



## MDR-TB treatment needs in patients previously treated for TB in Cotonou, Benin

S. Ade,<sup>1,2</sup> A. Trébuq,<sup>2</sup> A. D. Harries,<sup>2,3</sup> D. Affolabi,<sup>1</sup> G. Ade,<sup>1</sup> G. Agodokpessi,<sup>1</sup> P. Wachinou,<sup>1</sup> S. Anagonou,<sup>1</sup> M. Gninafon<sup>1</sup>

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**Setting:** Centre National Hospitalier de Pneumo-Phthisiologie, Cotonou, Benin.

**Objective:** To determine the proportion of individuals needing treatment for multidrug-resistant tuberculosis (MDR-TB) among patients previously treated for TB.

**Design:** A retrospective cross-sectional study of all patients previously treated for TB in Cotonou from 2003 to 2011.

**Results:** Of 956 patients on retreatment, 897 (94%) underwent culture and/or a line-probe assay. For different reasons, 594 (66%) underwent drug susceptibility testing for rifampicin (RMP), of whom 95 (16%) had RMP resistance (68 multidrug-resistance [MDR] and 27 other RMP resistance) and therefore needed treatment for MDR-TB. These represent 39% of patients who failed/relapsed after standardised retreatment, and 20% of those who failed, 19% of defaulters and 11% of relapses after first-line treatment. Residence outside of Benin was associated with a higher risk of RMP resistance (RR 3.13, 95%CI 2.19–4.48,  $P < 0.01$ ). From 2003 to 2011, the prevalence of RMP resistance decreased from 25% to 5% among patients living in Benin. Human immunodeficiency virus (HIV) prevalence was 25%; no association was found between HIV and RMP resistance. Of patients failing treatment, 48% were fully susceptible, 22% were mono-resistant and 8% poly-resistant.

**Conclusion:** The majority of patients who fail retreatment or first-line treatment in Cotonou do not require empirical treatment for MDR-TB.

In the last decade, tuberculosis (TB) control worldwide has been disrupted due to associated human immunodeficiency virus (HIV) infection and multidrug-resistant TB (MDR-TB, defined as resistance to at least rifampicin [RMP] and isoniazid [INH]). As a result, national tuberculosis programmes (NTPs) have been advised by the World Health Organization (WHO) to develop strategies to better detect and treat the growing number of MDR-TB cases.<sup>1</sup> According to the 2011 WHO report, there were an estimated 650 000 MDR-TB patients in the world.<sup>2</sup>

Management of MDR-TB requires local strategies that identify and diagnose affected patients as early as possible. In this regard, RMP-resistant patients have almost the same profile of response to the retreatment regimen, which uses first-line anti-tuberculosis drugs, as patients who have MDR-TB, and it is recommended that these patients be treated for MDR-TB.<sup>3</sup>

Since 2009, NTPs have been advised by the WHO to use their country-specific drug resistance data on

patients who have failed, relapsed or returned to treatment after default to determine levels of MDR-TB in their countries. In settings where this information is not available, it is advised that empirical treatment with MDR-TB treatment be started among all failure cases.<sup>4</sup>

Using data from TB patients in Benin, the aim of the current study was to report on the spectrum of failure, relapse and treatment after default in patients previously treated for TB, and to determine the drug susceptibility patterns of these patients to assess whether all failure patients should indeed receive empirical MDR-TB treatment. The specific objectives of the study were to determine in retreatment patients (stratified by types of retreatment), over the 9 years from 2003 to 2011: 1) the proportions with sputum submitted for culture and/or rapid test for drug susceptibility testing (DST) and who are resistant to RMP and/or INH, 2) the drug resistance pattern in relation to country of residence, 3) the association of drug resistance with HIV status, and 4) other patterns of drug resistance.

### STUDY POPULATION, DESIGN AND METHODS

#### Study design

This was a retrospective study involving a review of patient records.

#### Setting—general and study site

##### Country

Benin is a country in West Africa with a population of 9 million. The country registers about 3500 TB patients each year, of whom fewer than 10% have been previously treated. The NTP follows the DOTS strategy and uses recognised international criteria for the diagnosis and treatment of patients with TB.<sup>5,6</sup> Diagnosis, registration and care are decentralised to 57 Basic Management Units (BMUs) in the country. Cotonou, the economic capital, is served by three BMUs, including the Centre National Hospitalier de Pneumo-phthisiologie (CNHPP), the largest BMU in the country, which houses the NTP. Almost all retreatment patients in Cotonou are registered and treated in this centre. Because of its good reputation and its geographic situation, the CNHPP also receives patients from other countries, especially Nigeria.

