IN-05 Antibiotics: salvage, expiry, choice and stewardship

HEALING after the FALL, research library, IN-05

Researched 10 October 2026 by Claude Opus agent for THRIVING after the FALL, Book Four. Library document, unverified.

Findings by section

1. Scope and the three voices

This report asks four questions. What is a salvaged antibiotic worth years after the date on its box? Which ten should a village take first? How is each dosed by syndrome and weight without a laboratory? How does a village of 300 ration a chest that will never be refilled?

Three kinds of source are used: the stability record (the US Shelf Life Extension Program, FDA decisions on stockpiled doxycycline, laboratory studies of expired and heat-stressed stock), the clinical record (the MSF Essential Drugs guide, WHO AWaRe dosing, the AFRINEST newborn trials, Cochrane reviews), and the record of harm (degraded tetracycline case reports, anaphylaxis registries, cohort studies of tendon, ear and marrow damage). Three voices are kept apart throughout. The folklore says old drugs either "turn to poison" or "last for ever". The record says what was measured. The inference is what a careful reader may conclude where the record is silent, and it is marked [VERIFY] wherever it carries a number.

None of the related reports named in the brief (IN-03, IN-04, IN-06, ME-09, OR-06, SY-09) was in the library when this was written. IN-01 was read and supplies the death rates that antibiotics change (THRIVING library, IN-01). IN-01 found no plant that replaces amoxicillin for pneumonia, and none is assessed here.

2. What expiry means

2.1 The date and the Shelf Life Extension Program An expiry date marks the end of the period over which the maker has shown that the product keeps at least 90 per cent of its stated content and stays within limits for impurities and dissolution, when stored as labelled. It is the date beyond which nobody checked, not the date the drug fails. Neither the FDA nor the American Medical Association recommends dosing with expired drugs (Culbertson 2011, abstract only).

The US military's Shelf Life Extension Program (SLEP) tests stockpiled drugs and extends their dates lot by lot. Lyon and colleagues (2006) reviewed 3,005 lots of 122 products. About 88 per cent were extended, by a mean of about 66 months, with wide variation between lots (abstract and secondary accounts only. One secondary source gives 62 months [VERIFY]). Aronson (2019) adds that 479 lots (16 per cent) eventually failed, on potency, impurities, pH, water content, dissolution or appearance, that no lot failed within a year of its date, and that doxycycline tablets had no failures until the sixth year of testing. He notes that the published counts do not add up cleanly and warns that "previous stability does not guarantee future stability". SLEP drugs were unopened, kept in controlled stores, and every lot was tested before it was extended. Its 88 per cent describes well-kept stock that someone checks, not pills from a flooded pharmacy.

2.2 Very old drugs: Cantrell 2012 and Zilker 2019 Cantrell and colleagues (2012) analysed eight long-expired prescription products, 28 to 40 years past date, containing 14 active ingredients. Twelve of the 14 were still at 90 per cent or more of label. Aspirin and amphetamine were not. There were no antibiotics among them, and the authors did not recommend using expired drugs (secondary accounts only, including NPR 2017).

Zilker (2019) tested 50 drug substances 20 to 30 years old and 14 ampoules over 40 years old. Forty-four of the 50 still met European Pharmacopoeia standards. Among the ampoules, procaine had fallen to about 70 per cent and adrenaline (epinephrine) to about 70 per cent (summary page read). Both matter here: procaine is half of procaine penicillin, and adrenaline is the antidote to penicillin anaphylaxis.

2.3 Antibiotics specifically **Doxycycline.** Five lots of stockpiled doxycycline hyclate 100 mg capsules, with original dates from March 2015 to April 2018, were extended to June 2020 and then to July 2022. In February 2023 the FDA refused a third extension because "degradants exceeded acceptable limits" (FDA 2023). These capsules lasted roughly four to seven years past their printed date in controlled storage and then failed on impurities, not content. FDA guidance allows two-year extensions at a time, with a stricter protocol for lots not stored as labelled or more than six years past date (RAPS 2019).

Ciprofloxacin. Expired ciprofloxacin 500 mg batches from public hospitals in Jimma, Ethiopia, assayed at 100.9 to 104.7 per cent of label and norfloxacin at 90 to 99.6 per cent. One ciprofloxacin batch released only 78.7 per cent of its drug in 30 minutes, failing the 80 per cent dissolution standard. Time past expiry was not stated (Getahun et al 2024). The paper cites 242 SLEP ciprofloxacin lots all passing, with inconsistent attribution [VERIFY].

Amoxicillin and co-amoxiclav in heat and damp. Water opens the beta-lactam ring, and heat speeds it. Of 59 co-amoxiclav samples bought in Cambodia, 13.6 per cent failed content, 16.9 per cent content uniformity and 33.9 per cent dissolution. Ten of 12 samples with damaged packaging failed, against 14 of 47 intact. At 37 °C and 100 per cent humidity both components decomposed significantly within a day (Khan et al 2013). A review of tropical stability reports amoxicillin capsules from the Democratic Republic of the Congo losing 6 to 24 per cent in six months at 40 °C and 75 per cent humidity, Yemeni co-amoxiclav losing 10 to 33 per cent of its amoxicillin, and capsules in plastic bags or flip-top bottles losing 11 to 16 per cent in one simulated Durban day (PMC8274755 review n.d., search summary only [VERIFY]).

Clavulanic acid is the weakest link. In children's suspensions it lost up to 72 per cent in seven days at 28 °C against about 13 per cent at 8 °C, while amoxicillin lost about 15 per cent at 28 °C. Dissolved dispersible tablets lost 15 per cent of clavulanate in 24 hours at 23 °C and 22 per cent at 28 °C (Mack et al 2021, abstract only).

