Instructive ID Cases in People with HIV from New York City

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Disclosures

- None

Case 1: 50s M with well controlled HIV presenting with fever and altered mental status

HIV History

- Diagnosed: mid 2000s, risk factor IVDU
- OIs: Remote dermatomal zoster around time of diagnosis
- CD4 nadir: >200
- ARV History: DTG + TAF/FTC, LPV/r + TDF/FTC
- Resistance: None known

Medical/Social History

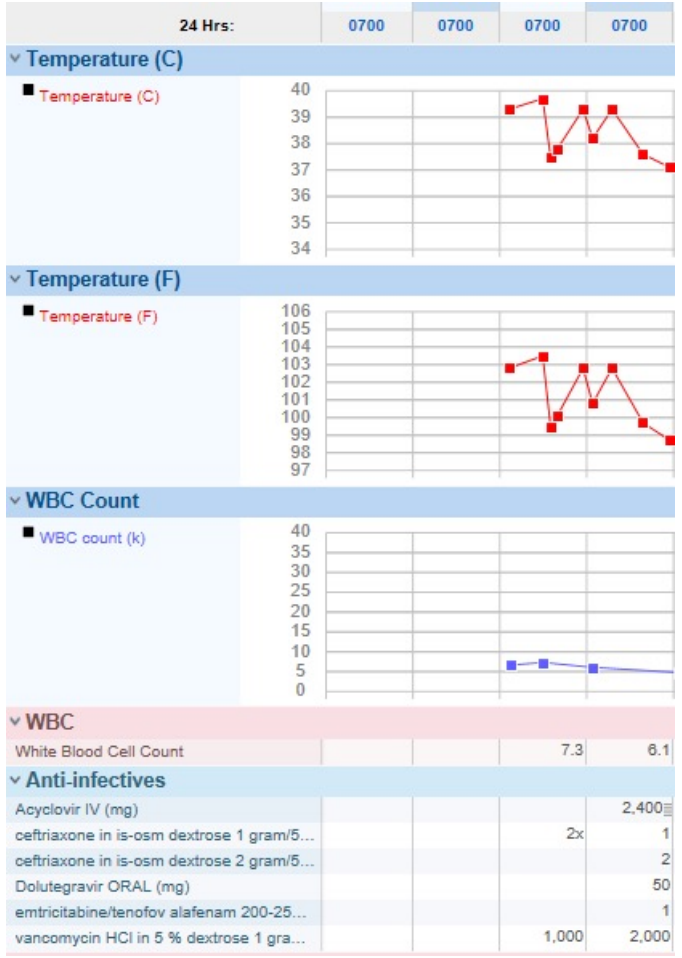
- HIV, virally suppressed for >5 years with most recent CD4 cell count 926/30% 2.5 months prior to presentation
- Opioid use disorder (last use >10 years ago)
- Intermittent/ongoing cocaine use
- Treated HCV
- Lives with wife (HIV negative) who is only sexual partner

50s M with well controlled HIV presenting with fever and altered mental status

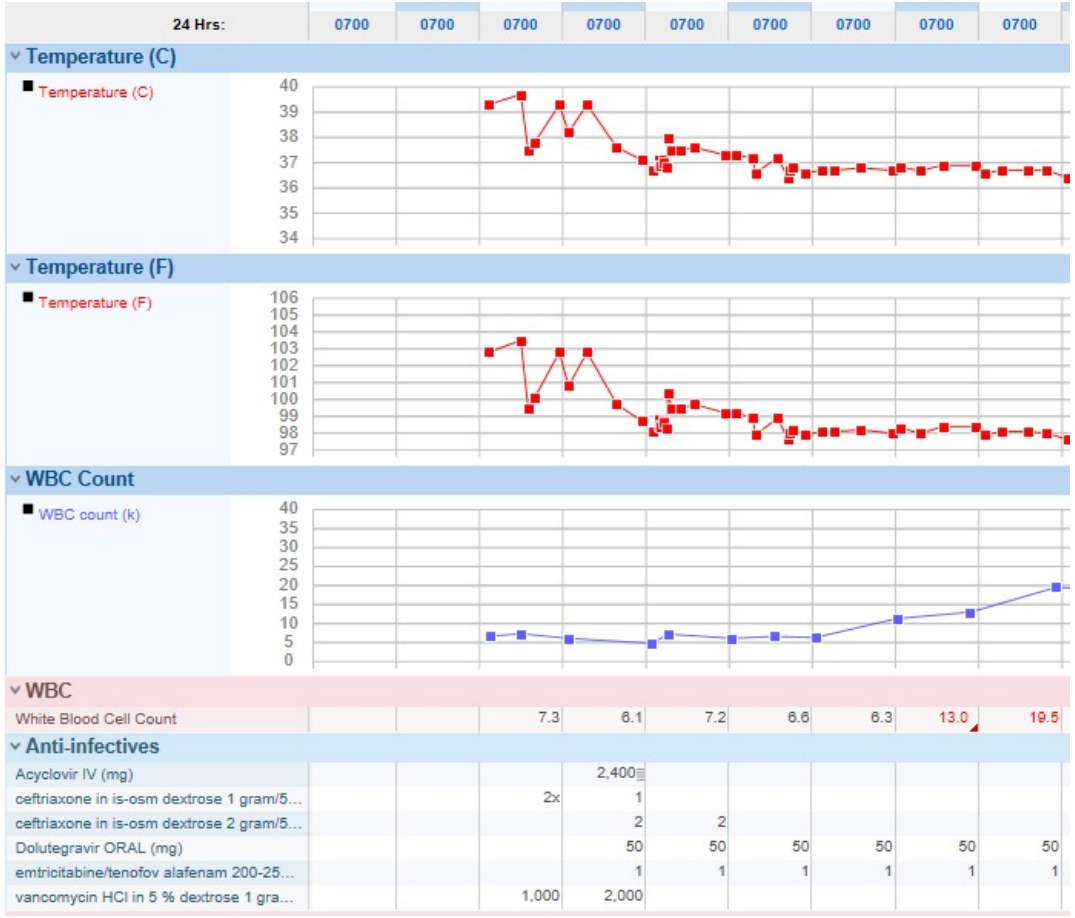
Admission Labs:

- BUN 18, Creatinine 1.39
- ALT 86, AST 85, ALP 49, T bili 0.9
- WBC 7.3, HCT 43.9, PLT 33
- SARS-CoV-2 PCR negative

- Head CT: No acute process



HIV-1 VL from admission 1,646,577 copies/mL with CD4 cell count 237/17%



Retroviral Rebound Syndrome

BRIEF COMMUNICATION

Retroviral Rebound Syndrome after Cessation of Suppressive Antiretroviral Therapy in Three Patients with Chronic HIV Infection

Roy Colven, MD; Robert D. Harrington, MD; David H. Spach, MD; Calvin J. Cohen, MD; and Thomas M. Hooton, MD

Background: Although viral rebound follows cessation of suppressive antiretroviral therapy in chronic HIV infection, a viremic clinical syndrome has not been described.

Objective: To describe a retroviral syndrome associated with cessation of effective antiretroviral therapy in chronic HIV infection.

Design: Case reports.

Setting: Outpatient HIV specialty clinics in Seattle, Washington, and Boston, Massachusetts.

Patients: Three patients with chronic HIV infection who discontinued suppressive antiretroviral therapy.

Measurements: Clinical course, plasma HIV RNA levels, and CD4 cell counts before, during, and after cessation of antiretroviral therapy.

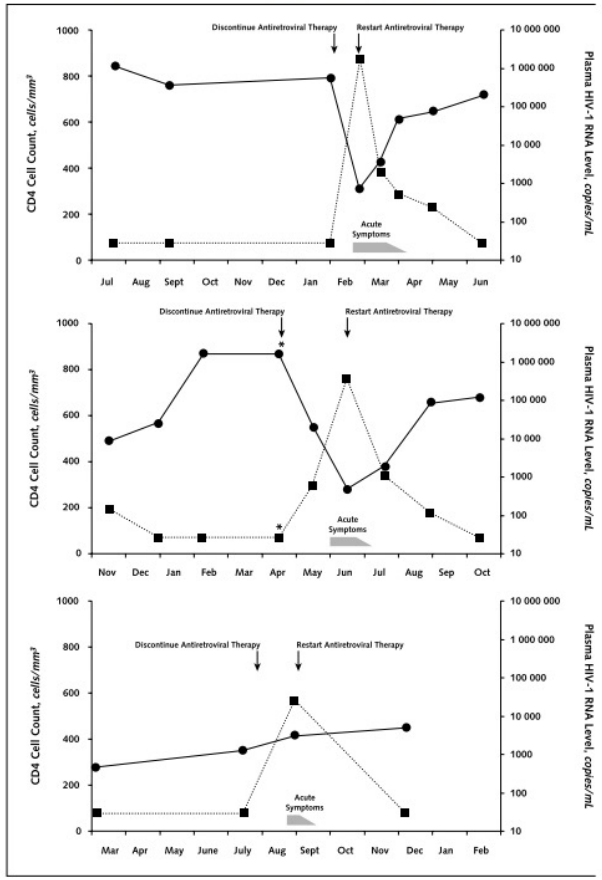
Results: Within 6 weeks after stopping antiretroviral therapy, each patient experienced a clinical illness that resembled a primary HIV syndrome. This coincided with a marked increase in HIV RNA level and, in two of three patients, a decrease in CD4 cell count. After antiretroviral therapy was restarted, each patient's symptoms rapidly resolved in association with resuppression of HIV RNA and increase in CD4 cell count or percentage.

Conclusion: A retroviral rebound syndrome similar to that seen in primary HIV syndrome can occur in patients with chronic HIV infection after cessation of suppressive antiretroviral therapy.

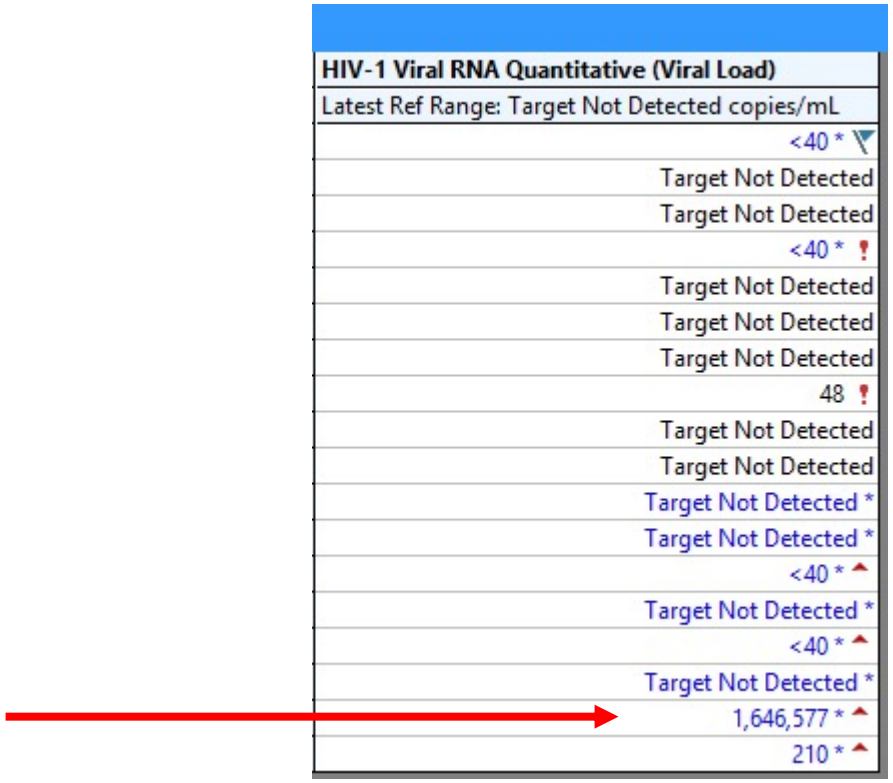
Ann Intern Med. 2000;133:430-434.

For author affiliations, current addresses, and contributions, see end of text.

CD4 cell counts (*circles*) and HIV RNA levels (*squares*) before, during, and after antiretroviral cessation.



Viral loads over the last 8 years for patient



HIV-1 Viral RNA Quantitative (Viral Load)
Latest Ref Range: Target Not Detected copies/mL
<40 *
Target Not Detected
Target Not Detected
<40 *
Target Not Detected
Target Not Detected
Target Not Detected
48
Target Not Detected
Target Not Detected
Target Not Detected *
Target Not Detected *
<40 *
Target Not Detected *
<40 *
Target Not Detected *
1,646,577 *
210 *

Simultaneously: counterfeit HIV medications reported in NYC

Company Statements

Gilead Warns of Counterfeit HIV Medication Being Distributed in the United States

Foster City, Calif., August 5, 2021 – Gilead Sciences has become aware of tampered and counterfeit versions of its once-daily single tablet HIV treatment regimen Biktarvy® (bictegravir 50 mg, emtricitabine 200 mg, and tenofovir alafenamide 25 mg tablets) and its HIV treatment and prevention medication Descovy® (emtricitabine 200 mg and tenofovir alafenamide 25 mg tablets) in circulation within U.S. drug distribution networks. Distributors not authorized by Gilead to sell Gilead-branded medicine have sold these counterfeits to pharmacies where genuine Gilead bottles have been tampered with a counterfeit foil induction seal or label and contain incorrect tablets. Working in communication with the U.S. Food and Drug Administration (FDA), Gilead has alerted potentially impacted pharmacies to investigate the potential for counterfeit or tampered Gilead medication sold by distributors not authorized by Gilead that may be within their recent supply and to remain vigilant to the potential for this to occur in the future. The authenticity and safety of Gilead-branded medicines can only be secure when obtained directly through Gilead's authorized distributors.

Gilead continues to work closely with the FDA, pharmacies, and legal authorities to remove counterfeit and tampered medication from circulation and to prevent future distribution of these medications.

"The safety of individuals taking Gilead medication is always our first priority," said Merdad Parsey, MD, PhD, Chief Medical Officer, Gilead Sciences. "We are taking aggressive action to ensure that healthcare providers and people who rely on our medicines can confidently distinguish authentic Gilead products from counterfeit drugs."

