionalism of physicians at a major teaching hospital during the Fukushima nuclear disaster

M. Narita[1], Y. Tokuda[2] and P. Barnett[3]

Discussion

An employee leaving the hospital without permission or without having a replacement is a serious issue, whether that employee is a physician, nurse, pharmacist or building maintenance person. All are essential to the patients' wellbeing and to the safety and functioning of the hospital team.

Physicians work under a variety of 'contracts', both formal and informal, with many duties and expectations being 'understood'. In all military services leaving without permission is clearly desertion, which is a criminal offense. In civilian organizations, contracts are likely to be less rigid and consequences of breach of contract are less explicit and less severe. In Fukushima, this was the case, made worse by the insidious threat of radiation sickness and all of its historic significance for Japan. The pressure on all concerned was immense. Difficult decisions had to be made with high regard and compassion for all of those involved, including those who needed to leave for whatever reason.

As the principles of medical professionalism state, 'Excellence, humanism, accountability and altruism should be upheld during an unprecedented disaster'[2]. It has been stated that, even for trainee physicians, their behaviors should be aligned with this principle and they are expected to help sick

Acknowledgement

We thank Dr. Thomas Hurt, Dr. Richard Birrer for judicious elaborating and Dr. Kazuaki Shinohara for inspiring us to leave this article.

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QJM: An International Journal of Medicine, 2016, 447–448

論文を書く「コツ」
まず「骨」格から
いきなり書き始めないこと

- アウトラインを作成すること
- 図　表を作成すること
- 自分の時間を確保すること
- 一日少しでも（10分でも）コツコツやること

Your lifework
あなたが一生かけて成すべきことは

440

The Masqueraders presenting a multi-system disease
Unusual and atypical clinical features of Scrub Typhus in Fukushima, Japan

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Background: Scrub typhus (ST) is endemic in Fukushima, where the highest number has been reported from 2006 to 2011 in Japan. Atypical clinical presentation of ST makes the diagnosis difficult followed by treatment delay which is unfortunate because ST is eminently treatable.

Methods: We reviewed the clinical features of ST in adults from 2008 to 2017 at Ohta Nishinouchi General Hospital, a major teaching hospital in Fukushima, Japan.

Results: 55 cases (serotype Karp 24, Irie/Kawasaki 21, Hirano/Kuroki 10) of ST were confirmed by elevated IgM and IgG in paired sera and PCR positivity within eschars. Complications were documented in 13% (7/55: 4 Karp and 3 Irie/Kawasaki), cardiovascular (4 cases of paroxysmal atrial fibrillation), neurological (2 cases of syncope, encephalitis) and metabolic/electrolyte abnormalities (hyponatremia /SIADH). In terms of atypical clinical features, the cases without triad (fever, rash and eschars) were found in 31% (17/55). The cases of "eschar negative scrub typhus" were found in 11% (6/55: Karp 1, Irie/Kawasaki 1, Hirano/Kuroki 4). Patients without fever and rash were 18% (10/55: Karp 2, Irie/Kawasaki 6, Hirano/Kuroki 2) and 9% (5/55: Karp 2, Irie/Kawasaki 1, Hirano/Kuroki 1). Severe cases complicated with shock and DIC (7%, 4/55) including one fatal case (2%, 1/55: Hirano/Kuroki). Besides the typical cases with triad 53% (29/55), the unusual complications and atypical features were found in total 40% (22/55).

Conclusion: The diagnosis of ST becomes a clinical challenge if typical features are absent. In an endemic area, atypical presentation of ST involving multi-system disease is common.

Table 1. Serotypes, Phylogenic types and Vectors of ST

	The summer type		The autumn-winter type
Serotype	Karp		Irie/Kawasaki, Hirano/ Kuroki
Phylogenetic type	JP-1/Matsuzawa	JP-2/KNP1	Kawasaki, Kuroki
Vector chigger mites	*L.Intermedium* 	*L.pallidum* 	*L.Scutellare* 
Regional distribution	North, middle and east coast (Abukuma mountains) of Fukushima		South to middle of Fukushima
Preference to human	"Slow biter" to soft skin after migration		"Quick-biter" without migration

L: Leptotrombidium

Figure 1. Categorized Clinical Features of ST in Fukushima 2008-2017

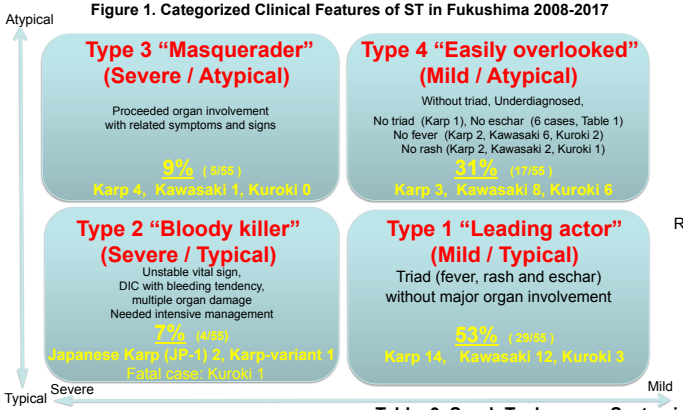


Figure 2. Clinical Features of Scrub Typhus (% of total 55 cases)