Suspensions, injectables and eye drops. Dry amoxicillin powder keeps at room temperature. Once mixed, the US label says discard after 14 days, refrigeration "preferable but not required" (amoxicillin label n.d.). A Sudanese thesis found mixed suspension above 90 per cent for seven days even at 40 °C, but down to 67 to 72 per cent by day 14 at 40 °C (SUST n.d., search summary [VERIFY]). Reconstituted ceftriaxone must be used immediately (MSF ceftriaxone). Opened preserved eye drops are conventionally discarded at 28 days and preservative-free units at 24 hours. Contamination of in-use dropper bottles has been reported at 0.07 to 70 per cent (OHSU n.d., search summary). The danger of old opened drops is infection, not weakness.

2.4 The tetracycline story and modern doxycycline The fear that expired drugs become poison has one real root. Frimpter and colleagues (1963) reported three patients, a woman of 54 and two children of 13, who took degraded tetracycline and developed nausea, vomiting, acidosis and protein, sugar and amino acids in the urine, at first mistaken for diabetes. This is the Fanconi syndrome, a failure of the kidney tubules. All recovered in about a month. Gross reported an adult case the same year (cited in Whelton 1978). Wegienka and Weller (1964) described a woman of 39, admitted in September 1961 with severe acidosis after taking capsules dispensed five to six years earlier, whose kidneys were normal again about a year and a half later. Cleveland and colleagues (1965) added a case with low potassium, confusion and sun sensitivity (search summary).

Only anhydro-4-epitetracycline, of three degradation products given to rats and dogs, reproduced the kidney findings (Benitz and Diermeier 1964, search summary). Tetracycline degrades by reversible epimerisation, which gives an inactive but non-toxic product, and by dehydration at carbon 6, favoured below pH 2, which gives the toxic anhydro forms (Young et al 2013). Heat, damp and acid drive it.

Doxycycline and minocycline lack the carbon-6 hydroxyl group whose loss forms the anhydro compounds, so teaching sources state they cannot follow this route (secondary sources only [VERIFY]). Heated doxycycline degrades instead to 4-epidoxycycline, 6-epidoxycycline and methacycline (Young et al 2013). No case of Fanconi syndrome from expired doxycycline was found. The FDA's 2023 refusal shows doxycycline does accumulate impurities, but not that they harm kidneys. The survival-literature claim that a citric acid excipient caused the 1960s cases could not be confirmed [VERIFY].

The record supports a narrow rule. Old plain tetracycline, and by inference its relatives that share the carbon-6 hydroxyl [VERIFY], should be destroyed if brown, sticky or ever hot or damp. Doxycycline in intact packs is among the more stable antibiotics on record, and its main risk with age is inferred to be weakness and impurity rather than kidney poisoning [VERIFY].

2.5 Potency by years past date: an inference No study gives antibiotic potency at 10 or 20 years past date. The table below is an inference from the record above, for planning only [VERIFY throughout].

Form and storage	5 years past	10 years past	20 years past
Tablets, sealed blister or bottle, below 25 °C, dry, dark	Likely above 90 per cent (SLEP mean 66 months, no doxycycline failures to year 6)	Probably usable, failures accumulating	Unknown
Capsules, same storage	Probably usable	Doubtful (doxycycline capsules failed on impurities at 4 to 7 extra years)	Last resort
Any form loose, hot or humid	May be badly degraded within months	Assume weak	Assume inactive
Co-amoxiclav	Treat as plain amoxicillin	Treat as weak amoxicillin	Discard
Dry injectable powders, sealed	Probably usable	Unknown	Unknown
Procaine penicillin suspension	Doubtful without cold	Discard	Discard
Mixed suspension	7 days without cold, 14 with		

The folklore that expired drugs turn toxic is true only for degraded tetracycline. The folklore that they last for ever is false for liquids, co-amoxiclav and anything kept hot and damp. Storage decides more than date.

2.6 The storage rule Water, heat, acid and light destroy antibiotics, roughly in that order. Keep every drug in its original sealed blister or bottle, never decanted into bags or pill boxes (Khan et al 2013). Keep it below 25 °C, the MSF storage line for every antibiotic here, in a cellar or earth-cooled store rather than a kitchen shelf. Keep it dry in a sealed tin or jar with a renewed desiccant such as dried rice or baked clay [VERIFY]. Keep it dark. Never freeze liquids or injectables. Mix suspensions on the day of use, date the bottle and discard at seven days without cold or 14

with it. Use the perishable stock first (mixed liquids, co-amoxiclav, capsules, damaged packs) and hold sealed tablets of amoxicillin, doxycycline, ciprofloxacin, metronidazole and co-trimoxazole for later years.

3. Which antibiotics

3.1 AWaRe WHO's AWaRe system sorts antibiotics into Access (first or second choice for common infections, lower resistance risk), Watch (broader, higher risk, to be monitored) and Reserve (last resort). WHO's target is that at least 60 per cent of use should be Access (Wikipedia n.d.). The 2023 list covers 41 essential antibiotics for more than 30 infections. By the WHO-based lists, amoxicillin, co-amoxiclav, doxycycline, metronidazole, co-trimoxazole, flucloxacillin, benzylpenicillin, gentamicin, cefalexin and clindamycin are Access, and ciprofloxacin, azithromycin and ceftriaxone are Watch. Chloramphenicol is Access in the WHO list but Watch in the UK adaptation (UKHSA 2024).