NYC DOHMH Advisory about Tampered and/or Counterfeit Versions of Biktarvy and Descovy

Uncategorized

On Aug. 5, 2021, Gilead Sciences, Inc. (Gilead) issued a Company Statement warning of tampered and/or counterfeit versions of HIV treatment regimen Biktarvy (bictegravir 50 mg, emtricitabine 200 mg, and tenofovir alafenamide 25 mg tablets) and HIV treatment and prevention medicine Descovy (emtricitabine 200 mg and tenofovir alafenamide 25 mg tablets) in circulation in the U.S. Gilead is working with the U.S. Food and Drug Administration (FDA), pharmacies, and legal authorities to remove tampered and/or counterfeit medicines from circulation and to prevent further distribution. **The Company Statement includes information to determine whether dispensed Biktarvy and Descovy are authentic, and sets forth the following instructions on reporting potentially tampered and/or counterfeit medicines**:

HIV related thrombocytopenia is associated with viral load

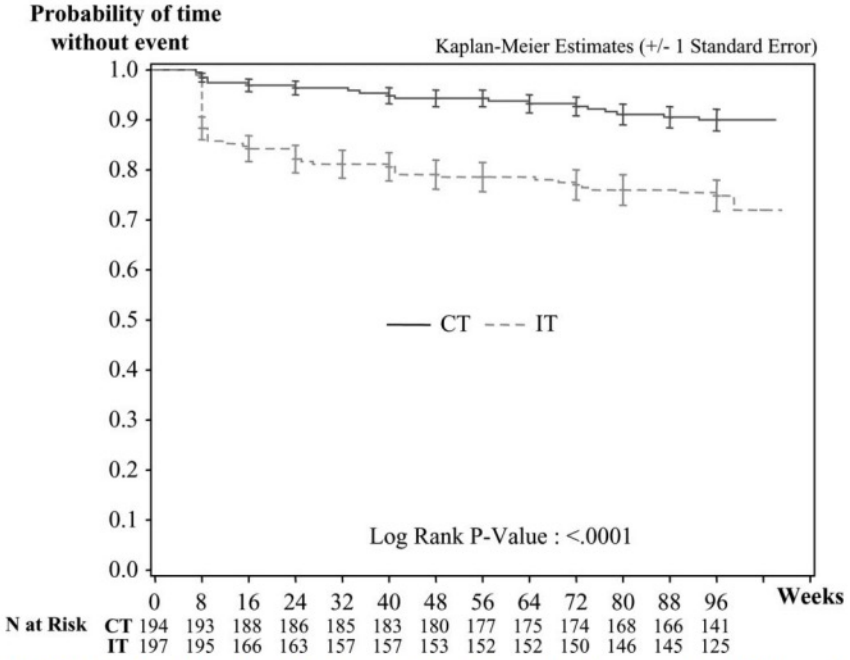


FIGURE 1. Kaplan–Meier estimates of the probability of a first episode of thrombocytopenia ($<150 \times 10^3/mm^3$) over 96 weeks in patients randomly assigned to intermittent or continuous therapy—intent to treat analysis. This figure shows obtained data within 2 weeks before or after a scheduled visit. CT, continuous arm; IT, intermittent arm.

Bouldouyre, Marie-Anne MD[*]; Charreau, Isabelle MD[†]; Marchou, Bruno MD[‡]; Tangre, Philippe MD[†]; Katlama, Christine MD[§]; Morlat, Philippe MD[¶]; Meiffredy, Vincent MD[†]; Vittecoq, Daniel MD[‖]; Bierling, Philippe MD[#]; Aboulker, Jean-Pierre MD[†]; Molina, Jean-Michel MD[*] and the ANRS 106 Study Group Incidence and Risk Factors of Thrombocytopenia in Patients Receiving Intermittent Antiretroviral Therapy: A Substudy of the ANRS 106-Window Trial, JAIDS Journal of Acquired Immune Deficiency Syndromes: December 2009 - Volume 52 - Issue 5 - p 531-537 doi: 10.1097/QAI.0b013e3181be73e3

O'Bryan *et al. BMC Res Notes (2015) 8:595*
DOI 10.1186/s13104-015-1548-3

BMC Research Notes

SHORT REPORT Open Access

Impact of the highly active antiretroviral therapy era on the epidemiology of primary HIV-associated thrombocytopenia

Thomas A. O'Bryan[1,2,3*], Jason F. Okulicz[1,3], William P. Bradley[1,2], Anuradha Ganesan[1,2,4], Xun Wang[1,2] and Brian K. Agan[1,2]

Abstract

Background: Primary HIV-associated thrombocytopenia (PHAT) typically improves with highly active antiretroviral therapy (HAART); however, cases continue to occur. Data comparing the epidemiology of PHAT between the pre-HAART and HAART eras are limited. We retrospectively examined the incidence of PHAT over 28 years in the US Military HIV Natural History Study (NHS) from 1986 to 2013.

Results: Subjects had a nadir platelet count $<100 \times 10^9$/l with no other identifiable cause. Time periods were categorized as pre-HAART (1986–1995), early HAART (1996–2001), and later HAART (2002–2013). Incidence, demographic data, and CD4 count were compared across the three eras. A generalized estimating equations model was used to assess any association of platelet count and HIV viral load in cases diagnosed during the HAART eras. 218 participants met the case definition. 86.2 % of cases occurred prior to 2002. The incidence of PHAT per 1000 person-years of follow-up was 16.3, 4.6, and 1.9 during pre-HAART, early HAART and later HAART eras respectively. CD4 cell counts were significantly higher in the HAART eras at the time of thrombocytopenia ($p < 0.001$). Of patients diagnosed after 1996, 96.4 % were viremic within six months preceding the platelet nadir and over half were antiretroviral naïve. Viral load (per $\log_{10}$ copies/ml) inversely correlated with platelet count throughout the HAART eras ($p < 0.0001$).

Conclusions: The incidence of PHAT has markedly decreased in the HAART era. However, viremic individuals, including those with healthy CD4 cell counts, may be at risk. Achieving viral suppression as early as possible may decrease the incidence further.

Keywords: HIV, Primary, Thrombocytopenia, Antiretroviral, HAART, Incidence, Viremia, CD4

Case 2: 40s M with HIV with cold like symptoms and right hand/left foot pain and weakness

HIV History

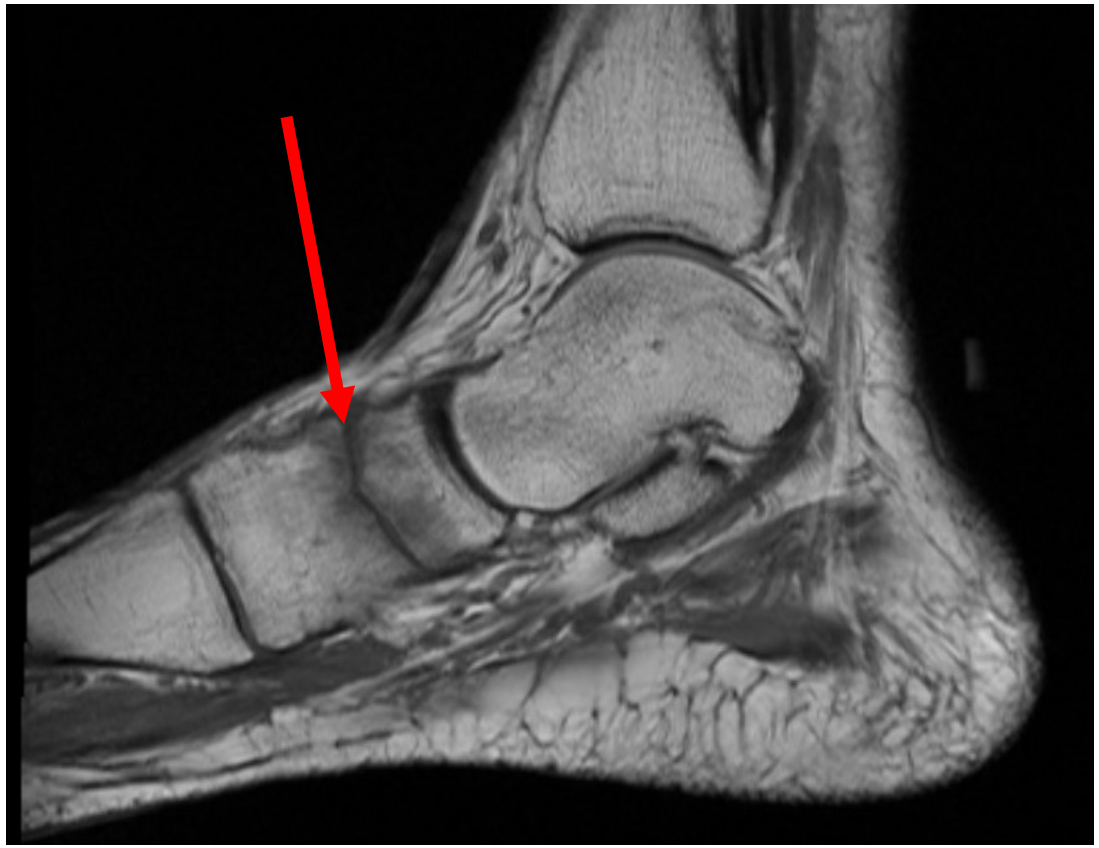
- Diagnosed: mid 1990s, risk factor MSM
- OIs: disseminated VZV about 4 years before current presentation
- CD4 nadir: <50 around 2010, but closer to 200 more recently
- ARV History: EVG/c/TAF/FTC (current), prior EVG/c/TDF/FTC, TDF/FTC + ATV/r
- Resistance: None known (though long history of intermittent adherence)

Medical/Social History

- HIV: most recent VL <40 with CD4 cell count 134/9% 1 month ago; 2 months ago VL was 82,925 copies/mL
- Genital HSV-2 (episodic valacyclovir)
- Syphilis
- Multiply recurrent chlamydia/gonorrhea of various sites
- Rectal abscess
- Lives alone, no IVDU

40s M with HIV with cold like symptoms and right hand/left foot pain and weakness

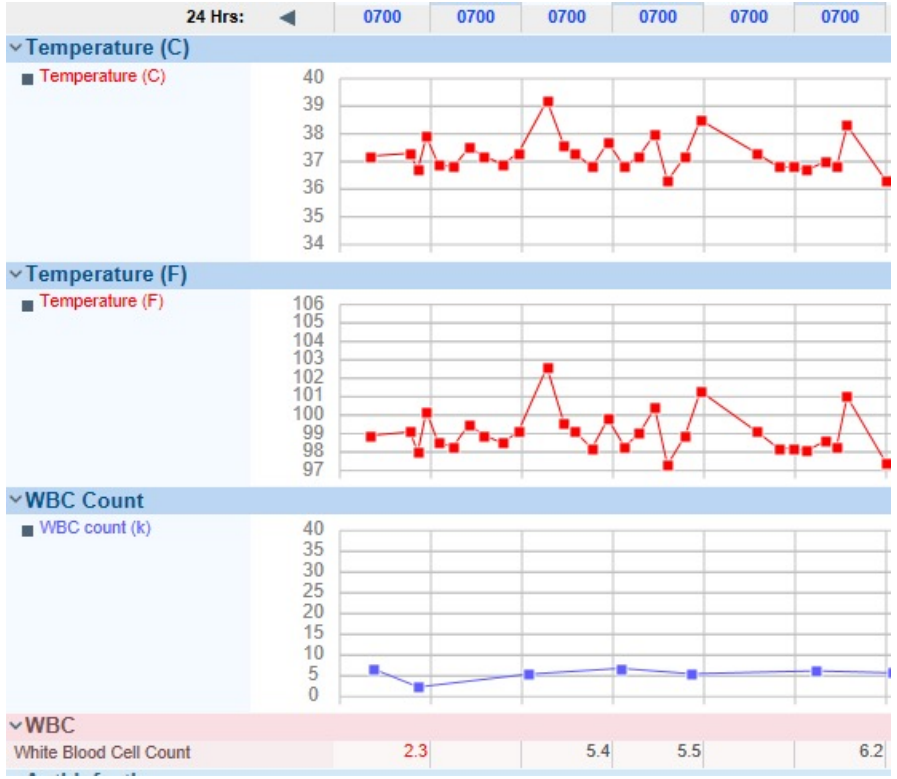
- On exam, he has left ankle and right third finger proximal interphalangeal joint swollen and erythematous
- Joints are exquisitely tender to palpation with micromotion tenderness
- “Weakness” is secondary to pain
- MRI Left Foot: “diffuse marrow signal abnormality involving multiple tarsal bones and base of second and third metatarsal. Erosive changes along margins of navicular/medial cuneiform joint line. Small effusion.”



40s M with HIV with cold like symptoms and right hand/left foot pain and weakness

Admission Labs:

- BUN 13, Creatinine 0.84
- ALT 18, AST 46, ALP 60, T bili 0.84
- WBC 2.3 (bands 10%), HCT 41.8, PLT 129
- ESR 108, CRP 13.5
- SARS-CoV-2 PCR negative
- Cryptococcal serum antigen negative



40s M with HIV with cold like symptoms and right hand/left foot pain and weakness

Blood, Bacteriology Culture

Growth of

Haemophilus influenzae !

Beta Lactamase Negative

This organism was identified using test methods dev
Drug Administration has not approved or cleared thi
be used as the sole means for clinical diagnosis or
laboratory is certified under the Clinical Laborato

Gram Stain

From Aerobic Bottle: Gram negative bacilli,tiny

Resulting Agency: MOSES

Susceptibility

	Haemophilus influenzae MIC/INTERPRETATION
Ampicillin	Sensitive
Azithromycin	Sensitive
Ceftriaxone	Sensitive
Ciprofloxacin	Sensitive
Identification	Identificat...
Tetracycline	Intermediate
Trimethorprim/Sulfamethoxazole	Sensitive

- Blood Cultures:
  - Admission: 1/2 H flu
  - Day 3: Negative
  - Day 4: Negative
- No fluid was able to be extracted from hand or ankle despite attempts
- TTE normal
- Diagnosed with presumed disseminated H flu infection
- Treated with 4-week course of IV ceftriaxone -> PO levofloxacin with resolution of symptoms

HIV and risk for invasive Haemophilus influenza infection

JAMA | Original Investigation

Invasive Nontypeable *Haemophilus influenzae* Infection Among Adults With HIV in Metropolitan Atlanta, Georgia, 2008-2018

Lauren F. Collins, MD; Fiona P. Havers, MD, MHS; Amy Tunali, MPH; Stephanie Thomas, MSPH; Julie A. Clennon, PhD, MSc; Zanthia Wiley, MD; Melissa Tobin-D'Angelo, MD, MPH; Tonia Parrott, PhD; Timothy D. Read, PhD; Sarah W. Satola, PhD; Robert A. Petit III, PhD, MS; Monica M. Farley, MD

Supplemental content

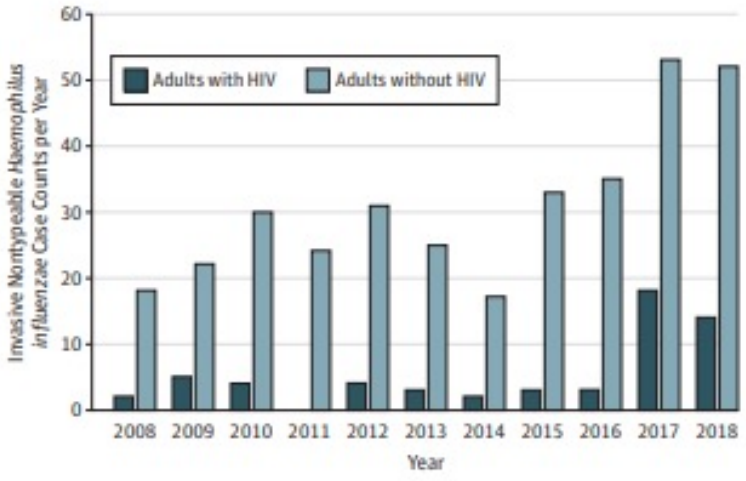
IMPORTANCE Invasive nontypeable *Haemophilus influenzae* (NTHi) infection among adults is typically associated with bacteremic pneumonia. Nontypeable *H influenzae* is genetically diverse and clusters of infection are uncommon.

