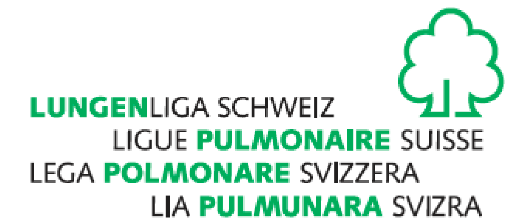
LUNGENLIGA SCHWEIZ
LIGUE PULMONAIRE SUISSE
LEGA POLMONARE SVIZZERA
LIA PULMUNARA SVIZRA

Concluding remarks/Jean-Paul Janssens

Introduction/ OFSP-BAG/ Andrea Arz de Falco/ Thomas Burgener



Duration of hospital stay for TB inSwitzerland / Otto Schoch

- 2002-2015: 7726 patients with TB in CH (OFSP). 500-600 /cases/year stable since 2007
- 7395 hospitalizations. ***81% hospitalization rate***; 14% readmission rate
- 76%: TB of airways; mostly male, median age: 40; any resistance: 1.1%; MDR: 0.7%
- Median duration of stay: 14 (IQR: 7-22), longer if > 65 yrs, M, (MD)R, miliary pattern or CNS, co-morbidities (HIV, endocrine, metabolic disorders, malnutrition, lung and liver disorders)
- Wide differences between Cantons: room for improvement by encouraging earlier outpatient care to decrease length of stay

Access to care for vulnerable TB patients / Constantin Bandolfi

Unisanté, Centre universitaire de médecine générale et santé publique, Lausanne

- Concept of vulnerability: *medical & social*; people on the move, poor (8.7% in CH); working poor (4.2% in CH): impact on renouncing to care
- Illustrative clinical case: delayed diagnosis of TB spondylodiscitis in a 46 year old male gambian
- « People on the move »: *systemic* and individual vulnerability; high risk of treatment interruption
- Screening systems (Centres for asylum seakers, prisons, referral in the Cantons to specialized structures: USMI, PSM)
- Importance of correctly identifying situations medically at risk *(« urgent »)* to ensure access to appropriate care and insurance coverage: major role of HCWs
- Among industrialized countries, Switzerland is 4th for equity of care and 8th for access to care

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What does thoracic surgery bring us today for the treatment of TB?

Jean Y. Perentes, Chirurgie thoracique, CHUV

- Historical perspective: Forlanini (1882), modalities of collapsotherapy, thoracoscopy (1910), thoracoplasty (1920's), pulmonary resection and reexpansion/drainage (as of ≈ 1950); regain of interest with MDR/XDR
- Present role of surgery: 1.Resection of persistent cavitary lesions in MDR/XDR (« reservoir ») added to medical treatment. In MDR/XDR : 47-95% cure rate; combination most often superior to medical treatment alone; mortality rates depend on extension of disease. Treatment after surgery: 12 months for MDR, 24 for XDR
- 2. Importance of treating « residual spaces »; 3. Correction of pleural restrictive sequellae (decortication)
- 4. Treatment of proximal airway stenosis (with endoscopic approach)
- General condition important for prognosis as well as having localized lesions. Multidisciplinary management mandatory.

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Pulmonary TB and COVID-19 /Jesica Mazza-Stalder

- TB during the pandemic: > 500'000 deaths; *1.4 M cases may not have received care for TB*. Many countries report *a decrease in case notification* (India, China, Brazil)
- Mortality has increased in emergent countries because of delayed diagnosis: poor access to care?
- Disruption of care for TB because of COVID. ***Worsening economic situation of vulnerable populations***.
- Illustrative case of co-infection with delayed diagnosis of TB in patient under anti-TNF
- Decrease in contact tracing, and management and treatment of LTBI. Marked increase in working poor and precarity
- No positive impact of social distancing.
- Potential positive and helpful contribution of digital technologies , and co-screening (COVID & TB)

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Therapeutic drug monitoring (TDM) during treatment for TB /