3.2 What each drug buys In Gadchiroli, India, child pneumonia case fatality was 0.8 per cent with village antibiotic treatment against 13.5 per cent in control villages, and newborn sepsis fatality fell from 16.6 to 2.8 per cent. A village of 300 has about 13 child pneumonia episodes a year. Before antibiotics, adult pneumonia killed 11 per cent under 30, 27 per cent at 30 to 59 and 69 per cent at 60 and over (all THRIVING library, IN-01). Pneumococcal meningitis was close to 100 per cent fatal before 1937, with one Louisiana series of 110 deaths in 111 cases, and untreated meningococcal meningitis killed 70 to 90 per cent (APS Rockefeller archive n.d., search summaries [VERIFY]). Typhoid killed 10 to 21 per cent in nineteenth-century hospital series, for example 27 of 244 at St Bartholomew's, London, in 1860 to 1864 (NLM historical text n.d. [VERIFY]), against 1 to 4 per cent treated (Sindh EPI n.d.). Antibiotics after sore throat cut rheumatic fever from 1.7 to 0.7 per cent, mostly in trials before 1961 (Spinks et al 2021). In cholera, fluids save the life and antibiotics cut stool volume by up to half (GTFCC n.d., Leibovici-Weissman et al 2014).

Against these stand conditions where antibiotics buy almost nothing. For the common cold there is no benefit and some harm (Kenealy and Arroll 2013). For acute bronchitis, 17 trials in 5,099 patients showed no difference in clinical improvement, about half a day less cough and more side effects (Smith et al 2017). For childhood ear infection, antibiotics did not reduce pain at 24 hours and one child in 14 had a side effect, while benefit concentrated in under-twos with both ears affected (NNT 4) and those with discharge (NNT 3) (Venekamp et al 2023).

A 10 kg child with pneumonia needs 20 tablets of 250 mg amoxicillin for five days. If treatment moves fatality from 13.5 to under 1 per cent, about eight children are treated per life saved, about 160 small tablets per life [VERIFY, inference from Gadchiroli, whose controls may overstate the effect]. A course spent on a cold saves no one and uses the same tablets.

3.3 The ranked list The ranking weighs lives saved per tablet, breadth of use, safety in lay hands, stability and AWaRe group. It is this report's judgement.

Rank	Drug	AWaRe	Why it ranks here	Grade
1	Amoxicillin	Access	Most lives per tablet. Child and adult pneumonia, newborn sepsis, ear in under-twos, sinus, throat, typhoid	A

Rank	Drug	AWaRe	Why it ranks here	Grade
2	Gentamicin	Access	With amoxicillin, the home newborn sepsis regimen tested in AFRINEST. Also adult sepsis and kidney infection	A
3	Doxycycline	Access	Stable, oral, broad. Atypical pneumonia, typhus, leptospirosis, plague, cholera single dose, chlamydia, syphilis	B
4	Ceftriaxone	Watch	Once daily for meningitis, severe sepsis, severe typhoid, gonorrhoea	A
5	Metronidazole	Access	Only common drug for anaerobes, amoebae and Giardia. Abdominal and pelvic infection, deep wounds, dental abscess	A
6	Co-trimoxazole	Access	Cheap and stable. Pneumocystis prophylaxis in HIV, typhoid where susceptible, pertussis. Severe skin reactions	B
7	Benzathine penicillin	Access	One injection for syphilis and strep throat, and four weeks' rheumatic fever prophylaxis	A
8	Ciprofloxacin	Watch	First line for bloody diarrhoea, also kidney infection. Tendon harm, resistance	A
9	Azithromycin	Watch	Single dose for cholera, trachoma, chlamydia. Typhoid, dysentery back-up	A
10	Cloxacillin or cefalexin	Access	Staphylococcal skin and wound infection	B

Rank	Drug	AWaRe	Why it ranks here	Grade
Also	Procaine penicillin	Access	Daily injection where oral fails. Short life, needs cold	B
Also	Chloramphenicol	Access or Watch	Meningitis and typhoid when nothing else is left. Fatal marrow failure 1 in 24,000 to 40,000	X for routine use

4. Dosing by syndrome and weight

4.1 Rules Weigh the patient, with a spring balance and sling if need be. Treat the syndrome, not the germ, as the MSF and WHO tables are built to do. Give the full dose, because half doses to stretch stock are the error that fails. Give the shortest course that works: three days of amoxicillin was non-inferior to five in Malawian children with chest indrawing, and CAP-IT found lower doses and shorter courses non-inferior (Dharmapalan et al 2023). Review at 48 to 72 hours. Write everything down.