RESULTS Among 553 adults with invasive NTHi infection (median age, 66 years [Q1-Q3, 48-78 years]; 52% male; and 38% black), 60 cases occurred among persons with HIV. Incidence of invasive NTHi infection from 2017-2018 among persons with HIV (41.7 cases per 100 000) was significantly greater than from 2008-2016 among those with HIV (9.6 per 100 000; $P < .001$) and from 2008-2018 among those without HIV (1.1 per 100 000; $P < .001$). Among adults aged 18 to 55 years with invasive NTHi infections from 2017-2018 (n = 179), persons with HIV (n = 31) were significantly more likely than those from 2008-2018 without HIV (n = 124) to be male (94% vs 49%, respectively; $P < .001$), black (100% vs 53%; $P < .001$), and have septic arthritis (35% vs 1%; $P < .001$). Persons with HIV who had invasive NTHi infection from 2017-2018 (n = 31) were more likely than persons with HIV who had invasive NTHi infection from 2008-2016 (n = 24) to have septic arthritis (35% vs 4%, respectively; $P = .01$). Pulsed-field gel electrophoresis of 174 of 179 NTHi isolates from 18- to 55-year-olds identified 2 genetically distinct clonal groups: cluster 1 (C1; n = 24) and cluster 2 (C2; n = 23). Whole-genome sequencing confirmed 2 clonal lineages of NTHi infection and revealed all C1 isolates (but none of the C2 isolates) carried IS*1016* (an insertion sequence associated with *H influenzae* capsule genes). Persons with HIV were significantly more likely to have C1 or C2 invasive NTHi infection from 2017-2018 (28/31 [90%]) compared with from 2008-2016 among persons with HIV (10/24 [42%]; $P < .001$) and compared with from 2008-2018 among those without HIV (9/119 [8%]; $P < .001$). Among persons with C1 or C2 invasive NTHi infection who had HIV (n = 38) (median age, 34.5 years; 100% male; 100% black; 82% men who have sex with men), 32 (84%) lived in 2 urban counties and an area of significant spatial aggregation was identified compared with those without C1 or C2 invasive NTHi infection.

CONCLUSIONS AND RELEVANCE Among persons with HIV in Atlanta, the incidence of invasive nontypeable *H influenzae* infection increased significantly from 2017-2018 compared with 2008-2016. Two unique but genetically related clonal strains were identified and were associated with septic arthritis among black men who have sex with men and who lived in geographic proximity.

Emergence of invasive nontypeable H flu associated with septic arthritis in MSM

Figure 1. Invasive Nontypeable *Haemophilus influenzae* Case Counts From 2008-2018 in Atlanta, Georgia, by HIV Status



Among persons with HIV, the rate of invasive nontypeable *H influenzae* significantly increased from the time period of 2008-2016 to 2017-2018 ($P < .001$).

Table 1. Characteristics of Adults Aged 18 to 55 Years With Invasive Nontypeable *Haemophilus influenzae* (NTHi) Infection in Metropolitan Atlanta, Georgia, by HIV Status

	No./Total No. of Invasive NTHi Infection Cases (%)[a]			
	In 2008-2016 With HIV (n = 24)	In 2017-2018 With HIV (n = 31)	In 2008-2016 Without HIV (n = 85)	In 2017-2018 Without HIV (n = 39)
Age, median (range), y	39 (21-53)	35 (19-50)	39 (18-55)	42 (21-55)
Clinical syndrome[d]				
All types of bacteremia	24/24 (100)	29/31 (94)	83/85 (98)	36/39 (92)
Pneumonia or empyema	9/24 (38)	7/31 (23)	31/85 (36)	16/39 (41)
Septic shock	5/24 (21)	5/31 (16)	7/85 (8)	5/39 (13)
Bacteremia without focus	3/24 (13)	7/31 (23)	33/85 (40)	12/39 (31)
Meningitis	1/24 (4)	2/31 (6)	1/85 (1)	2/39 (5)
Septic arthritis	1/24 (4)	11/31 (35)	1/85 (1)	0
Pericarditis	1/24 (4)	0	0	2/39 (5)
Other	6/24 (25)[e]	2/31 (6)[f]	11/85 (11)[g]	6/39 (15)[h]
Intensive care unit stay	9/24 (38)	6/29 (21)[i]	29/60 (48)	15/33 (45)
Died	2/24 (8)	2/31 (6)	11/85 (13)	5/39 (13)
Isolates with clustering by pulsed-field gel electrophoresis[j]	10/24 (42)	28/31 (90)	2/82 (2)	7/37 (19)
Cluster 1	1/10 (10)	21/28 (75)	0/2	2/7 (29)
Cluster 2	9/10 (90)	7/28 (25)	2/2 (100)	5/7 (71)

Case 3: 50s F with well controlled HIV presenting with 2 months of worsening cough and fever

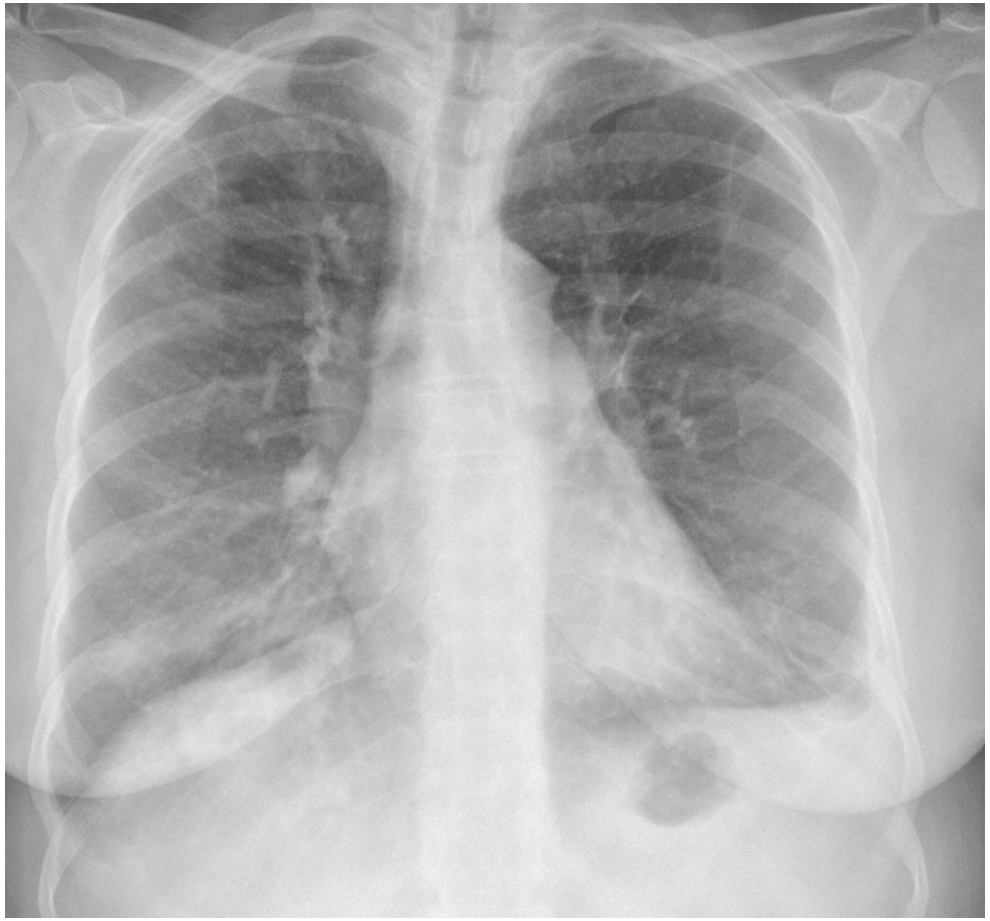
HIV History

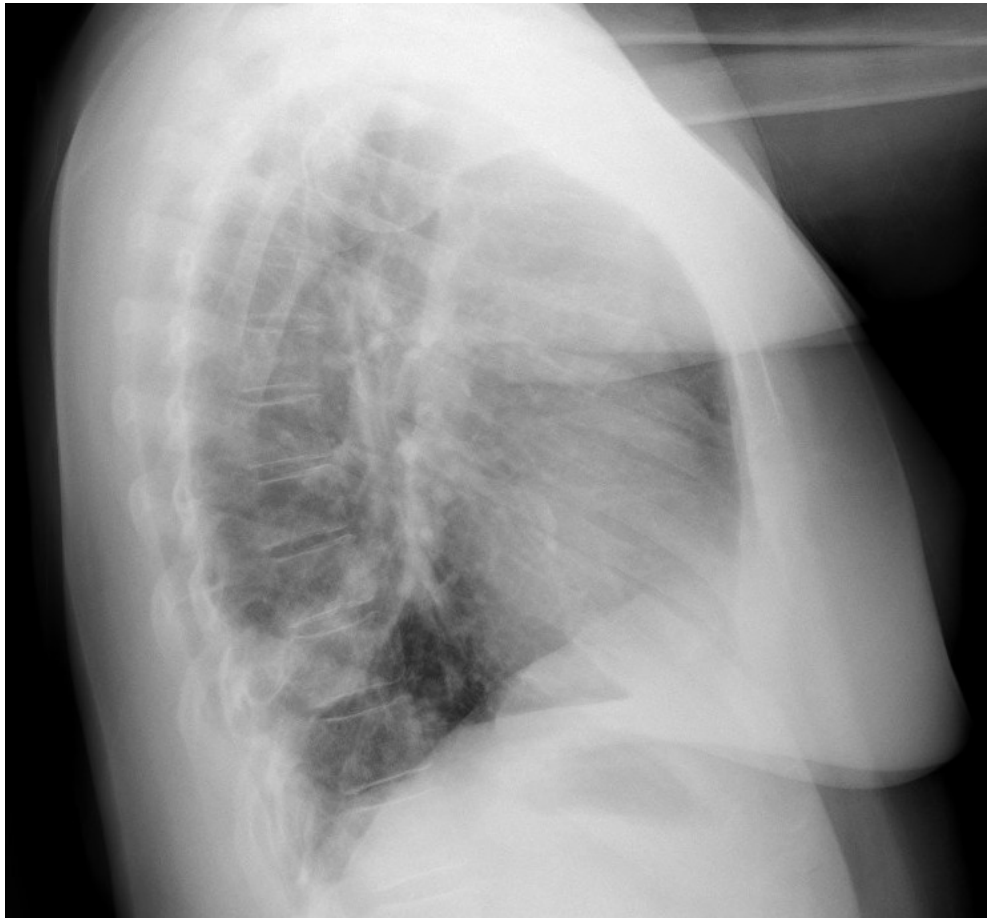
- Diagnosed: late 1990s, risk factor: husband with HIV
- OIs: none
- CD4 nadir: 300/24%
- ARV History: DTG/3TC/ABC
- EFV + 3TC/ABC
- Resistance: None known

Medical/Social History

- HIV: most recent VL undetectable with CD4 cell count 542/37% 4 months prior to presentation
- “Recurrent pneumonia” (treated 3 months and 2 months prior to presentation)
- Grave’s disease (treated)
- Born in the Dominican Republic, moved to US about 35 years ago and returns annually
- Never smoker

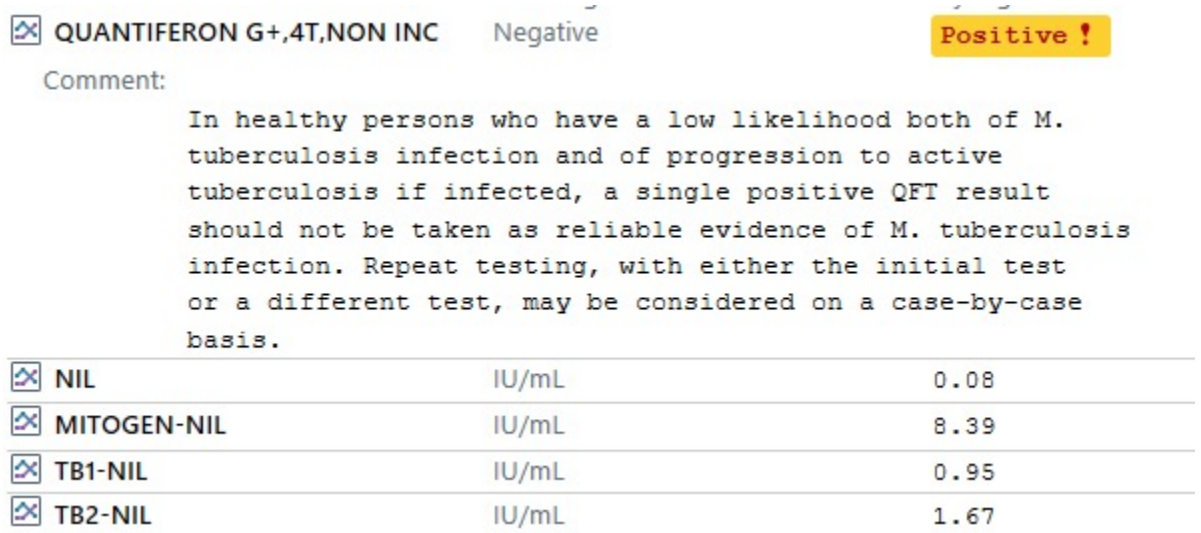
Diagnosed with RLL pneumonia and treated with levofloxacin 2 months before presentation