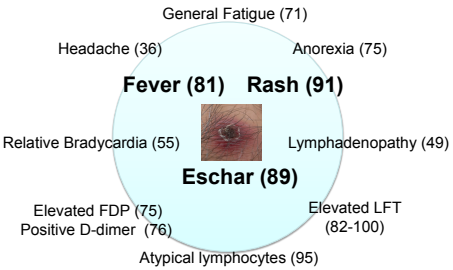


Table 2. Clinical overview of "non-eschar" ST (11% 6/55)

Age/ Sex	Serotypes	Serology titer (IP IgG/IgM)	Fever (℃)	Rash Distribution	Treatment	PD/HD/DTT	VNT	Comorbidities /CCI	Prognosis /From onset to death (Days)
62/M	Karp	-/2560 2560/5120	37.1	None	None	6/N/N	2	DM. HTN, Adrenal tumor /1	Survival
72/F	Hirano/Kuroki	10240/20480 10240/10240	39.4	Neck, chest	None	0/N/N	4	HTN, DLP/ 0	Survival
52/F	Hirano/Kuroki	2560/20480 20480/20480	38.5	Scalp	DOXY po:10D	0/5/5	2	ITP/ 0	Survival
68/M	Irie/Kawasaki	80/640 5120/5120	38.7	chest	DOXY po: 7D	5/2/7	1	PD, Autoimmune bullous disease / 1	Death (PD,PNA) / 1642
62/F	Hirano/Kuroki	1280/-	40.0	Trunk	MINO po:14D	0/7/7	6	HTLV-1 positive (f/b ATL) / 0	Survival
85/M	Hirano/Kuroki	10240/2560 20480/5120	37.5	Trunk	MINO iv:8D DOXY po:5D	5/17/23	2	Bladder Ca, AA, ILD / 2	Death (ILD) / 279

ST: Scrub Typhus M: Male F: Female IP: Immnoperoxidase DOXY: Doxycyline MINO: Minocycline po: per os D:Days PD: Patient delay HD: Hospital delay DTT: Days to treatment N: Not to detect VNT: Visits number of times to the diagnosis CCI: Charlson Comorbidity Index DM: Diabetes Mellitus HTN: Hypertension DLP: Dyslipidemia ITP; Idiopathic thrombocytopenia PD: Parkinson Disease HTLV-1: Human T-cell Lymphotropic Virus f/b; followed by ATL: Adult T-cell Leukemia Ca: carcinoma AA: Aortic aneurysm ILD: Interstitial Lung Diseases PNA: Pneumonia

Table 3. Scrub Typhus as a Systemic Disease (% of total 55 cases)

	Signs and Symptoms	Lab abnormalities	Differential /Tentative Diagnoses	Organ/system Complications
Systemic, Skin	Fever (81) Rash (91) Eschar (89) General fatigue (71) Conjunctival suffusion (33)	Leukocytosis (18) Elevated CRP (87)	Drug fever, Influenza, Varicella Herpes Zoster, Viral infection Japanese Spotted Fever Murine Typhus Tularemia	
Cardiovascular	Hypotension (4) Relative bradycardia (55)		Arrthythmia Congestive Heart Failure	Paroxysmal atrial fibrillation (7)
Gastroenterology	Anorexia (75) Abd pain, nausea (45) GI bleeding (1)	Abnormal LFT AST (89) ALT (82) LDH (100)	Peptic Ulcer Diseases Acute Hepatitis Cholangitis	Acute peptic ulcer bleeding with exposed vessel (2) Peptic ulcer (2)
Neurology	Headache (36) Consciousness disturbance		Meningoencephalitis Cereverovascular diseases	Meningoencephalistis (2)
Pulmonary		Pulmonary infiltrations (16)	Pneumonia	
Renal / Metabolic		Hematuria (42) Proteinuria (51)	Renal failure (pre-renal/renal)	Acute renal failure (7) Hyponatremia/ SIADH (2)
Hematology	Lymphadenopathy (49)	Thrombocytopenia (29) Atypical lymphocytes (95) elevated FDP (75) Positive D-dimer (76) Hepatosplenomegaly (15)	Malignant Lymphoma Leukemia Infectious mononucleosis	DIC with bleeding tendency (7)
Musculoskeletal	Myalgia, Arthralgia (15)		Myositis, arthritis	Arthritis (synovial fluid PCR+) (2)