4.2 The dosing card All doses are from MSF Essential Drugs unless marked. “x2” means every 12 hours, “x3” every 8 hours.

Drug	Child	Adult	Courses
Amoxicillin, WHO child bands (40 to 50 mg/kg x2, Dharmapalan et al 2023)	5 to <7 kg 250 mg, 7 to <10 kg 375 mg, 10 to <15 kg 500 mg, 15 to <20 kg 750 mg, 20 to <30 kg 1 g, all x2	1 g x2 or x3	Pneumonia 5 days (3 where HIV is rare), throat 10 days where rheumatic fever is common
Amoxicillin, MSF high dose	30 mg/kg x3 (max 1 g): <6 kg 125 mg, 6 to <12 kg 250 mg, 12 to <25 kg 500 mg, ≥25 kg 1 g	1 g x3	Pneumonia, otitis 5 days, tonsillitis 6, sinusitis 7 to 10, typhoid 14
Doxycycline	<45 kg 2 to 2.2 mg/kg x2 (max 100 mg). Single dose 4 mg/kg (max 100 mg)	100 mg x2. Single dose 200 mg, 300 mg in cholera	Rickettsia 5 to 7 days, leptospirosis and chlamydia 7, atypical pneumonia 10 to 14, early syphilis 14, brucellosis 6 weeks
Metronidazole	Anaerobes 10 mg/kg x3. Amoebae 15 mg/kg x3. Giardia 30 mg/kg once daily	500 mg x3. Giardia 2 g daily. Trichomonas 2 g once	Amoebae 5 days, Giardia 3 days
Co-trimoxazole	From 6 weeks 20/4 mg/kg x2 (max 800/160). Pneumocystis prophylaxis 50/10 mg/kg daily	800/160 mg x2	Typhoid, pertussis, brucellosis [VERIFY durations]

Drug	Child	Adult	Courses
Ciprofloxacin	From 1 month 15 mg/kg x2 (max 500 mg). Suspension 250 mg/5 ml: 4 to <6 kg 1.5 ml, 6 to <8 kg 2 ml, 8 to <12 kg 2.5 ml, 12 to <15 kg 4 ml, 15 to <26 kg 5 ml, 26 to <36 kg 8 ml	500 mg x2	Dysentery 3 days, cystitis 3, kidney infection 10 to 14
Azithromycin	Single dose 20 mg/kg (max 1 g). Typhoid 10 to 20 mg/kg daily. Dysentery 12 mg/kg then 6 mg/kg. Atypical pneumonia 10 mg/kg daily	1 g single, 2 g early syphilis	Typhoid 7 days, dysentery 5, pneumonia 5
Cloxacillin	Over 10 years 15 mg/kg x3	1 g x3, between meals	7 days
Benzathine penicillin, deep IM, never IV	<30 kg 600,000 IU, ≥30 kg 1.2 MIU. Syphilis under 10 years 1.2 MIU	2.4 MIU (1.2 MIU each buttock)	Single dose. Prophylaxis every 4 weeks
Procaine penicillin, IM, never IV	50,000 IU/kg daily (max 1.2 MIU)	1.2 MIU daily	
Ceftriaxone, IM or IV	From 1 month, <50 kg: 50 to 100 mg/kg daily (max 4 g)	1 to 2 g daily, up to 4 g in meningitis and typhoid	Never in a jaundiced newborn or with calcium. Lidocaine solution IM only
Gentamicin, IM or slow IV, once daily	First week <2 kg 3 mg/kg, ≥2 kg 5 mg/kg. Day 8 to 1 month 5 mg/kg. From 1 month 4.5 to 7.5 mg/kg	5 to 6 mg/kg	"Do not prolong treatment unnecessarily"

4.3 Syndrome card Fast breathing is 60 or more a minute under 2 months, 50 or more at 2 to 11 months and 40 or more at 1 to 5 years (Pocket book table n.d., secondary).

Syndrome	First drug	Second choice
Child 2 to 59 months, cough with fast breathing or chest indrawing	Amoxicillin, WHO bands, 5 days	Refer or inject if danger signs
Infant under 2 months, fast breathing only	Oral amoxicillin 7 days (AFRINEST 2015)	Add gentamicin if worse
Infant under 2 months, any other danger sign	Gentamicin 2 to 7 days plus oral amoxicillin 7 days	Ceftriaxone if not jaundiced
Adult pneumonia, walking	Amoxicillin 1 g x3, 5 days	Doxycycline
Meningitis, severe sepsis	Ceftriaxone, or gentamicin with amoxicillin or benzylpenicillin	Chloramphenicol last
Bloody diarrhoea	Ciprofloxacin 3 days	Azithromycin, metronidazole if amoebae

Syndrome	First drug	Second choice
Watery diarrhoea	No antibiotic. Fluids and zinc	Suspected cholera: single-dose doxycycline or azithromycin
Sore throat where rheumatic fever occurs	Benzathine once, or amoxicillin 10 days	Azithromycin
Ear pain	None, unless under 2 with both ears, or discharge	Amoxicillin 5 days
Cold, cough without fast breathing, bronchitis	None	
Skin and wound infection	Cloxacillin or cefalexin 7 days	Add metronidazole if deep or foul
Fever after floods, rats, ticks or lice	Doxycycline	Azithromycin
Typhoid	Azithromycin 7 days, ceftriaxone if severe	Amoxicillin 14 days
Kidney infection	Ciprofloxacin 10 to 14 days	Gentamicin, ceftriaxone
Genital ulcer or syphilis	Benzathine 2.4 MIU	Doxycycline 14 days

5. Fish and veterinary antibiotics

Preppers hold that aquarium antibiotics are human tablets in a different box. The record partly agrees. Zhang and colleagues (2020) found fish antibiotics sold without prescription by 24 online vendors. Eight products, among them amoxicillin, doxycycline and ciprofloxacin, matched human generic tablets by imprint and appearance, though nothing was chemically tested. Of 2,288 customer reviews, 55 (2.4 per cent) related to human use. The FDA says these products are unapproved and that marketing them for humans is illegal. Roberts and colleagues (2022) assayed over-the-counter fish amoxicillin and cephalexin by HPLC and found 90 to 120 per cent of labelled content, with unidentified excipients (abstract only). The inference is that sealed fish capsules bearing a recognisable human imprint are worth about as much as the same capsules from a pharmacy, judged by the same storage rule, but no regulator stands behind them [VERIFY].