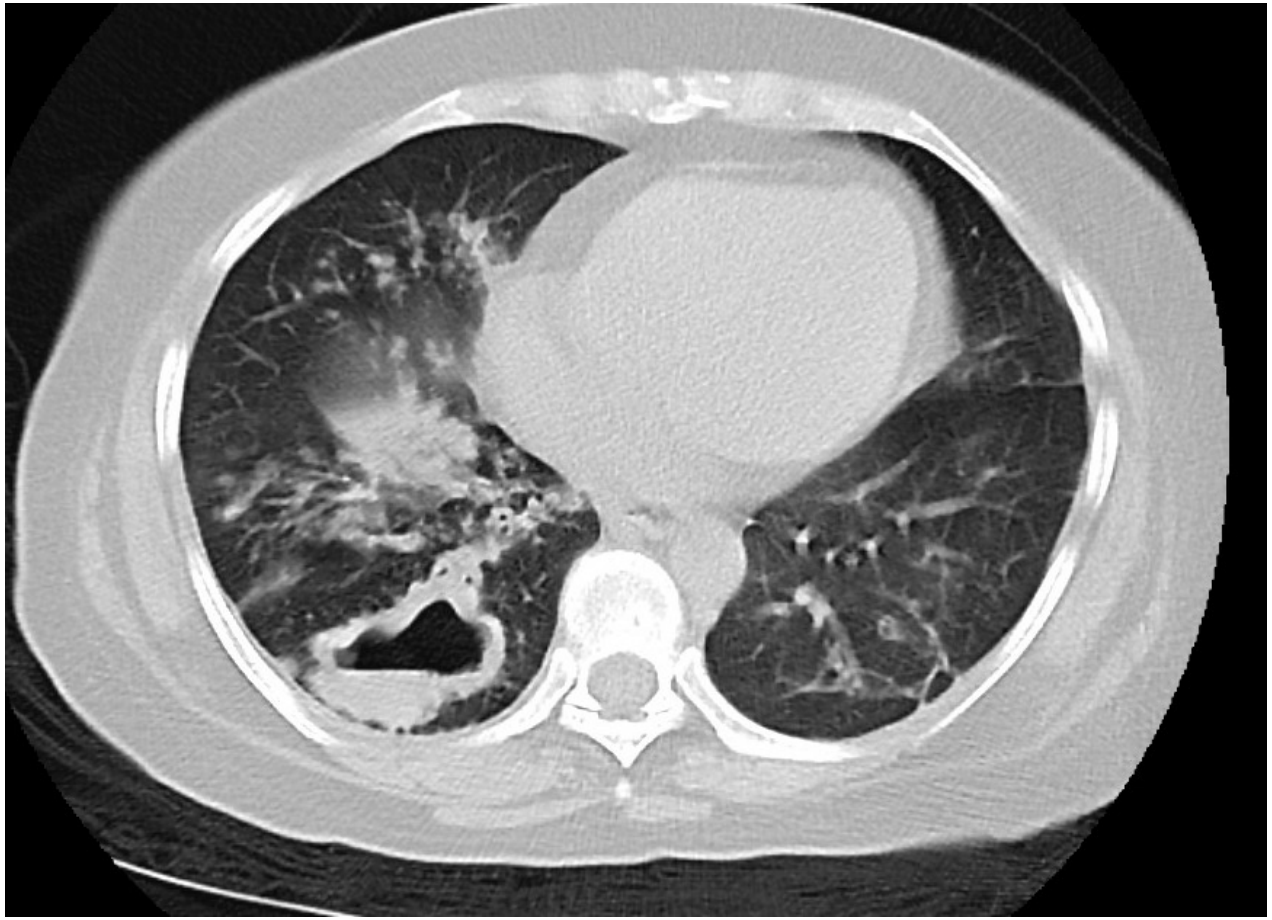
Had relatively new LTBI based on newly positive TB IGRA, and had not yet been treated

- TB IGRA (QuantiFERON Gold Plus)
  - 10 years ago: negative
  - 9 years ago: negative
  - 8 years ago: negative
  - 7 years ago: negative
  - 6 years ago: negative
  - 5 years ago: negative
  - 4 years ago: negative
  - 3 years ago: negative
  - 2 years ago: negative
- 1.5 years ago:



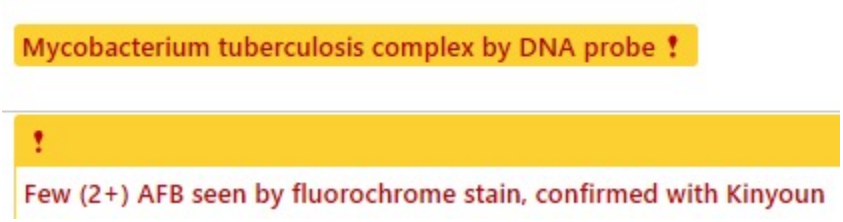
QUANTIFERON G+,4T,NON INC	Negative	Positive !	
Comment:	In healthy persons who have a low likelihood both of M. tuberculosis infection and of progression to active tuberculosis if infected, a single positive QFT result should not be taken as reliable evidence of M. tuberculosis infection. Repeat testing, with either the initial test or a different test, may be considered on a case-by-case basis.		
NIL		IU/mL	0.08
MITOGEN-NIL		IU/mL	8.39
TB1-NIL		IU/mL	0.95
TB2-NIL		IU/mL	1.67

New cavitary pneumonia



Confirmed pulmonary TB

- Sputum cultures are AFB smear positive and MTB DNA positive by Gene Xpert probe



- Pan-susceptible MTB confirmed by DOH
- Started RIPE and changed ART to DTG 50 mg BID + TDF/FTC
- Eventually in follow up with DOH changed to DTG/3TC + DTG
- Doing well on treatment, with plan to complete 9 months of treatment

Among 116,742 contacts of 2609 TB cases from 1-12/2015 with ~3 years follow up, 499 developed active TB (81.0% in the first 2 years)

Months After Notification Index Case	Contacts with TB, No.	(Cumulative %[a])
Total	499	
0–3	119	(23.8)
4–6	85	(40.9)
7–9	50	(50.9)
10–12	48	(60.5)
13–24	102	(81.0)
25–42	95	(100)

(Note no information in study about HIV status)

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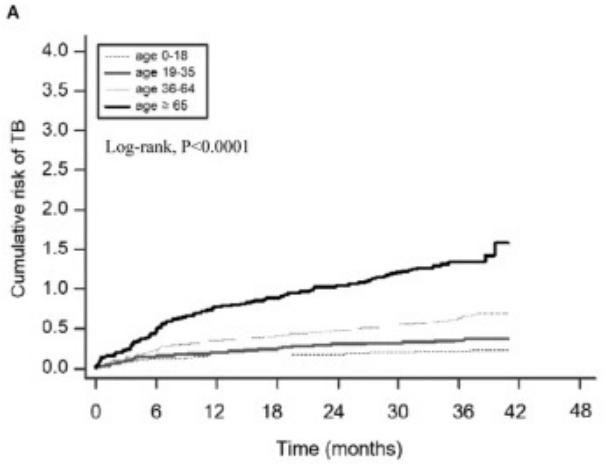
Article | Open Access | Published: 28 January 2020

Risk of active tuberculosis development in contacts exposed to infectious tuberculosis in congregate settings in Korea

Shin Young Park, Sunmi Han, Young-Man Kim, Jieun Kim, Sodam Lee, Jiyeon Yang, Un-Na Kim ✉ & Mi-sun Park ✉

Figure 2



Returning to the QFT-Plus (TB interferon gamma release assay)

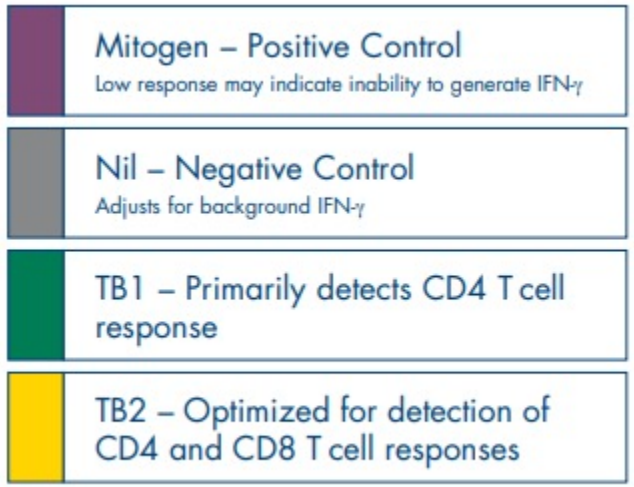
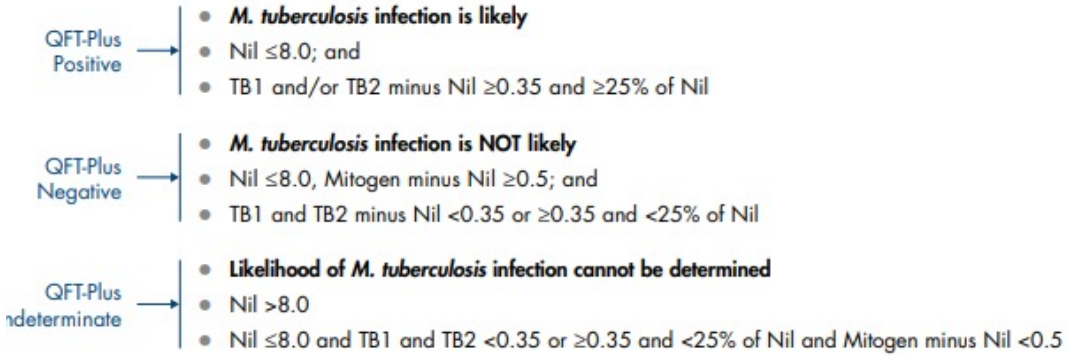


Figure 1. QFT-Plus Blood Collection Tubes.



https://www.quantiferon.com/us/wp-content/uploads/sites/13/2017/10/PROM-11186-001_1107785_BRO_QFT-Plus_GeneralSales_0717_US.pdf

QFT Gold Plus: TB2 allows for assessment of CD8 cell host response, believed to be higher in more recent exposure or in active disease

QUANTIFERON G+,4T,NON INC	Negative	Positive !	
Comment:	In healthy persons who have a low likelihood both of M. tuberculosis infection and of progression to active tuberculosis if infected, a single positive QFT result should not be taken as reliable evidence of M. tuberculosis infection. Repeat testing, with either the initial test or a different test, may be considered on a case-by-case basis.		
NIL		IU/mL	0.08
MITOGEN-NIL		IU/mL	8.39
TB1-NIL		IU/mL	0.95
TB2-NIL		IU/mL	1.67

TABLE 6 Backward stepwise multivariate logistic regression for predicting TB2–TB1 >0.6 IU·mL^{-1}

	OR (95% CI)	p-value
Country of birth		
Non-European	1	
European	3.46 (1.03–11.69)	0.0453
Sleeping proximity to the index case		
Different room	1	
Same room	5.90 (1.83–18.97)	0.0029

M. tuberculosis-specific CD8$^+$ T-cells have been more frequently detected in individuals with active TB when compared with LTBI and correlated with increasing antigenic burden [21–23, 34, 35], suggesting that the presence of CD8$^+$ T-cells in a small proportion of latently infected individuals may be predictive of *M. tuberculosis* active replication and more likely disease progression [22]. Consistent with these results, in a previous study we found that the difference in responses between the QFT-Plus tubes may positively correlate with increasing antigenic load in active TB patients, as it was significantly more common in smear-positive *versus* smear-negative active TB patients [36]. In the present study, we observed a greater TB2 antigen response (TB2–TB1 difference >0.6 IU·mL^{-1}) in 18 (15.13%) individuals, all QFT-Plus positive. We speculate that the small subgroup of latently infected contacts with TB2–TB1 difference >0.6 IU·mL^{-1} had a higher antigenic burden. However, to date, we do not have the tools to directly assess *M. tuberculosis* antigenic burden, as current LTBI tests rely on the (indirect) measurement of a specific immune response.

EUROPEAN RESPIRATORY *journal*
FLAGSHIP SCIENTIFIC JOURNAL OF ERS

First evaluation of QuantiFERON-TB Gold Plus performance in contact screening

Lucia Barcellini, Emanuele Borroni, James Brown, Enrico Brunetti, Daniela Campisi, Paola F. Castellotti, Luigi R. Codecasa, Federica Cugnata, Clelia Di Serio, Maurizio Ferrarese, Delia Goletti, Marc Lipman, Paola M.V. Rancoita, Giulia Russo, Marina Tadolini, Elisa Vanino, Daniela M. Cirillo

European Respiratory Journal 2016 48: 1411-1419; DOI: 10.1183/13993003.00510-2016

Contact screening study for 119 TB contacts with QFT-Plus

"Although QFT-Plus was launched with the promise of improved performance over QFT-GIT through the addition of the CD8 T-cell response, studies directly comparing QFT-Plus with QFT-GIT in TB patients, high-risk groups, and low-risk populations have not revealed any significant improvement in its performance."

Study reference	Country	Sample size	No. (%) of IC hosts	Population (median age [yr])	Sensitivity (%)			Median or mean IFN-γ (IU/ml)		
					QFT-Plus	QFT-GIT	Difference (95% CI)	TB1 in QFT-Plus	TB2 in QFT-Plus	TB Ag in QFT-GIT
30	Germany	24 (MRS) 33 (CRS)	4 (7.0)	Adult (NA)	95.8 84.8	95.8 84.8	0.0 (−11.3 to 11.3) 0.0 (−17.3 to 17.3)	3.10	3.70	4.67
12	USA and Japan	164 (MRS)	4 (2.4)	Adult (71)	93.0	94.3	−1.3 (−6.6 to 4.0)	3.07	3.56	4.45
13	Italy	27 (23 MRS, 4 CRS)	0 (0.0)	Adult (38)	85.0	89.0	−4.0 (−21.9 to 13.9)	NA	NA	NA
15	Italy	69 (49 MRS, 20 CRS)	0 (0.0)	Adult (35)	90.0	88.0	2.0 (−8.4 to 12.4)	1.90	2.50	2.60
31	Japan	162 (MRS)	9 (5.5)	Adult (59)	91.1	90.7	0.4 (−5.9 to 6.7)	2.36	2.85	4.24
16	South Korea	33 (16 MRS, 17 CRS)	0 (0.0)	Adult and pediatric (17)	93.9	93.9	0.0 (−11.5 to 11.5)	10.00	10.00	NA
19	Eswatini	5 MRS 7 CRS	5 (41.7)	Pediatric (NA)	80.0 14.0	80.0 14.0	0.0 (−49.6 to 49.6) 0.0 (−36.4 to 36.4)	NA	NA	NA

Collectively, these studies show nearly identical sensitivities between QFT-Plus (range, 85% to 100%) and QFT-GIT (range, 85% to 100%). As shown in Table 2, the difference in sensitivity ranged from –4.0 to 2.0%.