##### TB control

In Cotonou, since 2003, smear-positive patients with a previous history of TB have been requested to provide sputum for culture and DST; such patients are

#### AFFILIATIONS

- 1 National Tuberculosis Programme, Cotonou, Benin
- 2 International Union Against Tuberculosis and Lung Disease, Paris, France
- 3 London School of Hygiene & Tropical Medicine, London, UK

#### CORRESPONDENCE

Serge Ade  
National Tuberculosis Programme  
Cotonou, Benin  
Tel: (+229) 96545760  
email: adeserg@yahoo.fr

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#### KEY WORDS

multidrug resistance; rifampicin; retreatment; group

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classified as failure, relapse and treatment after default according to national and international guidelines.<sup>5,6</sup> The classical retreatment regimen consists of an initial phase of RMP, pyrazinamide, INH and ethambutol (EMB) for 3 months (with streptomycin [SM] in addition during the first 2 months) followed by a continuation phase of RMP, INH and EMB for 5 months. All cultures, DST and/or molecular tests and anti-tuberculosis drugs are free of charge.

Patients with MDR and other RMP resistance are treated with a shortened 9-month regimen recommended by the International Union Against Tuberculosis and Lung Disease (The Union). The patients take daily gatifloxacin (replaced by moxifloxacin since February 2013), prothionamide, ethambutol, clofazimine and pyrazinamide under direct observation for 9 months, with kanamycin and INH (at double dose) in addition during the first 4 months. Second-line drugs are provided only by the NTP and are not available in private pharmacies.

### Mycobacteria Reference Laboratory

Standard culture and DST are performed in the Mycobacteria Reference Laboratory, Cotonou, Benin. After decontamination by the modified Petroff method, sputum is cultured on solid medium (Löwenstein-Jensen) in two tubes. When the culture is positive, mycobacteria are identified using thiophene-2-carboxylic acid hydrazide medium and biochemical tests such as nitrate reductase test, niacin test and catalase test at 68°C. When the test is positive for *Mycobacterium tuberculosis* complex, DST is performed against RMP, INH, SM and EMB using the proportion method at the following concentrations: RMP 40 µg/ml, INH 0.2 µg/ml, SM 4 µg/ml and EMB 2 µg/ml. Since 2009, the Hain GenoType® MTBDRplus line-probe assay (LPA; Hain LifeScience GmbH, Nehren, Germany) for RMP and INH has also been used for the rapid detection of resistance to these drugs.

Quality control of the laboratory is regularly performed by the supranational laboratory at the Mycobacteriology Unit of the Institute of Tropical Medicine, Antwerp, Belgium, and shows excellent results.

### Patients

All patients with smear-positive sputum and previously treated for TB (failure, relapse or default after new treatment, and TB patients returning after retreatment) and registered at the CNHPP from 2003 to 2011 were included in the study.

### Data variables, source of data and collection tool and data validation

Information on all previously treated TB patients was systematically entered into an electronic database constructed from the TB register. DST results were entered later. Data variables collected

included epidemiological characteristics (sex, age, living in or outside Benin), diagnostic characteristics (type of patient, HIV status), culture results, and DST results for RMP, INH and other drugs. In case of discordance between culture and molecular test results, culture was used as the gold standard.

### Analysis and statistics

Data were analysed using EpiData version 3.1 (EpiData Association, Odense, Denmark). Frequency, percentage and proportions were used to describe the patient population. Comparisons were made using the  $\chi^2$  test. Levels of significance were set at 5%.

### Ethics

The study was approved by the NTP and the Ethics Advisory Group of The Union. It did not involve direct interaction with human subjects and was therefore deemed to represent minimal risk.

## RESULTS

### Patient characteristics and results of sputum culture and drug susceptibility testing

A total of 956 patients (mean age 36 years, male/female ratio 3.0) were started on a retreatment regimen. This represented 10% of the 9604 TB patients treated at the centre, 97% of the 985 retreatment patients treated in Cotonou and 40% of the 2516 retreatment patients registered in Benin during the same time period.