Pascal André/ Head pharmacist, CHUV

- Indications and modalities of TDM. Available for TB: 4 x 1st-line drugs & 12 x 2nd line drugs
- Reference levels: published in 1992…
- Interpretation: Steady state ?; Trough or peak?; doses and other drugs; clinical condition; suitability of result (or dose adjustment).
- Problem of drug levels in blood versus tissues (i.e. alveolar tissues); free vs linked levels..
- Clinical case: Messages: 1/Use of IBW for drug dosage; 2/drug interactions: no direct role for IPP but effect on gastric pH may affect solubility and dissolution of RIF; 3/Intrinsic variability; 4/ INH acetylor type: slow or intermediate type may have higher hepatotoxicity
- Case 2: CLO: many questions remain ; no correlation between TDM and effect
- THM: *still limited current knowledge*; may be helpful to explain poor clinical response or in case of comorbidities and drug interactions. More important potential for MDR/XDR

Treatment of TB with rifampicin: are we using the right doses?

Martin Boere, Nijmegen, NL

- Background: Relapse rate: 2.8% during 1st year. *Low INH and RIF peak levels and AUC precede acquired drug resistance*. Initially, tests looked for the lowest efficient dose to limit toxicity.
- Higher doses of RIF may decrease relapse rate & emergence of resistance, and decrease TTC
- Many studies in sub-saharan Africa looking at higher doses of RIF (PanACEA): 10 mg/kg vs 20-40 mg/kg: *well tolerated, no withdrawals*
- At 50mg/kg: higher withdrawal rates: « not happy patients »!
- 600-1200 mg RIF in intensive phase: no increase in bacteriological response: up to 20 mg/kg too low!
- ***RIF 35*** vs 10-20 mg/kg: decrease in time to culture conversion (adj HR: 1.99); toxicity stable
- *Team of M Boere uses 35 mg/kg of RIF in severe PTB, TBM, TB and HIV, severe EPTB, TB and diabetes*
- Doses of 40 mg/kg may allow shorter regimens (3-4 months) in the future (2100 mg)

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INTENSE TBM: Intensified TB treatment to reduce the mortality of tuberculous meningitis: on-going study / Alexandra Calmy, HUG

- Intense TBM project. Multicentric study in sub-saharan Africa (Ivory Coast, Uganda, Madagascar, South Africa). *Started Jan 2021*. Mortality of TBM: HIV-: 30%; HIV+ : up to 70 %; long term sequellae possible.
- Poor penetration of RIF in CNS.
- Aim: 4 arms (n=192/arm): Mortality: Intense tt for TBM during first 8 weeks vs SOC; 2/ aspirine (8W) vs placebo
- SOC: 2HRZE/7HR + DEX over 60 days; **Intensified REG: RIF 35 mg/kg 8 weeks** then 10mg/kg ; LIN 1200 4 weeks, 600 4 weeks, +HZE. **RIF: 300-750 g vs 1200-2550 mg**
- ***Evidence: High RIF safe, reduces TTC, may decrease mortality (Ph II, 2013); becomes detectable and reaches MIC in CSF at higher doses***
- LIN: interaction with RIF: 2 x increase in dosage; substudies ASP; Dble dose: Dolutegravir

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PRO-Con debate: measuring serum levels of anti-TB drugs: Waste of money or effective for individualized treatment?

Jan Fehr, ZH/ Gunar Günther, BE

- Toxicity matters and affects QoL: hearing loss, hepatatis, vomiting, depression , neuralgia
- Risk of MDR/XDR: 50% of all TB-treatment costs for MDR; 56% of MDR and 40% of XDR treated successfully
- Lower serum cc: higher risk of remaining C+
- Possible implications for transmission? Little/no impact on treatment failure.
- Meta-analysis (2020, 15 studies): Low PZA increases poor outcome; low RIF may slightly affect outcome; low EMB and INH: no documented difference
- WHO 2018: no demonstrated added value of TDM except in specific drug regimens (LIN, CYC)
- Many unanswered questions: when, how, what to measure, cost-effectiveness, low income areas…

SwissTB award 2021: and the winners are……..

- Fabian Arnold, ZH, Miriam Weber & Imre Gonda, ZH
- Congratulations! (and thanks to Swiss-TB!)

Mycobacterial siderophores (mycobactins)

Concluding remarks /Jean-Paul Janssens

- Many thanks to all our excellent speakers
- Many thanks to the organizers and interpreters
- Thank you for your participation
- Stay safe and in good health!
- See you next year hopefully in « real life »:
- Save the date: 24.3.2022

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