Shafeque A, Bigio J, Hogan CA, Pai M, Banaei N. Fourth-Generation QuantiFERON-TB Gold Plus: What Is the Evidence?. *J Clin Microbiol*. 2020;58(9):e01950-19. Published 2020 Aug 24. doi:10.1128/JCM.01950-19

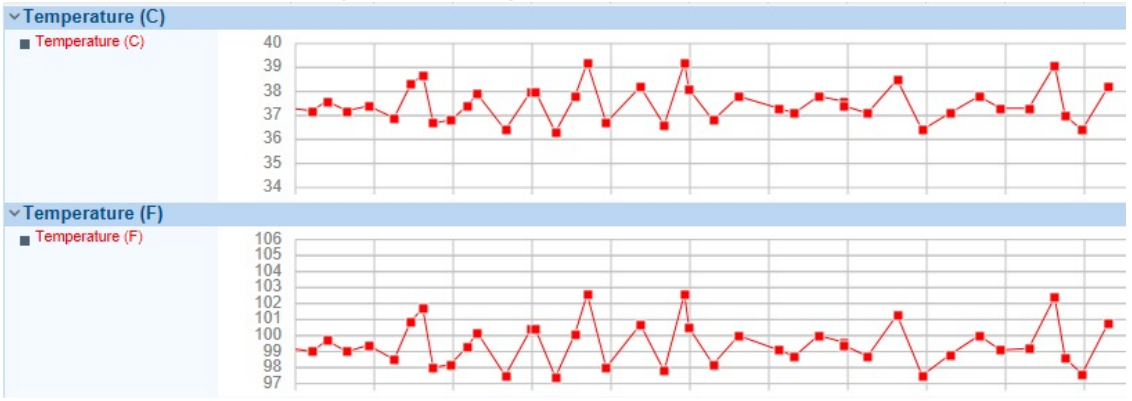
Case 4: 20s M with recently diagnosed HIV, now with 2 months of fever/weight loss, fatigue, diarrhea, right neck swelling

HIV History

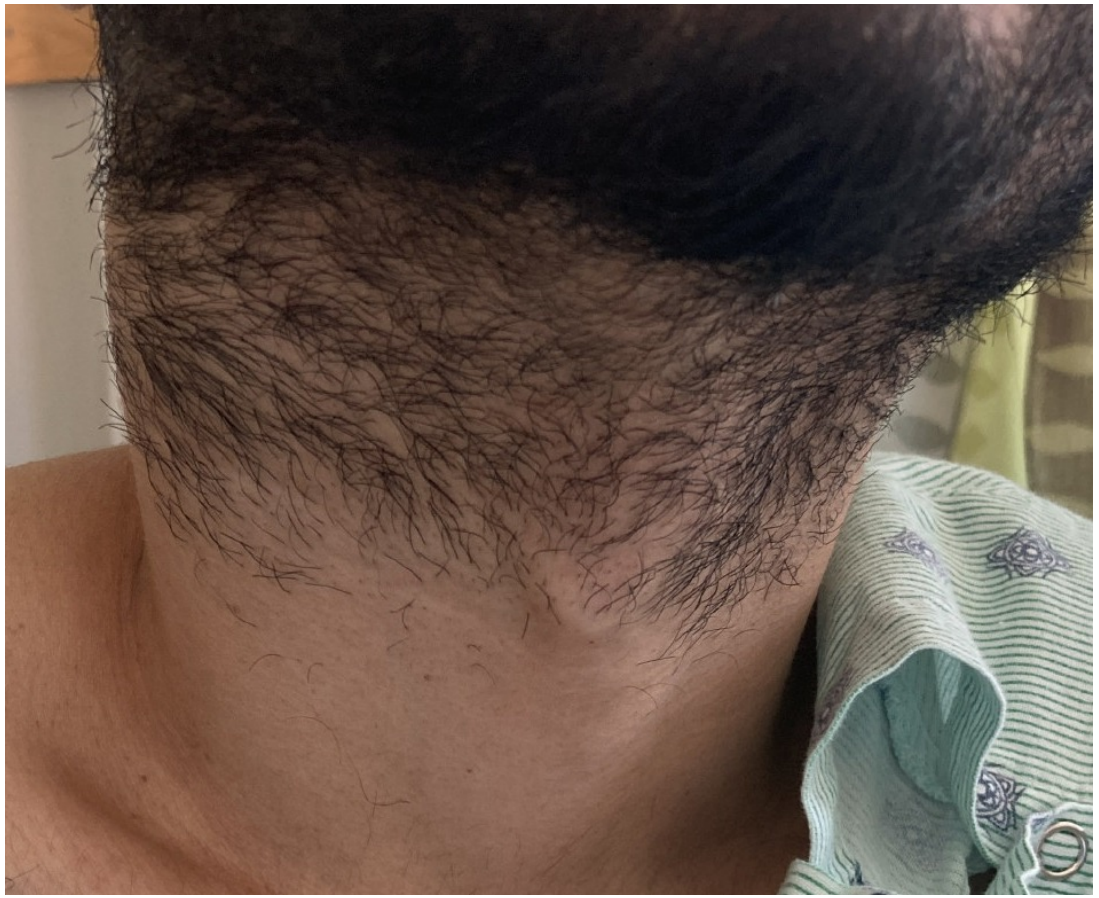
- Diagnosed: 4 months before presentation and had Pneumocystis pneumonia, risk factor: MSM
- OIs: Pneumocystis pneumonia at time of diagnosis
- CD4 nadir: 83 (percentage unknown) at time of diagnosis
- ARV History: BIC/TAF/FTC since diagnosis
- Resistance: None

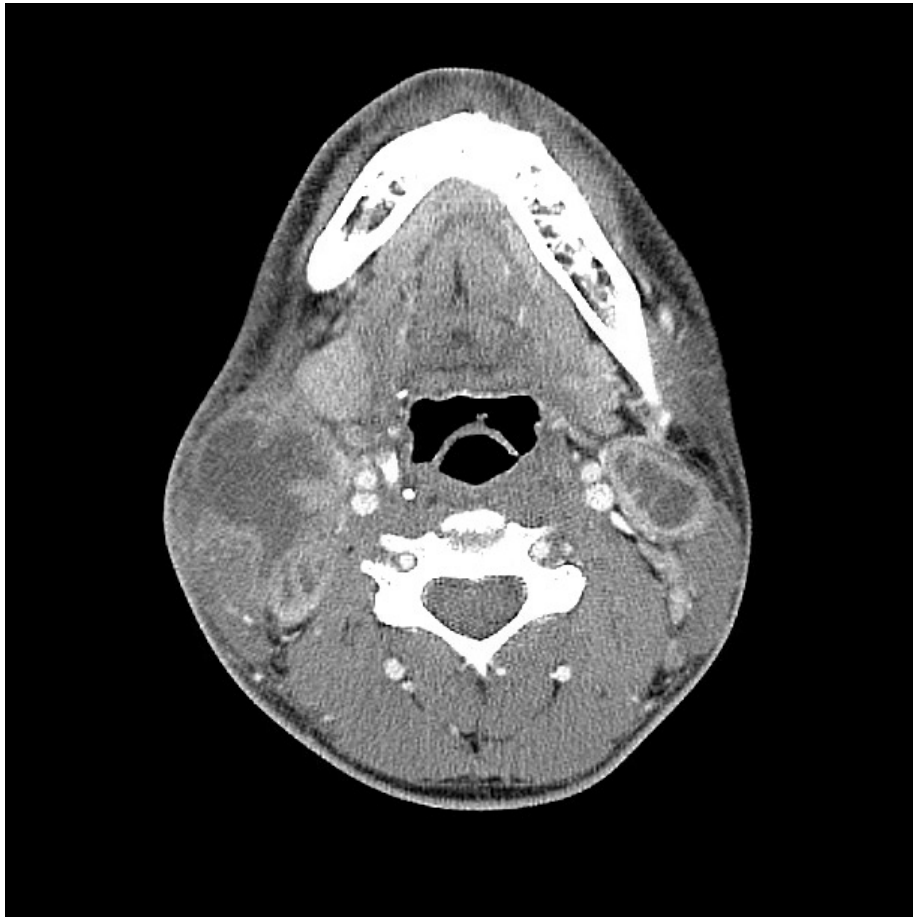
Medical/Social History

- No known prior significant medical history
- Discovered to have horseshoe kidney on imaging studies
- Born in Central America, in New York City >10 years

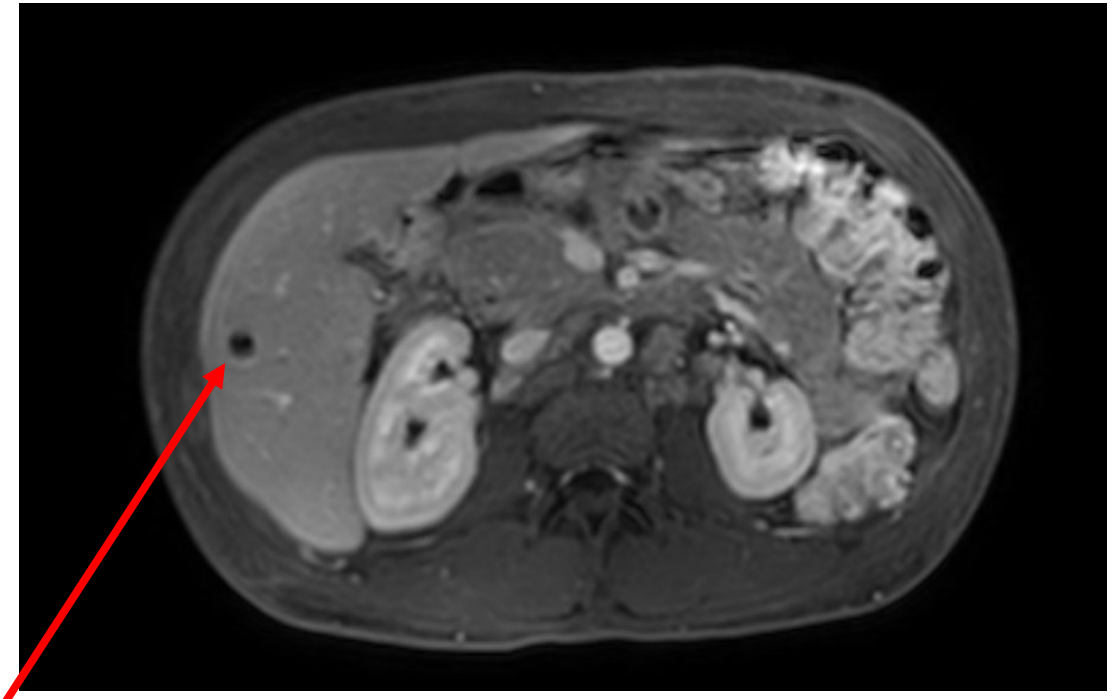


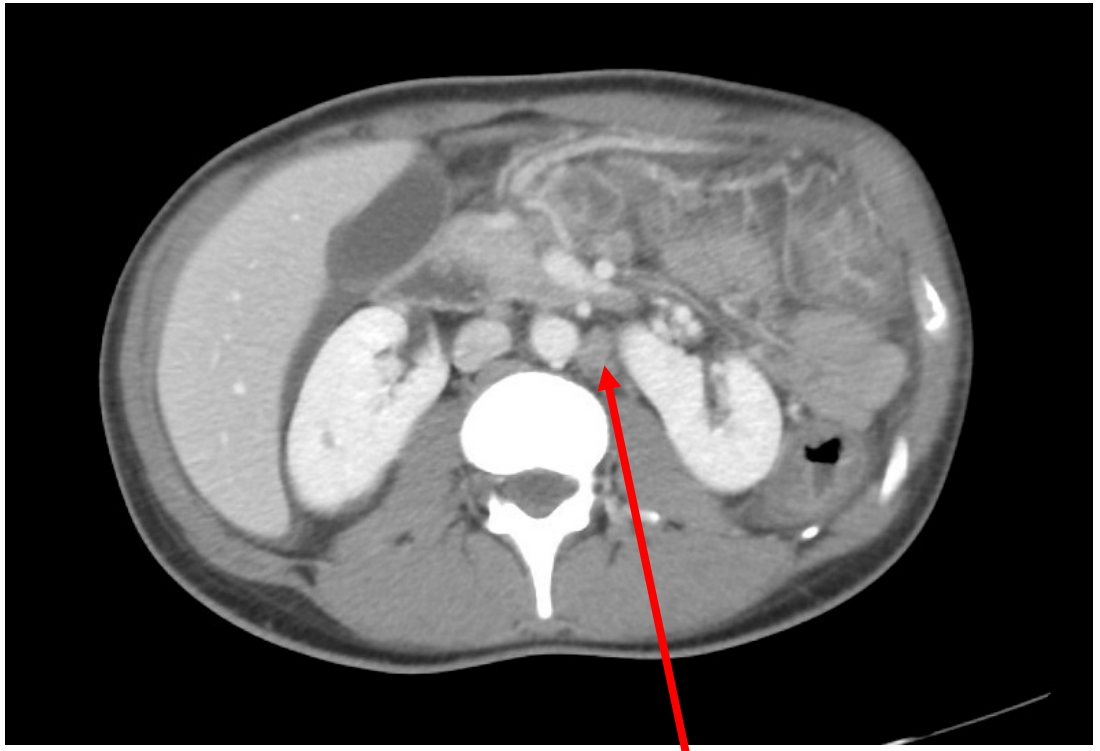
CD4 cell count now 252/27%, VL 395 (down from 780,000 at time of diagnosis)





Small roughly 1 cm ring enhancing liver lesions seen and mesenteric lymphadenopathy, including a 2.2 cm node with central necrosis





Undergoes FNA of right neck node

- Blood cultures negative
- AFB blood cultures negative

- ALT 11, AST <20, ALP 53, T bili 0.4
- WBC 7.0, Hgb 9.9, HCT 29.8, PLT 302
- LDH 218

Tissue, AFB Culture	Mycobacterium Avium Complex By DNA Probe
AFB Stain	!
	Rare (1+) AFB seen by fluorochrome stain, confirmed with Kinyoun

Resulting Agency: MOSES

A. Neck, Right, Level II, FNA:

Negative for Malignant Cells
Necroinflammatory debris with necrotizing granulomatous inflammation, compatible with acute granulomatous lymphadenitis; see comment

Comment: Sample sent to microbiology for evaluation. Please correlate with the microbiological results.