The number of retreatment cases and the numbers and proportions with culture and/or LPA, a DST result for RMP and evidence of RMP resistance, stratified by the different categories of retreatment, are shown in Table 1. A high proportion (94%) of patients provided sputum for culture and/or LPA; 66% underwent DST for RMP. For the remaining 34%, DST for RMP was not available for a number of reasons (negative culture, identification of atypical mycobacteria, inconclusive results, contamination). The culture contamination rate was low, at 2.6%. A total of 68 patients (11% of those with a DST for RMP) had MDR-TB; the highest rates were observed among smear-positive patients who had failed or relapsed after a retreatment regimen or on first-line treatment. Another 27 patients (5%) had resistance to RMP without resistance to INH. Altogether, 95 patients (16% of those with DST for RMP; mean age 34 years, male/female ratio 4.6) were diagnosed as RMP-resistant and required treatment for MDR-TB. The final diagnosis of RMP resistance was established using a phenotypic method for 92 patients and LPA for 3 (Figure 1).

### Patient distribution by place of residence and trends

The place of residence of the RMP-resistant patients in relation to the different types of retreatment is shown in Table 2. Most

**TABLE 1** Retreatment patients and their culture and DST results in relation to different types of retreatment in Cotonou, Benin, 2003–2011

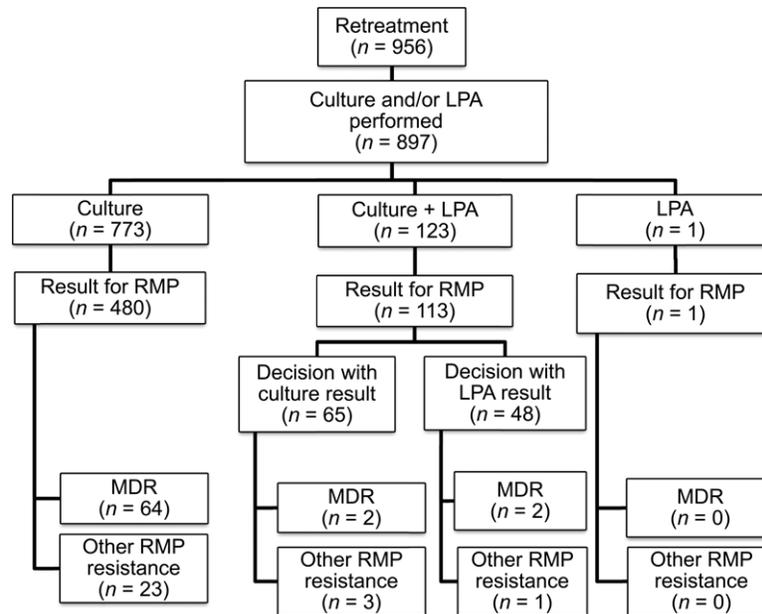
Type	Failure after first-line treatment n (%)	Relapse after first-line treatment n (%)	Default after first-line treatment n (%)	After retreatment (failure, relapse) n (%)	Total n (%)
All patients on retreatment	175	470	263	48	956
Patients with culture and/or Hain test performed	165 (94)*	440 (94)*	248 (94)*	44 (92)*	897 (94)*
Patients with a DST result for RMP (culture and/or LPA)	94 (57)†	300 (68)†	172 (69)†	28 (64)†	594 (66)†
MDR	18 (19)‡	22 (7)‡	21 (12)‡	7 (25)‡	68 (11)‡
RMP resistance (without MDR)	1 (1)‡	11 (4)‡	11 (6)‡	4 (14)‡	27 (5)‡
RMP resistance (without MDR) + MDR	19 (20)‡	33 (11)‡	32 (19)‡	11 (39)‡	95 (16)‡

\*Percentage calculated for all patients on retreatment.

†Percentage calculated for patients who had culture and/or Hain test performed.

‡Percentage calculated for patients with a DST result for RMP after culture and/or Hain test.

DST = drug susceptibility testing; RMP = rifampicin; LPA = line-probe assay; MDR = multidrug resistance.



**FIGURE 1** Number of patients with RMP resistance stratified by different methods of DST among retreatment patients. LPA = line-probe assay; RMP = rifampicin; MDR = multidrug resistance; DST = drug susceptibility testing.