Veterinary procaine penicillin G comes at 300,000 units per ml in multi-dose vials of 100 to 500 ml for intramuscular use, must be kept at 2 to 8 °C, and is labelled for not more than 10 ml per site and not more than seven days (veterinary labels n.d.). An adult human dose of 1.2 MIU is 4 ml. A punctured multi-dose vial can grow bacteria. Some cattle products combine benzathine and procaine penicillin for injection under the skin and must not be confused with plain procaine. Procaine penicillin can cause the Hoigné reaction, an episode of agitation, hallucinations and fear of death lasting 15 to 30 minutes and settling on its own. It is not allergy and does not forbid further penicillin (Pfizer n.d.). No incidence figure and no human-use purity study of veterinary penicillin were found.

6. The harms, quantified

Penicillin anaphylaxis. The brief's figure of 1 fatal reaction in 50,000 to 100,000 courses traces to a 1968 WHO review giving 0.002 per cent and collecting 151 deaths from 1951 to 1965, mostly after injections (Idsoe et al 1968, via Castells et al 2019). The denominator could not be confirmed [VERIFY]. The best modern pooled figure is for injected benzathine penicillin: 54 anaphylaxis cases in 2,028,982 people (0.002 per cent) and four deaths, about 1 death in 500,000, with no anaphylaxis in 1,244 pregnant women (Galvão et al 2013). Oral penicillins carry the lowest risk (Castells et al 2019). UK data from 1972 to 2007 recorded eight fatal anaphylaxis cases linked to amoxicillin, five after intravenous use (Lee and Shanson 2007 [VERIFY]).

Chloramphenicol. Fatal aplastic anaemia occurred in an estimated 1 in 24,200 to 1 in 40,500 courses in a California study (Wallerstein et al 1969, via label). It is unpredictable.

Fluoroquinolones. Current fluoroquinolone use tripled the rate of Achilles rupture (adjusted rate ratio 3.14), and with oral steroids multiplied it by 19.4. The absolute excess was 2.9 tendon ruptures per 10,000 patients overall, 5.6 at 60 and over, and 19.6 at 60 and over with steroids (Morales et al 2019). MSF adds QT prolongation and says to stop at the first tendon pain.

Doxycycline. Old tetracyclines stained the teeth of 23 to 92 per cent of exposed children. None of 58 children given doxycycline before age 8, mean 1.8 courses, had staining (95 per cent CI 0 to 5 per cent) (Todd et al 2015). MSF limits courses under 8 to 21 days, avoids doxycycline in the second and third trimesters except single doses, and warns of oesophageal ulcer from tablets swallowed dry or lying down.

Gentamicin. In about 10,000 patients in 144 trials, gentamicin was linked with kidney toxicity in 14 per cent, hearing damage in 8.3 per cent and balance damage in 3.2 to 3.7 per cent (Kahlmeter and Dahlager 1984, abstract only). Ear damage is irreversible. In one elderly series kidney toxicity was 3.9 per cent with seven days or fewer, 30 per cent at 8 to 14 days and 50 per cent beyond 14 days, and balance damage may appear up to ten days after stopping (search summaries, source not identified [VERIFY]).

Metronidazole and alcohol. Labels warn of a disulfiram-like reaction and advise no alcohol during and for three days after. A review of six case reports in eight patients found no convincing evidence that it exists (Williams and Woodcock 2000). Avoiding alcohol costs little, so the rule stands.

Co-trimoxazole. Stevens-Johnson syndrome and toxic epidermal necrolysis occurred in about 3.2 per 100,000 new users in one cohort (Eur J Clin Pharmacol 2018 [VERIFY]). MSF adds haemolysis in G6PD deficiency and forbids use under six weeks and in the first trimester or after 36 weeks except in HIV.

Resistance. Mass azithromycin cut child deaths by 13.5 per cent, but macrolide resistance determinants were 7.5 times higher in treated communities at 48 months (Keenan 2018, via THRIVING library, IN-01).

7. Stewardship

7.1 How big is the need? World antibiotic use in 2018 was 14.3 defined daily doses per 1,000 people per day, up 46 per cent since 2000, ranging from 5.0 in the Philippines to 45.9 in Greece (Browne et al 2021). Even at 5.0, a village of 300 would use about 550 daily doses a year [inference]. A village treating only the syndromes on the card might need 40 to 80 courses a year, many of them small children's courses [VERIFY]. A chest of a few thousand tablets can last years if it is not spent on coughs.

7.2 Where the chest leaks Colds, bronchitis and most ear and throat pain drain the chest without saving lives (section 3.2). Delayed prescribing, in which the patient waits at least 48 hours and returns only if worse, cut antibiotic use from 93 to 31 per cent with no difference in complications and satisfaction of 86 against 91 per cent (Spurling et al 2017).

7.3 The one-page stewardship rule for a village of 300

1. **One keeper, one key.** The trained lay healer alone dispenses. A second named person holds a duplicate list and checks the count monthly.
2. **One ledger.** Every course is written down: date, name, age, weight, syndrome, drug, dose, days, outcome at day 3 and day 7.
3. **The card decides.** No antibiotic for a syndrome not on the card. Colds, coughs without fast breathing, watery diarrhoea and most ear pain over age two get a return date in 48 hours instead.
4. **Access first.** Ciprofloxacin, azithromycin and ceftriaxone only for their named syndromes. Chloramphenicol last.
5. **The children's reserve.** All gentamicin, all dispersible tablets and a fixed share of amoxicillin, perhaps a third, are kept for under-fives and newborns [VERIFY].