In a prospective RCT of 203 patients between 12/1994 and 2/1998, C/E/R superior to dual regimen; proportion with complete microbiologic response at 12 weeks similar

A Prospective, Randomized Trial Examining the Efficacy and Safety of Clarithromycin in Combination with Ethambutol, Rifabutin, or Both for the Treatment of Disseminated *Mycobacterium avium* Complex Disease in Persons with Acquired Immunodeficiency Syndrome

Constance A. Benson,[1] Paige L. Williams,[2] Judith S. Currier,[3] Fiona Holland,[2] Laura F. Mahon,[5] Rob Roy MacGregor,[6] Clark B. Inderlied,[4] Charles Flexner,[6] Judith Neidig,[9] Richard Chaisson,[6] Gerard F. Notario,[10] Richard Hafner,[7] and the AIDS Clinical Trials Group 223 Protocol Team[a]

[1]Division of Infectious Diseases, University of Colorado Health Sciences Center, Denver; [2]Center for Biostatistics in AIDS Research, Harvard School of Public Health, Boston, Massachusetts; [3]University of California at Los Angeles CARE Center and [4]University of Southern California Children's Hospital, Los Angeles; [5]AIDS Clinical Trials Group Operations Center, Social and Scientific Systems, Silver Spring, [6]Johns Hopkins University School of Medicine, Baltimore, and [7]Division of AIDS, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland; [8]University of Pennsylvania Medical Center, Philadelphia; [9]Ohio State University College of Medicine, Columbus; and [10]Abbott Laboratories, Abbott Park, Illinois

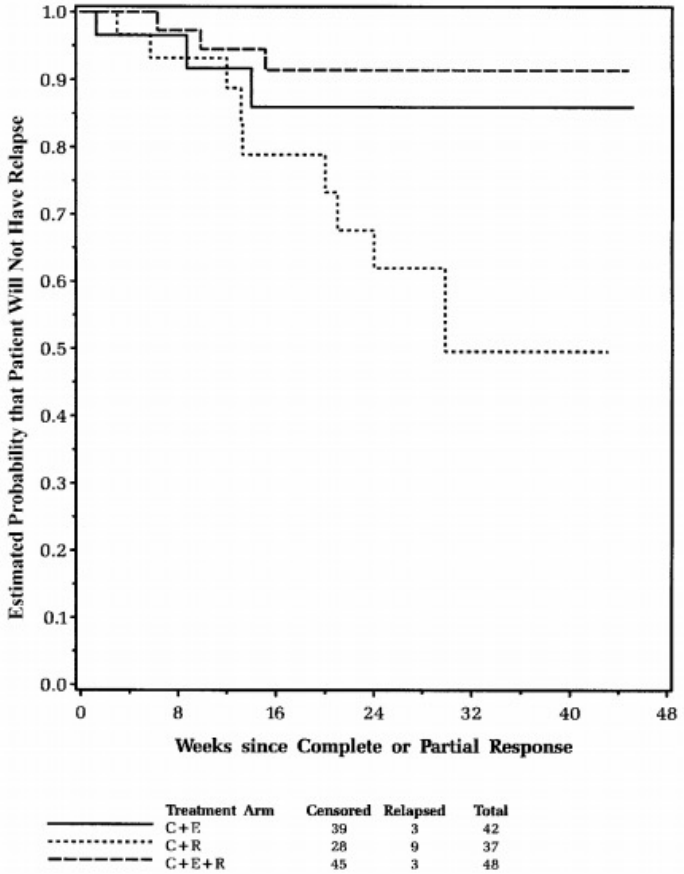
Table 2. Proportions of patients with AIDS with a complete microbiologic response and with a complete clinical response to combination clarithromycin therapy for *Mycobacterium avium* complex disease, by treatment arm and week of therapy.

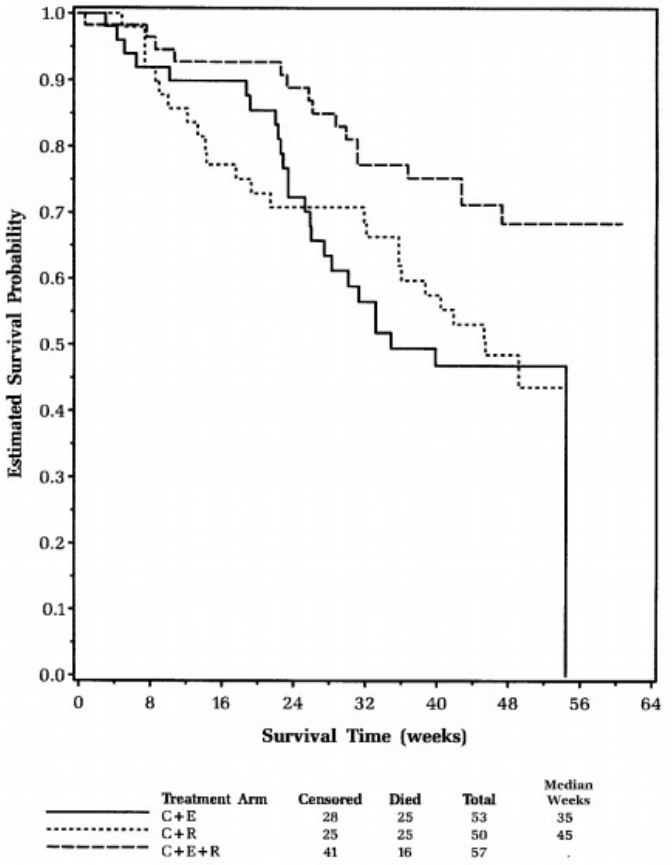
	No. (%) of patients in indicated treatment arm			
Response, week	C+E	C+R	C+E+R	*P*[a]
Complete microbiologic				
6	16 (30)	10 (20)	15 (26)	.497
8	20 (38)	17 (34)	20 (35)	.935
12	21 (40)	21 (42)	29 (51)	.454
16	25 (47)	23 (46)	36 (63)	.130
Complete microbiologic and clinical				
6	10 (19)	7 (14)	11 (19)	.755
8	9 (17)	12 (24)	13 (23)	.653
12	14 (26)	13 (26)	17 (30)	.903
16	11 (21)	12 (24)	21 (37)	.144

NOTE. C, clarithromycin; E, ethambutol; R, rifabutin.

[a] Calculated using a generalized version of Fisher's exact test for R × C tables.

Of 127 w complete or partial response, 15 had relapse. Relapse rates: for C/E (7%) and C/E/R (6%) vs 24% C/R
66 of 160 died during study, 25 deaths C/E, 25 deaths C/R, 16 deaths C/E/R. Adjusted for PI use, C/E/R had reduced rate of death compared to either other regimen





39 subjects had baseline blood cultures negative for MAC and were not included in the analysis

Table 1. Selected baseline characteristics and laboratory values for patients with AIDS who received combination clarithromycin therapy for *Mycobacterium avium* complex (MAC) disease, by treatment arm.

Variable	Total (n = 160)	Treatment arm[a] C+E (n = 53)	C+R (n = 50)	C+E+R (n = 57)
Sex				
Male	139 (87)	43 (81)	44 (88)	52 (91)
Female	21 (13)	10 (19)	6 (12)	5 (9)
Race/ethnicity				
White	56 (35)	21 (40)	17 (34)	18 (32)
African American	74 (46)	24 (45)	23 (46)	27 (47)
Latino	24 (15)	8 (15)	9 (18)	7 (12)
Other	6 (4)	0 (0)	1 (2)	5 (9)
Current/previous injection drug use	36 (23)	8 (15)	13 (26)	15 (26)
Protease inhibitor use	23 (14)	8 (15)	6 (12)	9 (16)
Age, median years (range)	36 (20–55)	35 (27–47)	35 (25–55)	37 (20–47)
Karnofsky score, median (range)	70 (30–100)	70 (40–100)	70 (30–100)	70 (30–90)
Median laboratory value (range)				
$CD4^+$ cell count, cells/μL	8 (0–408)	9 (0–89)	9 (0–63)	7 (0–408)
MAC bacteremia level, $\log_{10}$ cfu/mL	1.623 (−0.071 to 5.228)	1.696 (−0.071 to 5.228)	1.628 (0–3.690)	1.554 (−0.033 to 4.535)
SGOT/AST level, IU/L	41 (10–371)	40 (15–189)	41(13–371)	41 (10–309)
Alkaline phosphatase level, IU/L	127 (48–1805)	118 (50–1341)	135 (48–1805)	133 (60–1493)
SGPT/ALT level, IU/L	33 (6–160)	33 (8–128)	35 (8–157)	30 (6–160)
Hemoglobin concentration, g/dL	9.5 (5.3–14.6)	9.0 (6.3–12.0)	9.6 (6.2–14.4)	9.8 (5.3–14.6)

NOTE. Data are no. (%) of patients, unless otherwise indicated. ALT, alanine aminotransferase; AST, aspartate aminotransferase; C, clarithromycin; E, ethambutol; R, rifabutin; SGOT, serum glutamic oxaloacetic transaminase; SGPT, serum glutamic pyruvic transaminase.

[a] No statistically significant differences were detected among the treatment arms for any baseline characteristic.

Fever and lower hemoglobin associated with dMAC when comparing PWH to matched controls

Table 1. Risk factors for disseminated *M. avium* complex (MAC) bacteremia.

Enrollment characteristic (means)	Bacteremia (n = 102)	No bacteremia (n = 469)	P
Age (years)	38.0	37.6	NS
Weight (kg)	68.8	72.1	.02
Karnofsky score (%)	87.9	89.1	NS
CD4 cell count (/mm^3)	34.6	60.7	<.001
Hemoglobin (g/dL)	12.2	12.5	.06
WBCs (×10^9/L)	2.7	3.5	<.001
Platelets (×10^9/L)	200	205	NS
SGOT (U/L)	51	46	.02
SGPT (U/L)	53	48	NS
Bilirubin (mg/dL)	0.46	0.28	.01
Alkaline phosphatase (U/L)	116	108	.03

NOTE. WBCs, white blood cells; SGOT, serum glutamic-oxaloacetic transaminase; SGPT, serum glutamate-pyruvate transaminase; NS, not significant.

Table 2. Clinical and laboratory characteristics of cases at time of *M. avium* complex bacteremia and of matched controls.

Characteristic	Cases (n = 90)	Controls (n = 180)	P
Weight* (kg)	66.3	71.4	.001
Karnofsky score*	74.3	84.4	<.001
Fever (%)	48	26	.001
Night sweats (%)	24	14	.065
Abdominal pain (%)	23	13	.05
Diarrhea (%)	37	25	.07
Fatigue (%)	65	59	.39
Hemoglobin* (g/dL)	10.9	12.1	<.001
WBCs (×10^9/L)	3.08	3.02	.86
Platelets* (×10^9/L)	195	193	.88
SGOT* (U/L)	56	50	.29
SGPT* (U/L)	44	49	.30
Bilirubin* (mg/dL)	0.54	0.59	.24
Alkaline phosphatase* (U/L)	203	138	.038
LDH* (U/L)	334	280	.018

NOTE. WBCs, white blood cells; SGOT, serum glutamic-oxaloacetic transaminase; SGPT, serum glutamate-pyruvate transaminase; LDH, lactate dehydrogenase.
* Mean values.

Gordin FM, Cohn DL, Sullam PM, Schoenfelder JR, Wynne BA, Horsburgh CR Jr. Early manifestations of disseminated Mycobacterium avium complex disease: a prospective evaluation. J Infect Dis. 1997 Jul;176(1):126-32. doi: 10.1086/514014. PMID: 9207358.

Management: suspected dMAC with IRIS

- Inpatient: Started on azithromycin, ethambutol, rifabutin in hospital, and ART changed to DTG + TDF/FTC
- Outpatient: transitioned to azithromycin, ethambutol and back to BIC/TAF/FTC
- Considered addition of prednisone
- Completed 6 months of dMAC therapy and doing well
- CD4 cell count 474/23%

Case 5: 50s woman on PrEP presenting with new headache and rash on arm

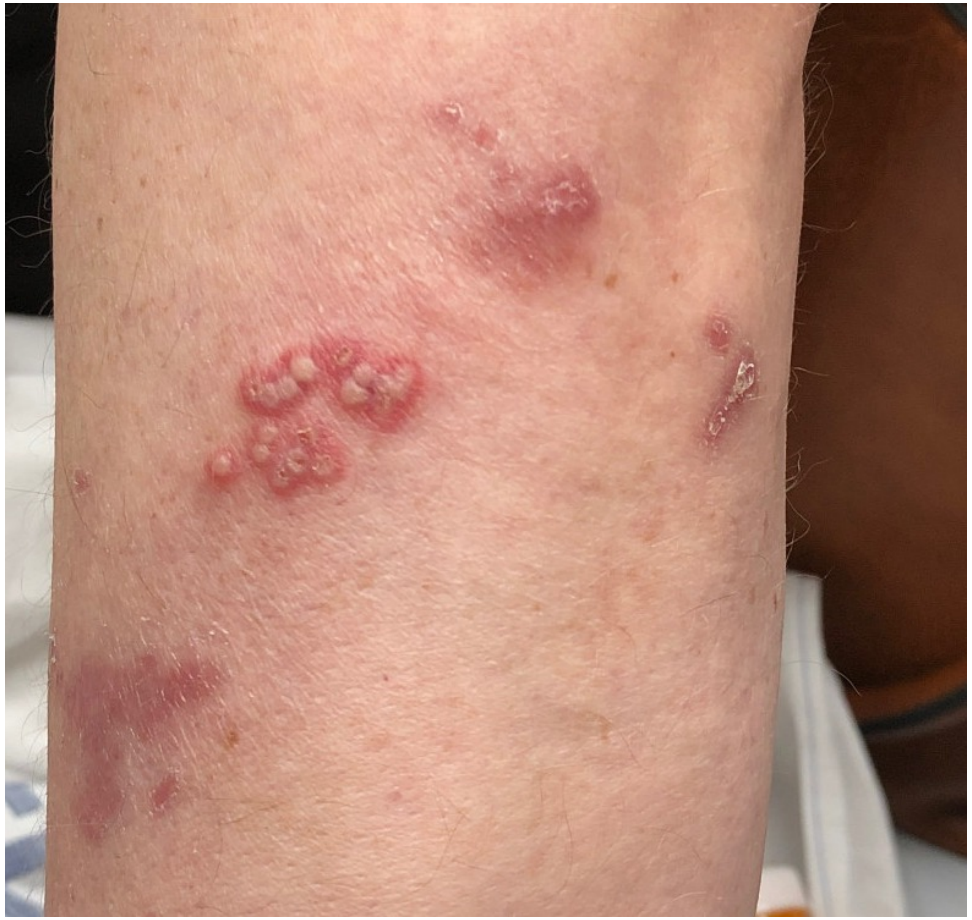
- Reports good adherence to PrEP with few missed doses
- Also reports last HIV test and provider visit was >7 months prior to presentation

HIV-1 POSITIVE !