**TABLE 2** Patients with RMP resistance and relationship between types of retreatment and residence inside or outside Benin, Cotonou, 2003–2011

Residence	Failure after first-line treatment		Relapse after first-line treatment		Default after first-line treatment		After retreatment		Total	
	N	n (%)*	N	n (%)*	N	n (%)*	N	n (%)*	N	n (%)*
Benin	88	12 (15)	270	26 (10)	71	5 (7)	19	5 (26)	441	48 (11)
Outside Benin	13	7 (54)	30	7 (23)	101	27 (27)	9	6 (67)	153	47 (31)

\*Proportion of patients with DST result who had RMP resistance.

RMP = rifampicin; N = total number of patients with a result for RMP after culture and/or LPA; n = total number of RMP-resistant patients; DST = drug susceptibility testing; LPA = line-probe assay.

**TABLE 3** Retreatment cases, culture and DST and MDR-TB, stratified by residence inside or outside Benin and by year, Cotonou, 2003–2011

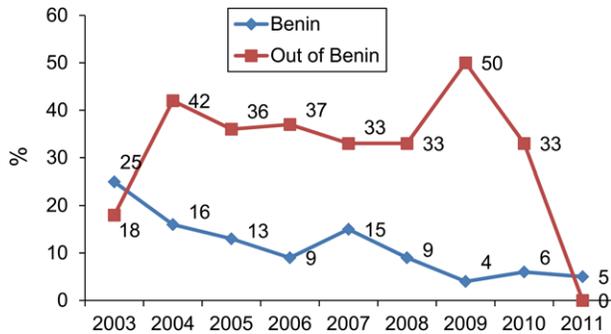
Year	Benin				Outside Benin			
	Retreatment n	Culture and/or LPA performed n (%)*	Patients with DST for RMP after culture or LPA n (%)†	MDR + other RMP resistance n (%)‡	Retreatment n	Culture and/or LPA performed n (%)*	Patients with DST for RMP after culture or LPA n (%)†	MDR + other RMP resistance n (%)‡
2003	88	81 (92)	48 (59)	12 (25)	76	74 (97)	50 (68)	9 (18)
2004	66	58 (88)	38 (66)	6 (16)	48	47 (98)	26 (55)	11 (42)
2005	77	73 (92)	48 (66)	6 (13)	49	49 (100)	27 (55)	10 (37)
2006	82	72 (88)	45 (63)	4 (9)	24	23 (96)	19 (83)	7 (37)
2007	94	86 (91)	55 (64)	8 (15)	21	15 (71)	9 (60)	3 (33)
2008	74	71 (96)	46 (65)	4 (9)	21	20 (95)	12 (60)	4 (33)
2009	78	76 (97)	48 (63)	2 (4)	6	6 (100)	4 (67)	2 (50)
2010	61	60 (98)	51 (85)	3 (6)	4	3 (75)	3 (100)	1 (33)
2011	82	78 (95)	62 (79)	3 (5)	5	5 (100)	3 (60)	0
Total	702	655 (93)	441 (67)	48 (11)	254	242 (95)	153 (63)	47 (31)

\*Percentage of number of patients on retreatment in each year.

†Percentage of those with culture and/or LPA performed.

‡Percentage of those with DST result.

DST = drug susceptibility testing; MDR-TB = multidrug-resistant tuberculosis; LPA = line-probe assay; RMP = rifampicin; MDR = multidrug resistance.



**FIGURE 2** Annual prevalence of MDR-TB and other RMP resistance in patients living inside and outside Benin, Cotonou, 2003–2011. MDR-TB = multidrug-resistant tuberculosis; RMP = rifampicin.

patients (73%) were living in Benin; the remainder had a permanent address outside the country, mostly in Nigeria. Residence outside Benin was associated with a higher risk of RMP resistance (relative risk [RR] 3.13, 95%CI 2.19–4.48,  $P < 0.01$ ). This difference was also maintained when stratified by different types of retreatment: the results for failures and defaulters were 54% vs. 15% ( $P < 0.01$ ) and 27% vs. 7% ( $P < 0.01$ ), respectively.