6. **Full dose, short course.** Never half doses.
7. **Perishable first.** Liquids, co-amoxiclav, capsules and damaged packs before sealed tablets.
8. **No prevention** except benzathine after rheumatic fever, co-trimoxazole in HIV, and contact cover in an epidemic if the district decides [VERIFY].
9. **Quarterly review.** Count stock, list failures and deaths, and ask whether any drug fails more often than before.
10. **Refuse kindly.** Explain why, name the danger signs, set the return date. The rule is the council's, not the healer's.

Evidence grades

Practice	Tradition	Record	Inference	Grade
Well-stored tablets after expiry	Poison, or eternal	88 per cent of SLEP lots extended, mean 66 months. Doxycycline 4 to 7 extra years	Usable for years, falling confidence	B
Loose or heat-exposed stock		Losses of 6 to 33 per cent, co-amoxiclav fails within a day in damp	Assume weak	B
Avoiding degraded tetracycline	Old tetracycline harms kidneys	Reversible Fanconi cases 1963 to 1965	Real for tetracycline, not shown for doxycycline	B
Amoxicillin for child pneumonia		Fatality 13.5 to 0.8 per cent	Most valuable tablet	A
Home gentamicin plus amoxicillin, or oral amoxicillin alone for fast breathing, in young infants		AFRINEST failure 8 against 10 per cent	Effective in trained lay hands	A
Short courses	Longer is safer	Non-inferior in Malawi and CAP-IT	Saves stock	A
Delayed prescribing		Use 93 to 31 per cent, no more complications	Core stewardship tool	A
No antibiotics for colds and bronchitis	Antibiotics cure coughs	No benefit, more harm		A
Antibiotics in cholera		Stool volume halved at most	Fluids first	A
Benzathine for strep throat		Rheumatic fever 1.7 to 0.7 per cent	Where rheumatic fever is common	B
Fish antibiotics	Same pills	Imprint match, one small assay	Probably usable	C
Veterinary procaine penicillin		No human data	Cold chain is the problem	D

Practice	Tradition	Record	Inference	Grade
Routine chloramphenicol		Fatal marrow failure 1 in 24,000 to 40,000		X
Old opened eye drops		Contamination up to 70 per cent		X
Metronidazole-alcohol reaction	Dangerous	No convincing evidence	Avoid anyway	D

Means ledger

Rung	Oral Access antibiotics	Injectables (gentamicin, ceftriaxone, penicillins)	Judging salvaged stock
Hands and knowledge	Recognise which syndromes need a drug and which do not. Count breaths. No drug, so child pneumonia fatality stays near 13.5 per cent	Nothing safe	Look, smell, feel. Reject discoloured, sticky, crumbling or swollen units
Hearth	A sealed household course or two, the card, a scale	A household should not inject	Sealed jar, coolest corner, original packs
Garden and still	Cool dry store, desiccant, spring balance, ledger	Boiled syringes only in emergency [VERIFY]	Earth-cooled store, sorted by perishability
Village dispensary	Lay healer as sole keeper, card, rule, review at 48 to 72 hours, microscope if found. Pneumonia fatality towards 0.8 per cent	IM gentamicin and benzathine, adrenaline at hand, 30 minutes' observation. Newborn sepsis fatality towards 2.8 per cent	Inventory cards, monthly count
District infirmary	Second-line drugs, resupply of villages, ledger review	IV access, ceftriaxone, cold store for procaine penicillin, whisper test during gentamicin	Possible agar bioassay against old and new stock [VERIFY feasibility]
Pre-Fall hospital	Culture and sensitivity	Drug levels, kidney tests, intensive care	HPLC and dissolution testing

Harm test

Drug	Harm	Never give	Stop sign and action
Penicillins	Anaphylaxis, rash, diarrhoea. Hoigné reaction with procaine	Known penicillin anaphylaxis. Benzathine or procaine into a vein. Amoxicillin in glandular fever	Hives, swelling, wheeze, faintness: adrenaline IM, lie flat, fluids, never again

Drug	Harm	Never give	Stop sign and action
Gentamicin	Permanent deafness and imbalance, kidney injury	Long courses, dehydration uncorrected	Ringing ears, dizziness, falling urine: stop at once
Ceftriaxone	Allergy	Jaundiced newborn, with calcium. Lidocaine solution into a vein	Stop for allergy
Doxycycline and tetracycline	Oesophageal ulcer, sunburn. Fanconi syndrome from degraded tetracycline	Degraded tetracycline. Late pregnancy except single doses. Over 21 days under age 8	Pain on swallowing, vomiting and thirst after old tetracycline: stop, fluids
Ciprofloxacin	Tendon rupture, QT, seizures	Previous quinolone tendon injury. Pregnancy unless no alternative	Tendon or joint pain: stop, rest
Metronidazole	Nausea, metallic taste		Avoid alcohol to 3 days after
Co-trimoxazole	Stevens-Johnson syndrome, haemolysis	Under 6 weeks, first trimester and after 36 weeks unless HIV, sulfa allergy	Fever with rash and mouth ulcers: stop for ever
Azithromycin	QT, pyloric stenosis in infants	Caution under 6 weeks	
Chloramphenicol	Fatal aplastic anaemia	Routine use	
Any stock	Unknown identity, contamination	Unlabelled loose tablets, punctured multi-dose vials of unknown age, eye drops opened over 28 days	

The systemic harm is that every unneeded course empties the chest and breeds resistance.

Red flags

These signs mean the patient may die or be disabled without oxygen, intravenous treatment or surgery.