POSITIVE FOR HIV-1

Positive for HIV-1 Antibodies. Laboratory evidence of HIV-1 infection is present.

An initial HIV Ag/Ab Combo (Abbott Architect) was performed and found to be reactive. Follow up HIV antibody differentiation testing confirmed the presence of HIV-1 Antibodies.



Case 5: 50s woman on PrEP presenting with new headache and rash on arm

HIV History

- Diagnosed: 2021, risk factor: male sexual partners
- OIs: presumptive zoster
- CD4 nadir: unknown (new diagnosis)
- ARV History: None
- Resistance: Unknown, though concern for high level NRTI resistance given reported TDF/FTC use around time of seroconversion

Medical/Social History

- Treated for pulmonary TB for 6 months in another part of the US 25 years before presentation
- Obesity, BMI >35
- On PrEP for >5 years
- Syphilis (treated)
- Notes rash recurs on left arm roughly each year for ~8 years
- Lives alone in NYC. Reports male and female sexual partners. Remote prior smoking history.

50s woman on PrEP presenting with new headache and rash on arm

- Work up reveals:
  - CBC with diff, BMP, LFTs: within normal limits
  - HIV-1 VL 886,911 copies/mL
  - CD4 cell count 201/12%
  - CMV IgG positive
  - Genotype: pending
- Patient with chronic (unchanged) cough. Primary team sends off sputum which eventually returns:
  - Pneumocystis PCR POSITIVE
- Serum beta-d-glucan <31

Clinical Questions:

1) What is the cause of the rash?
2) Does the patient have Pneumocystis pneumonia?
3) What ART regimen would you start the patient on?

1) What is the cause of the rash?

Open Forum Infectious Diseases

MAJOR ARTICLE

Herpes Zoster and Recurrent Herpes Zoster

Kimiyasu Shiraki,[1] Nozomu Toyama,[2] Tohru Daikoku,[1,a] and Misako Yajima;[1,b] for the Miyazaki Dermatologist Society

[1]Department of Virology, Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama, Japan; [2]Toyama Dermatologic Clinic, Aburatsu, Nichinan City, Miyazaki, Japan

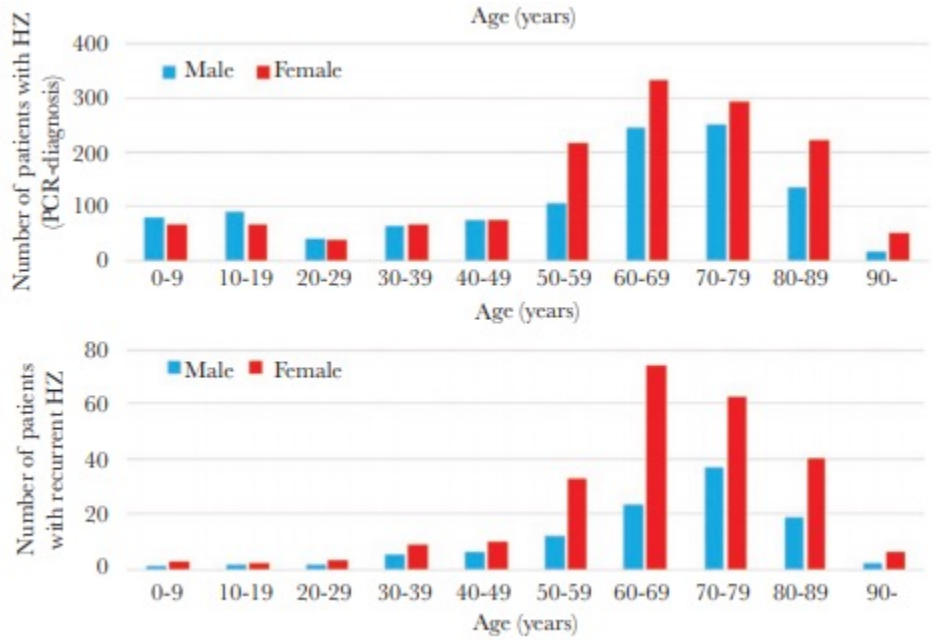
Background. The incidence of recurrent herpes zoster (HZ) and the relationship between initial and recurrent HZ are not clear.

Methods. The Miyazaki Dermatologist Society has surveyed ~5000 patients with HZ annually since 1997. A questionnaire regarding HZ and its recurrence was completed by the dermatologists.

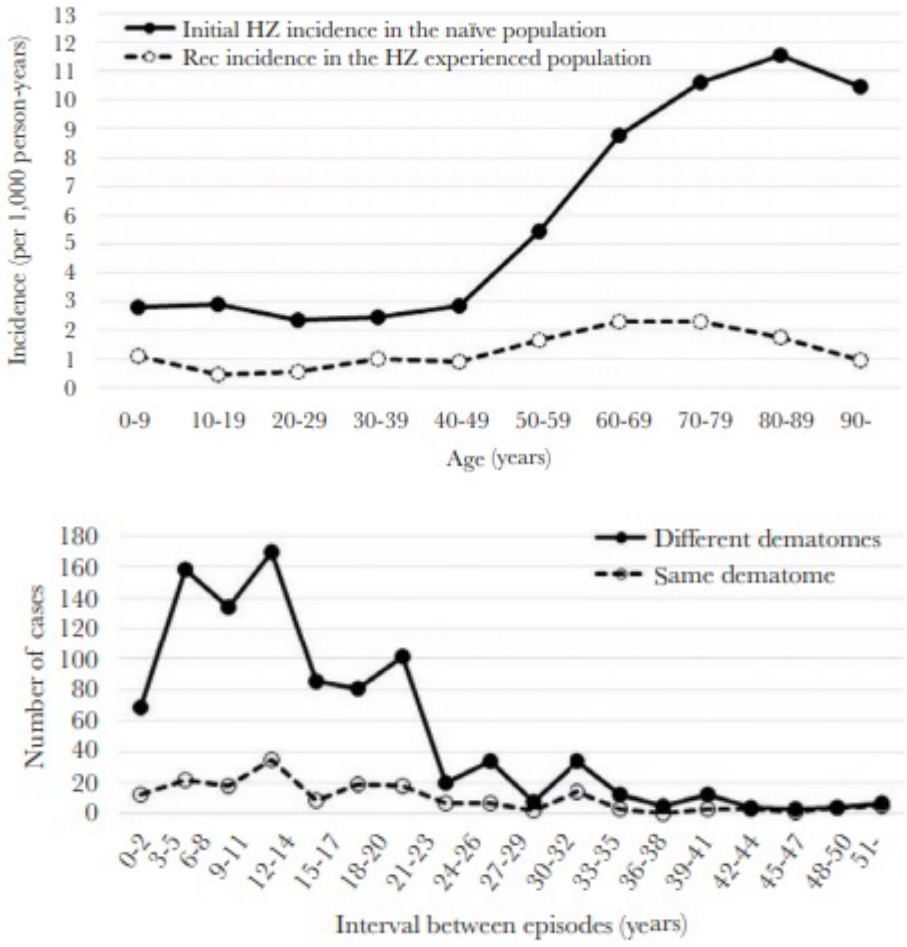
Results. A total of 34 877 patients with HZ were registered at 43 clinics between June 2009 and November 2015. Among 16 784 patients seen at 10 of the 43 clinics, 1076 patients (6.41%) experienced recurrence. Herpes zoster was more frequent in female than in male patients (5.27 vs 4.25 in 1000 person-years, $P < .001$), as was HZ recurrence (7.63% vs 4.73%, $P < .001$). Two and three recurrences were observed in 49 and 3 patients, respectively. Recurrence in the same dermatome was observed in 16.3% of patients, and more frequently this occurred in the left side ($P = .027$). The number of HZ-experienced persons increased with age, and one third of the population had experienced HZ by the age of 80.

Conclusions. Recurrent HZ was observed in 6.41% of patients, with a higher incidence in women. Moreover, HZ experience reduced the HZ incidence to 31.7% of the incidence in the HZ-naive population.

Keywords. epidemiology; herpes zoster; recurrence; varicella-zoster virus.



Recurrence is rare and more likely in different dermatomes



- "The intervals between the prior and recurrent episodes among 1125 cases ranged from 2 months to 73 years with a mean period of 13.71 ± 10.96 years, peaked at 3–11 years, and then decreased gradually with time "
- Episodes within 8 years occurred more frequently in a different dermatome (361 of 942, 38.3%) than in the same dermatome (53 of 183, 29.0%) (P = .016), indicating that recurrence was more likely to occur in a different dermatome than in the same dermatome during that period

Cause of rash was confirmed to be HSV-2. Patient placed on PO valacyclovir, with plan for suppression given frequency of recurrences

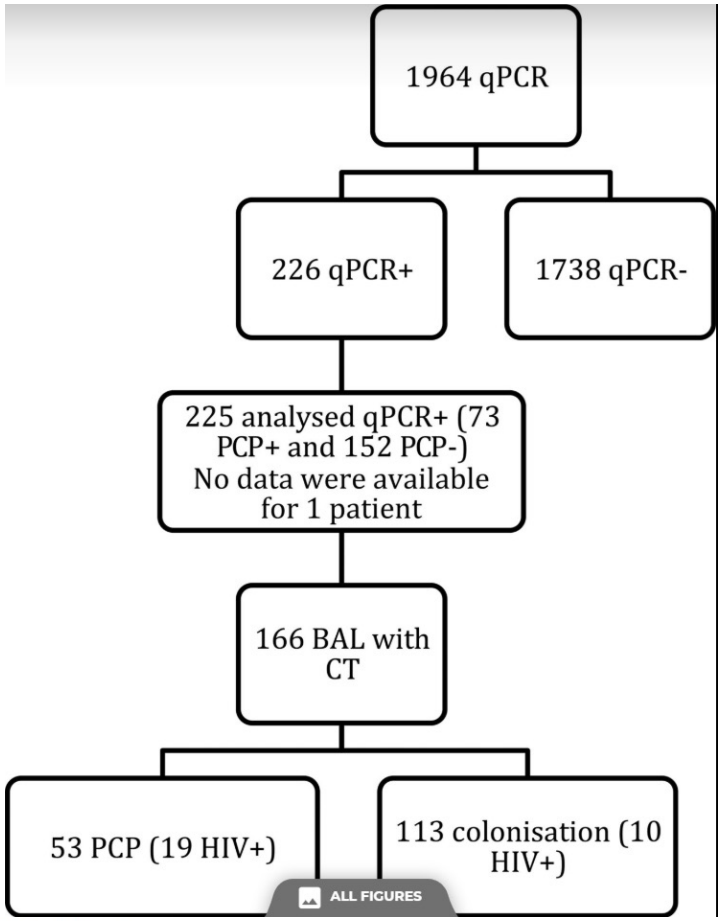
Herpes Simplex Virus (HSV) Types 1 and 2 by PCR

HSV1 & HSV2 DNA Detection (Swabs)

Collected:	09/30/21 1248
Result status:	Final
Resulting lab:	MOSES
Reference range:	Negative for HSV 1 and HSV 2
Value:	HSV 2 POSITIVE !
Comment:	The ARIES HSV assay is an FDA approved in-vitro diagnostic test for the detection and differentiation of Herpes Simplex Virus types 1 & 2. This assay is approved only for use with appropriately collected swabs from cutaneous and mucocutaneous lesions. The ARIES® HSV 1&2 Assay is not FDA cleared for use with cerebrospinal fluid (CSF) or for prenatal screening. The results from this assay must be interpreted within the context of all relevant clinical and laboratory findings.

2) Does the patient have Pneumocystis pneumonia?

- In a study from Nice University Hospital, France, a quantitative Pneumocystis PCR was used to help distinguish colonization from infection
- Diagnosis of PCP made by a panel of pulmonologist and ID physicians
- No patient with PCP had a negative qPCR
- Note this was used on BAL samples



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Volume 54, Issue 6, June 2016, Pages 1487-1495
https://doi.org/10.1128/JCM.03174-15

Mycology

Detection of Pneumocystis jirovecii by Quantitative PCR To Differentiate Colonization and Pneumonia in Immunocompromised HIV-Positive and HIV-Negative Patients

T. Fauchier [a], L. Hasseine [a], M. Gari-Toussaint [a], V. Casanova [b], P. M. Marty [a,c,d], and C. Pomares [a,c,d]

In a study of 282 patients with HIV, those with PCP had median beta-D-glucan 408 versus 37 pg/mL in those without

MAJOR ARTICLE HIV/AIDS

Blood (1→3)-β-D-Glucan as a Diagnostic Test for HIV-Related *Pneumocystis jirovecii* Pneumonia

Paul E. Sax,[1] Lauren Komarow,[2] Malcolm A. Finkelman,[3] Philip M. Grant,[4] Janet Andersen,[2] Eileen Scully,[1] William G. Powderly,[5] and Andrew R. Zolopa[4] for the AIDS Clinical Trials Group Study A5164 Team