Fever > 38.0℃ Hypotension: Systemic BP <70 mmHg Relative bradycardia:<108 bpm (beats per minutes) on 38.3℃, <132 bpm on 40℃ Leukocytosis >9800/μL Elevated CRP >2.5 mg/dL AST, ALT >40 IU/L LDH >250 IU/L Hematuria and Proteinuria: urine dipstic positive Thrombocytopenia <10,000/μL Elevated FDP (Fibrin/fibrinogen degradation products) >4 μg/mL Positive D-dimer > 1 μg/mL

Mentorship
メンターを信頼すること

論文を書く「コツ」など存在しないが....あるとすれば

「骨の髄から」　　自分が好きと言える執筆テーマを
「骨格」　　アウトライン、図、表を吟味してから

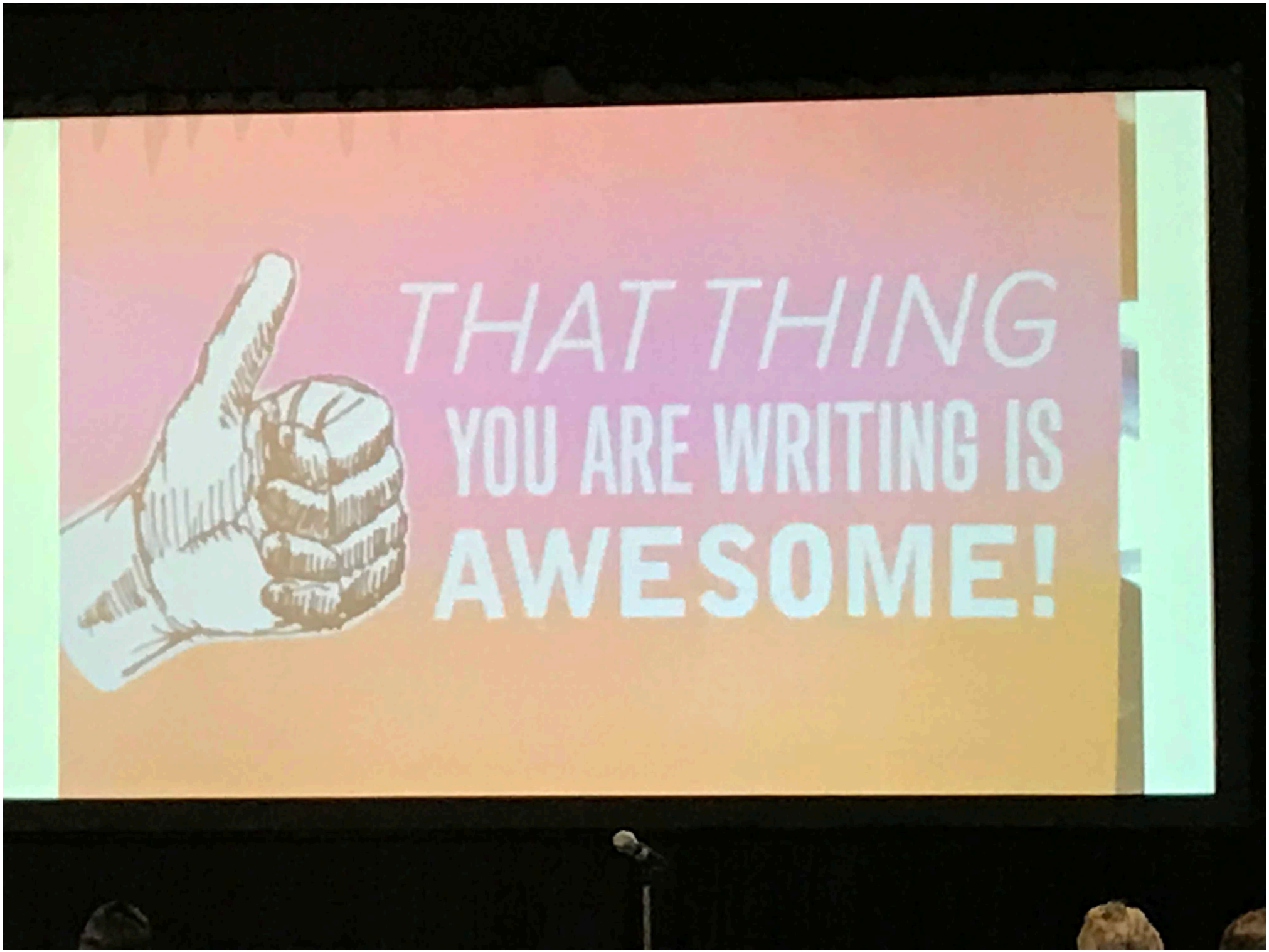
「骨のある」
「骨を拾ってくれる」　　メンターと常に相談しながら

「骨身を惜しまず」　　「社会・後世に資する使命感」を持ち

「骨骨（コツコツ）」　　毎日少しずつ

「骨を埋める」つもりで　自身のライフワークを仕上げる

秋田県健康環境センター　佐藤　寛子先生　提供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AWESOME!