The annual numbers of retreatment cases with culture, DST and RMP resistance results between 2003 and 2011 for those living in and outside Benin are shown in Table 3 and Figure 2. The number of retreatment cases living in Benin remained stable during this period, but the proportion with RMP resistance (MDR-TB

**TABLE 4** Retreatment patients with MDR-TB and RMP resistance in relation to known HIV status, Cotonou, Benin

Known HIV status	Total <i>n</i>	MDR + other RMP resistance <i>n</i> (%)
HIV-positive	68	4 (6)
HIV-negative	221	25 (13)

MDR-TB = multidrug-resistant tuberculosis; RMP = rifampicin; HIV = human immunodeficiency virus; MDR = multidrug resistance.

included) decreased from 25% in 2003 to 5% in 2011. For patients living outside Benin, the numbers of retreatment cases declined over time, but the proportion with RMP resistance (MDR-TB included) remained high, at 30–50%.

### Association between HIV infection and MDR-TB

Since 2007, 99% of TB patients have been tested for HIV and systematically reported. Of the 289 retreatment patients tested, no association was found between HIV infection and RMP resistance, including MDR-TB (RR 0.52, 95%CI 0.19–1.44,  $P = 0.28$ ; Table 4).

### Other patterns of resistance

Phenotypic DST results in retreatment patients are shown in Table 5. Of the 545 patients with phenotypic DST performed, 53% were fully susceptible to all four first-line anti-tuberculosis drugs, while in patients who had failed treatment (both first-line and

**TABLE 5** Patterns of anti-tuberculosis drug resistance in retreatment patients, stratified by type of retreatment, Cotonou, Benin, 2003–2011\*

	Failure after first-line treatment <i>n</i> (%)	Relapse after first-line treatment <i>n</i> (%)	Default after first-line treatment <i>n</i> (%)	After retreatment <i>n</i> (%)	Total <i>n</i> (%)
Phenotypic DST	81	268	170	26	545
Fully susceptible	39 (48)	155 (58)	85 (50)	11 (42)	290 (53)
Any resistance	43 (53)	113 (42)	85 (50)	14 (54)	255 (47)
S	31 (38)	84 (31)	64 (38)	12 (46)	191 (35)
R	19 (23)	31 (11)	32 (19)	10 (38)	92 (17)
H	28 (35)	50 (19)	40 (23)	7 (26)	125 (23)
E	13 (16)	24 (9)	15 (9)	5 (20)	57 (10)
Monoresistance	18 (22)	56 (21)	40 (24)	4 (15)	118 (22)
E	1 (1)	6 (2)	0	0	7 (1)
H	5 (6)	9 (3)	10 (6)	0	24 (4)
S	12 (15)	41 (15)	30 (18)	4 (15)	87 (16)
Polyresistance	5 (6)	26 (10)	13 (8)	0	44 (8)
ES	1 (1)	5 (2)	4 (2)	0	10 (2)
HE	0	0	1 (1)	0	1 (0.2)
HES	0	5 (2)	1 (1)	0	6 (1)
HS	4 (6)	16 (6)	7 (4)	0	27 (5)
RMP resistance	1 (1)	11 (4)	11 (7)	3 (12)	26 (5)
R	0	6 (2)	5 (3)	0	11 (2)
RE	0	0	0	1 (4)	1 (0.2)
RES	0	2 (1)	1 (1)	0	3 (0.6)
RS	1 (1)	3 (1)	5 (3)	2 (8)	11 (2)
MDR	18 (22)	20 (7)	21 (12)	7 (27)	66 (12)
RH	3 (4)	7 (3)	5 (3)	0	15 (3)
RHE	2 (2)	1 (0.4)	0	1 (4)	4 (1)
RHS	4 (5)	7 (3)	8 (5)	3 (12)	22 (4)
RHSE	9 (11)	5 (2)	8 (5)	3 (12)	25 (5)

\*Hain test results are not included in this table.

DST = drug susceptibility testing; S = streptomycin; R, RMP = rifampicin; H = isoniazid; E = ethambutol; MDR = multidrug resistance.

retreatment regimens) over 40% were fully susceptible to these four drugs. Resistance to SM was the most frequent type of resistance encountered, regardless of the type of retreatment, followed by INH. Overall, monoresistance to any single drug was found in 22% of patients and polyresistance in 8%.