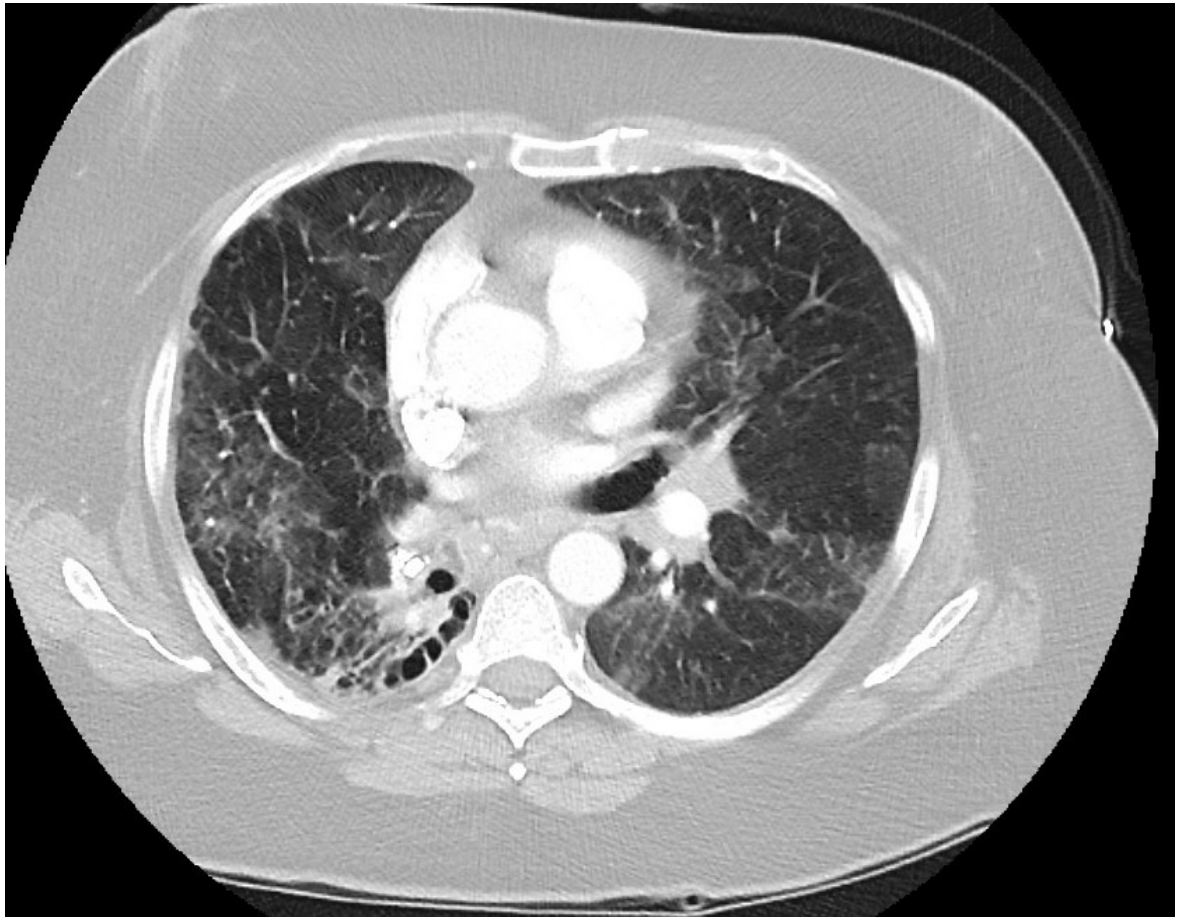
[1]Division of Infectious Diseases, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, and [2]Harvard School of Public Health, Boston, [3]Associates of Cape Cod, East Falmouth, Massachusetts; [4]Division of Infectious Diseases and Department of Medicine, Stanford University School of Medicine, Stanford, California; and [5]School of Medicine, University College Dublin, Ireland

Table 3. Positive (≥80 pg/mL) and Negative (<80 pg/mL) β-Glucan Results by *Pneumocystis jirovecii* Pneumonia (PCP) Diagnosis

	PCP		
Beta-glucan ≥80	Yes	No	*P*
Negative <80 pg/mL	13 (8%)	51 (65%)	<.001[a]
Positive ≥80 pg/mL	160 (92%)	28 (35%)	

NOTE. [a] Fisher's exact test.

On review with radiologists: CT scans dating back 7 years had been stable with chronic right lung scarring, bronchiectasis and diffuse air trapping



I’m not sure if patient had mild PCP or was colonized

- Pneumocystis PCR returned about day 5 after starting ART and placing patient on daily TMP-SMX
- The patient was improving and continued to report baseline respiratory status
- I recommended continuing the prophylactic dose of TMP-SMX at least through viral suppression since CD4 cell % was 12 (and we did not treat)

3) What ART regimen would you start the patient on? What is the risk of drug resistance when HIV seroconversion happens on PrEP?

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Drugs. 2019 April ; 79(6): 609–619. doi:10.1007/s40265-019-01108-x.

Drug Resistance during HIV Preexposure Prophylaxis

Kevin M. Gibas[#1], **Polly van den Berg**[#1], **Victoria E. Powell**[1], and **Douglas S. Krakower**[1,2,3]

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[2]The Fenway Institute, Fenway Health, Boston, MA

[3]Department of Population Medicine, Harvard Medical School, Boston, MA

[#] These authors contributed equally to this work.

Abstract

Clinical studies have demonstrated that use of tenofovir disoproxil fumarate with or without emtricitabine as antiretroviral preexposure prophylaxis (PrEP) can decrease the risk of HIV acquisition when medication adherence is high. However, the potential for PrEP to promote antiretroviral resistance remains an important public health consideration. We performed a search of the medical literature to identify studies that address HIV drug resistance during PrEP use. In this review, we summarize findings about emergent drug resistance during clinical trials of PrEP, case reports of seroconversions in adherent PrEP patients, and animal studies of PrEP effectiveness against drug resistant viral strains. We also discuss the potential utility of novel PrEP formulations for protection against drug resistant HIV, the impact of drug resistance on HIV treatment options, and mathematical models that estimate the potential contribution of PrEP to population-level drug resistance. Evidence suggests that selection for HIV drug resistance with PrEP use is infrequent and most likely to occur when PrEP is used during undiagnosed acute HIV infection. Breakthrough infections during PrEP use with high adherence are possible, but appear to be rare. The prevalence of drug resistant HIV strains needs to be monitored as PrEP is scaled-up. However, the benefit of decreased HIV incidence with wider PrEP use is likely to outweigh the risk of harms from possible increases in the prevalence of HIV drug resistance.

Key Points

- HIV Preexposure prophylaxis (PrEP) using tenofovir disoproxil fumarate (TDF) with or without emtricitabine (FTC) can decrease the risk of acquiring HIV when used with high adherence, but there is potential for PrEP to promote antiretroviral drug resistance.
- Evidence from clinical trials, case reports, animal studies, and mathematical models suggests that selection for HIV drug resistance with PrEP use is likely to be infrequent and most likely to occur when PrEP is used inadvertently during undiagnosed HIV infection.
- The benefit of decreased HIV incidence with wider PrEP use is likely to outweigh the risk of harms from possible increases in the prevalence of HIV drug resistance.

In these studies, there were 699 participants with seroconversion after receiving PrEP or placebo; drug resistance rare

Table 3.

Drug resistance mutations in study participants with incident HIV infection.

Study	Reference	TDF/FTC Arm			TDF Arm			Placebo			All Arms			Total
		FTC Mutation[a]	TDF Mutation[b]	TDF and FTC Mutation[c]	FTC Mutation	TDF Mutation	TDF and FTC Mutation	FTC Mutation	TDF Mutation	TDF and FTC Mutation	FTC Mutation	TDF Mutation	TDF and FTC Mutation	
Bangkok Tenofovir Study	Choopanya et al. (2013)	-	-	-	-	0	-	-	0	-	-	0	-	0
HPTN 082/Partners Demonstration Project	Baeten et al. (2016), Heffron et al. (2017)	0	0	0	-	-	-	-	-	-	0	0	0	0
FEM-PrEP	Van Damme et al. (2012), Grant et al. (2015)	4[d]	0	0	-	-	-	1	0	0	5	0	0	5
HPTN 067/ADAPT	Sivay et al. (2017)	0	0	1	-	-	-	-	-	-	0	0	1	1
IPERGAY	Delaugerre et al. (2018)	0	0	0	-	-	-	0	0	0	0	0	0	0
iPrEx[e]	Liegler et al. (2014)	2[f]	0	0	-	-	-	1	1	0	3	1	0	4
iPrEx OLE	Grant et al. (2014)	1	0	0	-	-	-	-	-	-	1	0	0	2
Partners PrEP + Open Label Extension/ Continuation Study[e,g]	Baeten et al. (2012), Lehman et al. (2015)	2	0	1	1	0	0	2	0	0	5	0	1	6
Project PrEPare 2	Hosek et. (2017)	0	0	0	-	-	-	-	-	-	0	0	0	0
PROUD	McCormack et. (2016)	0	0	0	-	-	-	-	-	-	0	0	0	0
TDF2	Thigpen et al. (2012), Chirwa et al. (2014)	0	0	0	-	-	-	0	1[h]	0	0	1	0	1
US MSM Safety Trial	Grohskopf et al. (2013)	-	-	-	-	-	-	-	0	-	0	0	0	0
VOICE[i]	Marrazzo et al. (2015)	1	0	0	0	0	0	0	0	0	1	0	0	1
Total		10	0	2	1	0	0	4	2	0	15	2	2	19

Among those with high adherence, M184V common, K65R/TAMs possible

Table 4.

Cases of incident HIV during PrEP use with confirmed high adherence.

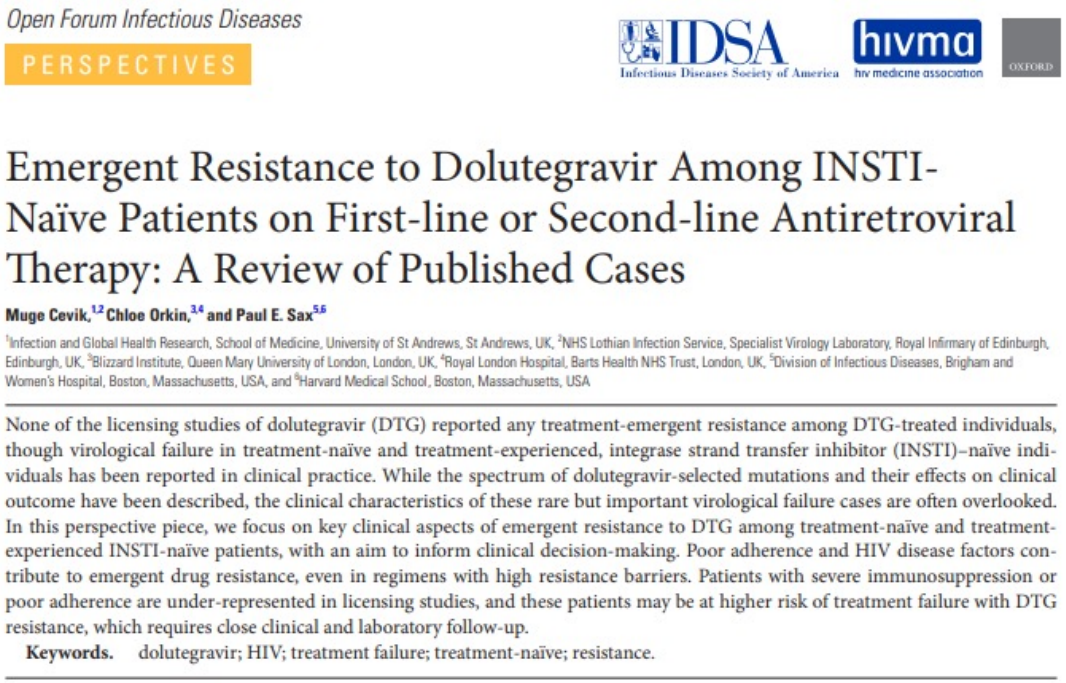
Case	Reported	Method of Confirming PrEP Adherence	Clinically Significant NRTI Resistance Mutations			NNRTI Resistance Mutations	Other Mutations
			M184V (FTC Resistance)	K65R (TDF Resistance)	Other Resistance Mutations		
1	Knox et al. (2017)	Dried Blood Spot	Present	Not present	M41L, D67G, T69D, K70R, Y215E	Y181C	H51Y, E92Q, L10I
2	Markowitz et al.(2017)	Dried Blood Spot	Present	Present	None reported	K103S, E138Q, Y188L	K46M, S68G, G93E, A98S, I142T, S163Y, Q174K, V179I, T200A, Q207E, R211K, F214L, V245M
3	Thaden et al.(2018)	Segmental Hair Analysis	Present	Present	K70T	K103N, V179I, V90I	None reported
4	Colby et al.(2018)	Dried Blood Spot	Present	Not present	None reported	A98G, K103N	None Reported
5	Hoornenborg et al.(2017)	Hair Analysis & Dried Blood Spot	Not present	Not present	None reported	None Reported	None Reported
6	Cohen et al. (2019)	Segmental Hair Analysis & Dried Blood	Present	Not present	L74V	K103N, L100I	D30N, G73S, G48E

NRTI, nucleos(t)ide reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor. Resistance mutation abbreviations reflect standard amino acid nomenclature.

Our patient's Genotype showed M184V

	Drug			Assessment*		Comments
	Generic Name	Brand Name	Drug	Drug		
NRTI	Abacavir	Ziagen	M184M/I/V	ABC	Sensitive	
	Didanosine	Videx	M184M/I/V	ddI	Resistance Possible	
	Emtricitabine	Emtriva	M184M/I/V	FTC	Resistant	
	Lamivudine	Epivir	M184M/I/V	3TC	Resistant	
	Stavudine	Zerit	None	d4T	Sensitive	1
	Tenofovir	Viread	None	TFV	Sensitive	1
	Zidovudine	Retrovir	None	ZDV	Sensitive	1
NNRTI	Doravirine	Pifeltro	V90V/I, I178L	DOR	Sensitive	
	Efavirenz	Sustiva	None	EFV	Sensitive	
	Etravirine	Intelence	V90V/I, V179I	ETR	Sensitive	
	Nevirapine	Viramune	V179I	NVP	Sensitive	
	Rilpivirine	Edurant	None	RPV	Sensitive	

3) What ART regimen would you start the patient on?



Open Forum Infectious Diseases

PERSPECTIVES

Emergent Resistance to Dolutegravir Among INSTI-Naïve Patients on First-line or Second-line Antiretroviral Therapy: A Review of Published Cases

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None of the licensing studies of dolutegravir (DTG) reported any treatment-emergent resistance among DTG-treated individuals, though virological failure in treatment-naïve and treatment-experienced, integrase strand transfer inhibitor (INSTI)–naïve individuals has been reported in clinical practice. While the spectrum of dolutegravir-selected mutations and their effects on clinical outcome have been described, the clinical characteristics of these rare but important virological failure cases are often overlooked. In this perspective piece, we focus on key clinical aspects of emergent resistance to DTG among treatment-naïve and treatment-experienced INSTI-naïve patients, with an aim to inform clinical decision-making. Poor adherence and HIV disease factors contribute to emergent drug resistance, even in regimens with high resistance barriers. Patients with severe immunosuppression or poor adherence are under-represented in licensing studies, and these patients may be at higher risk of treatment failure with DTG resistance, which requires close clinical and laboratory follow-up.

Keywords. dolutegravir; HIV; treatment failure; treatment-naïve; resistance.

- Of 15 cases of emergent DTG resistance reviewed, 10 had suboptimal levels and/or poor adherence and 3 had multiple OIs
- 4 treatment-naïve & 5 treatment experienced patients had a baseline VL >100,000 copies/mL
- Low CD4 cell count seen in some cases

ART regimen: BIC/TAF/FTC + DRV/c until suppression

- She has now been transitioned to BIC/TAF/FTC (after achieving viral suppression)

Thank you!

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