- **Child:** cannot drink, vomits everything, convulsion, very drowsy, severe indrawing with grunting or blue lips. Give the first dose at once, keep warm, cup-feed, carry to the district.
- **Newborn:** not feeding, too hot or too cold, breathing 60 or more, severe indrawing, no movement, convulsion. Start gentamicin and amoxicillin, skin to skin.
- **Meningitis:** fever with stiff neck, bulging fontanelle, purple rash that does not fade under a glass, confusion. Ceftriaxone at once if held.
- **Adult sepsis:** confusion, fast breathing, cold mottled limbs, little urine.
- **Anaphylaxis** after any drug.
- **Spreading necrotic infection:** crackling skin, pain out of proportion, black skin. Needs surgery.
- **Treatment failure:** no better at 72 hours on the right drug and dose. Think of wrong diagnosis, abscess, degraded stock or resistance.

Honest comfort: where death is likely whatever is done, the healer stays, keeps the patient warm, clean and drinking, eases pain and fear, and helps the family say what they need to say. The antibiotic may still be given, since some patients thought hopeless survive.

The case against

Against expired antibiotics. The FDA and the AMA do not recommend them (Culbertson 2011). Aronson (2019) warns that past stability does not guarantee future stability and that 16 per cent of SLEP lots failed eventually. The FDA's own doxycycline failed on impurities. SLEP tested every lot, and a village cannot. A weak drug may suppress symptoms while infection spreads and select resistance. The reply is that the alternative to weak amoxicillin for child pneumonia is none, and the untreated death rates are known. The case against holds in full for loose, hot, damp, liquid and tetracycline stock.

Against lay prescribing. Babu and Eisenberg (2010) evaluated Where There Is No Doctor and found considerable problems in its treatment recommendations (search summary only). Any dosing card here will contain errors too. The reply is that Gadchiroli and AFRINEST show lay workers saving lives with a narrow card, training and supervision.

Against antibiotics at the centre. Most diarrhoea deaths are prevented by fluids. Most coughs need nothing. Mass antibiotics save lives now and breed resistance later (Keenan 2018, via THRIVING library, IN-01). A village that treats every fever empties its chest in a year.

Against survivor stories. "I took expired pills and lived" proves nothing, since most infections resolve anyway.

Against the brief's allergy figure. Overstating the risk of oral amoxicillin pushes healers away from the safest and most valuable drug.

10-line summary

1. An expiry date marks the end of proven stability, not the start of toxicity.
2. Well-stored stockpile lots were extended by a mean of 66 months, and 16 per cent eventually failed.
3. Stockpiled doxycycline capsules lasted four to seven years past date before impurities exceeded limits.
4. Heat, damp and open packs destroy amoxicillin within months and clavulanic acid within days.
5. Only degraded plain tetracycline has caused documented harm from age, and doxycycline lacks the group responsible.
6. Amoxicillin is the most valuable tablet: child pneumonia fatality falls from 13.5 to 0.8 per cent.
7. Gentamicin with amoxicillin, or oral amoxicillin alone for fast breathing, treats sick infants at home.
8. Antibiotics do not help colds or bronchitis, and delayed prescribing cuts use by two-thirds safely.
9. Fatal anaphylaxis is about 1 in 500,000 for injected benzathine penicillin and rarer for oral amoxicillin.
10. A village of 300 may need only 40 to 80 courses a year if it spends only on the syndromes that kill [VERIFY].

Open questions

- What potency do sealed amoxicillin, ciprofloxacin, metronidazole and co-trimoxazole tablets keep at 10 and 20 years past date?
- Does any doxycycline degradation product harm people?
- Is the 1968 figure of 0.002 per cent per course, per patient or per injection?
- Can a district build an agar bioassay to compare old with new stock?
- How fast does resistance rise in a closed population of 3,000 on salvaged Access drugs?
- How long do sealed injectable powders and gentamicin solution stay usable past date?
- How often does the Hoigné reaction occur?

Sources to read in full

1. Lyon et al 2006, the core SLEP data.
2. FDA 2023 and the 2019 doxycycline stockpile guidance.

3. MSF Essential Drugs, the entry for each drug here.
4. Dharmapalan et al 2023 on amoxicillin dose and duration.
5. The WHO AWaRe antibiotic book (2022), not read here.
6. Khan et al 2013 on packaging and storage.
7. Frimpter et al 1963 and Wegienka and Weller 1964.
8. Galvão et al 2013 on benzathine safety.
9. AFRINEST 2015, read only in summary.
10. Idsoe et al 1968, not read.

At the bedside after the Fall

Household

Minimum viable version. An isolated household keeps one or two sealed courses of amoxicillin, dispersible for a small child, and one of doxycycline, in a dry jar in the coolest place, with the card. It knows the signs that need a drug (fast breathing with indrawing, bloody diarrhoea, spreading redness, a sick newborn) and those that do not. **What it needs to start.** The card, a scale, a way to count breaths, the jar. **First failure to expect.** The course goes on the first child with a cold, and nothing is left when the baby gets pneumonia.

Village of 300

Minimum viable version. One trained keeper, one ledger, the card and the stewardship rule. The chest is mostly amoxicillin, with doxycycline, metronidazole, co-trimoxazole, cloxacillin or cefalexin, benzathine penicillin, gentamicin with syringes, a few vials of ceftriaxone, ciprofloxacin and azithromycin for their named uses, adrenaline, and oral rehydration salts and zinc beside them. **What it needs to start.** A cool dry store, a spring balance, training in counting breaths, IM injection and anaphylaxis, and the council's backing. **First failure to expect.** A respected elder with bronchitis demands a course, the keeper gives in, and the rule collapses.