## DISCUSSION

During the study period, nearly 95% of recorded retreatment patients underwent culture or a rapid LPA, and two thirds underwent DST to assess RMP susceptibility. Altogether, 16% of the patients had either MDR-TB or other RMP resistance, both of which require treatment for MDR-TB. Higher rates of MDR-TB were identified in patients who had failed first-line treatment, who had failed or relapsed after a retreatment regimen and who resided in countries outside Benin. Interestingly, for those retreatment patients living in Benin, there was a decreasing prevalence of MDR-TB over the 9 years. Finally, amongst all retreatment cases with DST results, the most common pattern was full susceptibility to all four of the first-line anti-tuberculosis drugs; even amongst those failing the first-line or retreatment regimens, between 40% and 50% of patients had fully susceptible mycobacteria.

The strengths of the study were the large number of patients evaluated, the excellent monitoring and recording system and the fact that culture and DST were performed in a reliable laboratory, with contamination rates of 2.6%, lower than the 5% generally reported from other laboratories.<sup>7</sup> Limitations reflect the retrospective nature of the study, use of routinely collected data, which can be incomplete, and unusable results for 34% of the retreatment patients. In addition, during the first years, HIV testing and LPA had not been performed; these activities started later, in 2006 and 2009, respectively.

Benin is a low-burden country for MDR-TB, with about 0.5% of new patients reported as MDR-TB.<sup>8,9</sup> Overall, fewer than expected (16%) retreatment patients needed treatment for MDR-TB, and thus the majority can still be appropriately treated with first-line anti-tuberculosis drugs. The highest risk group for MDR-TB was those patients who failed or relapsed after a retreatment regimen, and where resources are tight priority must be given to these patients for culture and DST. The other high-risk group included patients who failed after a first-line regimen, likely due to poor adherence.

The WHO currently recommends empiric MDR treatment for failure patients, if individual or country-specific DST information is not available.<sup>4</sup> The results of our study suggest that this recommendation would be inappropriate for Cotonou, where 80% of failure cases do not have MDR-TB and could be treated with a retreatment regimen using first-line anti-tuberculosis drugs. Giving empirical MDR-TB treatment to so many patients unnecessarily might also promote the emergence of resistance to second-line anti-tuberculosis drugs, particularly if the administration and monitoring of MDR-TB treatment is weak.

The prevalence of MDR-TB among failure patients varies from country to country. For example, respectively 50% and 94% of failure patients from Bangladesh and Peru had MDR-TB, while none were found in Malawi.<sup>10-12</sup> A study in Tehran, Iran, found no significant differences in MDR-TB rates in recurrent and new TB patients, with the authors suggesting that empirical MDR-TB treatment should be avoided and decisions on use of this regimen should only be made when DST results become available.<sup>13</sup> The WHO recommendation on empirical treatment for failure cases should therefore be adjusted to the country's specific situation.

In contrast to patients who fail treatment, defaulters are usu-

ally attributed a lower MDR-TB risk, varying from 0.4% to 4%.<sup>14</sup> However, in our study, the risk of MDR-TB (when adding the results of monoresistance to RMP) was much higher, at nearly 20%, and thus this group of patients might also be accorded priority for DST in Cotonou. Patients with relapse TB had the lowest risk of MDR-TB; this may be because their recurrent TB arises from reinfection rather than endogenous reactivation, although we have no evidence to back up this statement.

Our findings might be useful when it comes to the practical application of the new nucleic acid amplification test, Xpert<sup>®</sup> MTB/RIF (Cepheid Inc, Sunnyvale, CA, USA). According to validation studies,<sup>15-18</sup> when the prevalence of RMP resistance exceeds 15% in any group of patients, the positive predictive value of an RMP-resistant result with Xpert MTB/RIF is >90%, but this declines to 32% when the prevalence of RMP resistance is low, at <1%. Therefore, in our patients who failed or relapsed after retreatment and failed or returned after default with first-line treatment, an RMP-resistant result could be accepted without the need for a confirmatory culture and DST. For relapse cases, however, confirmation would be necessary before treatment for MDR-TB.

In this study, we found no association between HIV and MDR-TB, similar to other studies in sub-Saharan Africa.<sup>9,19</sup>

While the decreasing prevalence of MDR-TB in retreatment patients over 9 years in those residing in Benin is reassuring for the NTP, we are not sure of the reasons for this. The higher numbers recorded during the first years of surveillance may relate to a backlog of previously unknown cases. The decrease in numbers of retreatment cases among those with permanent addresses outside Benin is likely due to referral to centres in their country of residence close to their homes before registration, a policy that began in 2009.

## CONCLUSION

Patients who failed or relapsed after retreatment or failed and defaulted after first-line treatment had a higher risk of requiring treatment for MDR-TB in Cotonou. However, the majority of these patients did not have MDR-TB and could thus be successfully treated with first-line anti-tuberculosis drugs.

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**Contexte :** Centre National Hospitalier de Pneumo-Physiologie, Cotonou, Bénin.

**Objectif :** Déterminer la proportion de patients nécessitant un traitement pour une tuberculose multirésistante (TB-MR) parmi les cas en retraitement.

**Schéma :** Etude rétrospective de type transversal ayant inclus tous les patients en retraitement contre la tuberculose (TB) à Cotonou de 2003 à 2011.

**Résultats :** Des 956 patients traités par un régime standardisé de retraitement, la culture et/ou le Hain test ont pu être réalisés chez 897 d'entre eux (94%). Pour diverses raisons, le résultat du test de sensibilité à la rifampicine (RMP) était exploitable chez 594 patients (66%). Parmi ceux-ci, 95 (16%) avaient une résistance à la RMP (68 en multirésistance [MR] et 27 résistances à la RMP mais non MR) et par conséquent, nécessitent un traitement de type TB-MR. Ils représentaient 39% des patients en échec/rechute après un régime de traite-

ment, et 20% des patients en échec, 19% des repris après interruption et 11% des patients en rechute après un régime de primo-traitement. Une résidence habituelle en dehors du Bénin était significativement associée à une résistance à la RMP (RR 3,13 ; IC95% 2,19–4,48 ;  $P < 0.01$ ). De 2003 à 2011, la prévalence de la résistance à la RMP parmi les patients ayant une résidence habituelle au Bénin a baissé de 25% à 5%. La prévalence de l'infection du virus de l'immunodéficience humaine (VIH) est de 25%. Nous n'avons pas retrouvé une association entre l'infection au VIH et la résistance à la RMP. Parmi les cas d'échecs à un primo-traitement, 48% étaient sensibles à tous les anti-tuberculeux de première intention, 22% étaient mono-résistants et 8% poly-résistants.

**Conclusion :** A Cotonou, la majorité des patients qui échouent à un traitement de première ligne ou à un régime standard de retraitement ne nécessitent pas un traitement empirique de TB-MR.

**Marco de referencia:** El Centro Nacional Hospitalario de Neumología de Cotonou, en Benín.

**Objetivo:** Determinar la proporción de pacientes tratados por tuberculosis (TB) que necesitan un régimen de tratamiento contra la TB multidrogorresistente (TB-MDR).

**Método:** Fue este un estudio transversal retrospectivo de todos los pacientes tratados previamente por TB en Cotonou entre el 2003 y el 2011.

**Resultados:** De los 956 pacientes inscritos en retratamiento, en 897 (94%) se practicó un cultivo o una prueba de Hain. Por razones variadas, se realizó una prueba de sensibilidad a rifampicina (RMP) en 594 pacientes (66%) y se obtuvieron 95 resultados de resistencia (16%; 68 MDR y 27 casos de otro tipo de resistencia a RMP), lo cual indicó la necesidad de un régimen contra la TB-MDR. Estos pacientes representaron 39% de los pacientes que fracasaron o recayeron después de un retratamiento normalizado y 20% de los fracasos, 19% de los

abandonos y 11% de las recaídas después de un régimen terapéutico con medicamentos de primera línea. La residencia fuera de Benín fue un factor que se asoció con un mayor riesgo de presentar resistencia a RMP (RR 3,13; IC95% 2,19–4,48;  $P < 0,01$ ). Entre el 2003 y el 2011, la prevalencia de resistencia a RMP disminuyó de 25% a 5% en los pacientes que residían en Benín. La prevalencia de infección por el virus de la inmunodeficiencia humana (VIH) fue 25%. No se observó ninguna asociación entre la infección por el VIH y la resistencia a RMP. De los pacientes que fracasaron el tratamiento el 48% era normosensible, el 22% monorresistente y el 8% presentaba resistencia a múltiples medicamentos.

**Conclusión:** La mayoría de los pacientes que fracasaron el retratamiento o el tratamiento con medicamentos de primera línea en Cotonou no necesitan un tratamiento empírico con un régimen contra la TB-MDR.