District of 3,000

Minimum viable version. A nurse runs a central store, resupplies villages by their ledgers, holds the injectables for meningitis and severe sepsis and the last-resort drugs, reviews ledgers each quarter for failure patterns, and keeps registers of true penicillin allergy and children on rheumatic fever prophylaxis. **What it needs to start.** A cool store, a stock register, a sterile room, IV equipment, a microscope. **First failure to expect.** Hoarding by villages and a run on the store in the first epidemic, unless sharing is agreed in advance.

Protocols

Protocol 1. Sorting a salvaged chest

1. Discard anything without a readable name and strength.
2. Discard past-date plain tetracycline (not doxycycline), any mixed liquid, opened eye drops, and any unit that is discoloured, crumbling, swollen, stuck together or smells wrong, or any vial whose powder has caked or changed colour.
3. Box A: sealed tablets. Box B: capsules, co-amoxiclav, damaged packs. Box C: dry powders for suspension and injectables.
4. Label each pack with where and when it was found.
5. Use Box B first, then C, then A.
6. Store all below 25 °C, dry, dark, never frozen.
7. Keep one inventory card per drug and count monthly.

Protocol 2. The antibiotic gate

1. Weigh. Count breaths for a full minute if there is cough.
2. Find the syndrome on the card. If it is not there, no antibiotic.
3. Cold, cough without fast breathing, watery diarrhoea, mild ear or throat pain: no antibiotic, danger signs explained, return in 48 hours.
4. Ask about allergy and pregnancy.
5. Choose the first drug. Check the dose against the band table twice.
6. Write the ledger entry before the first dose.
7. Watch for 30 minutes after any penicillin injection.
8. Review at day 3. Better: finish the short course. Not better: check diagnosis and abscess, then change drug.

Protocol 3. Child of 2 to 59 months with cough and fast breathing

1. Count breaths while calm: fast is 50 or more at 2 to 11 months, 40 or more at 1 to 5 years.
2. Check for danger signs (see Red flags).
3. Amoxicillin twice daily: 5 to <7 kg 250 mg, 7 to <10 kg 375 mg, 10 to <15 kg 500 mg, 15 to <20 kg 750 mg, 20 to <30 kg 1 g.
4. Dissolve dispersible tablets in breast milk or boiled water on a spoon.
5. Five days, or three where HIV is rare.
6. Keep breastfeeding and warm. Review at day 3.

Protocol 4. Sick young infant when the district cannot be reached

1. Danger signs: not feeding, convulsion, breathing 60 or more, severe indrawing, fever or low temperature, movement only when stimulated [VERIFY temperature thresholds].
2. Fast breathing only: oral amoxicillin 7 days.
3. Any other sign: gentamicin IM once daily (first week <2 kg 3 mg/kg, ≥2 kg 5 mg/kg, after first week 5 mg/kg) using the 10 mg/ml strength, drawn into a 1 ml syringe and checked by a second person.
4. Give gentamicin for 2 days (Malawi programme) up to 7, with oral amoxicillin for 7 days [VERIFY infant amoxicillin dose].
5. Skin to skin, expressed milk by cup.
6. Stop gentamicin if urine stops.

Protocol 5. Anaphylaxis

1. Within minutes to an hour: hives, swelling of lips or tongue, wheeze, hoarse voice, faintness.
2. Stop the drug. Call for help.
3. Adrenaline 1 mg/ml into the outer thigh: under 6 months 0.1 to 0.15 ml, 6 months to <6 years 0.15 ml, 6 to <12 years 0.3 ml, 12 years and adults 0.5 ml (0.01 mg/kg) (MSF 2024).
4. Lie flat with legs raised, or sitting if breathless.
5. Repeat every 5 minutes if not better, up to three doses.
6. Fluids by mouth if conscious, by vein if possible. Watch for some hours [VERIFY duration].
7. Record the allergy in the ledger and the district register, and tell the family.
8. Distinguish the Hoigné reaction: terror and hallucinations without swelling or wheeze, passing in 15 to 30 minutes. That patient may have penicillin again.

Protocol 6. Gentamicin safety

1. Weigh and calculate once-daily dose. Check twice.
2. Correct dehydration first.

3. Once daily only (except infants of 1 to 3 months with meningitis, 2.5 mg/kg every 8 hours).
4. Shortest course, 2 to 3 days where an oral drug can follow.
5. Ask daily about ringing ears and dizziness. Whisper test.
6. Stop for any ear symptom or falling urine.
7. Avoid in pregnancy unless life-threatening.

Numbers to carry

1. **88 per cent and 66 months.** Stockpile lots extended and mean extension.
2. **Below 25 °C, sealed, dry, dark.** The storage rule.
3. **7 and 14 days.** Life of a mixed suspension without and with cold.
4. **13.5 to 0.8 per cent.** Child pneumonia fatality without and with village antibiotics.
5. **60, 50, 40.** Fast breathing under 2 months, 2 to 11 months, 1 to 5 years.
6. **40 mg/kg twice daily for 5 days.** Amoxicillin for child pneumonia.
7. **5 mg/kg once daily.** Gentamicin for most patients over 2 kg.
8. **1 in 500,000.** Death from anaphylaxis to injected benzathine penicillin.
9. **0.01 mg/kg, adult 0.5 mg.** Adrenaline IM, repeat at 5 minutes.
10. **31 against 93 per cent.** Antibiotic use with delayed against immediate prescribing.

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