

Taking medicines properly?

95%...?



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Introduction

When you start HIV treatment, health care providers might tell you **"You have to take medicines properly", "If you fail, HIV virus will develop Resistance that means the treatment won't work effectively"**

Also, we sometimes hear from patients:

"I skipped a dose every other day until the next appointment because I was running out of medicines."

"I've heard that HIV treatment loses effectiveness because of **Resistance** in the future when I take it for long term"

"My doctor advised me to change medicines to better one, but I'm worried whether I lose treatment options when drug **resistant** viruses appear in the future."



The purpose of this booklet is to achieve your correct understanding on **Adherence** and **drug-resistant viruses**.

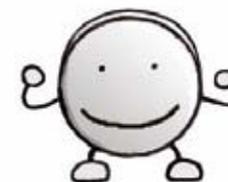
We personalize HIV for your better understanding.

「きちんと飲む」ってどんなこと？

<英語訳>

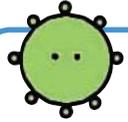
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Not Effective?	
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Drugs are Effective ? Not Effective ?

There are 3 types of viruses based on drug resistance degrees.



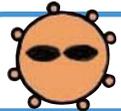
Viruses which drugs are effective (drug-sensitive viruses)

strength... **drug > viruses**

- They can replicate rapidly.
- They are also called wild-type viruses.
- They can't replicate when you take medicines properly.



When compared to military, they are unarmed infantry in a large number and try to fight stronger enemy.



Viruses which drugs are less effective (candidate for drug-resistant viruses)

strength... **drug > viruses**

- They are defective products of original **drug-sensitive viruses**.
- They are fragile and can't replicate efficiently.
- The virus which survived the drug attack can evolve into **drug-resistant viruses**.
- They can't replicate when you take medicines properly.



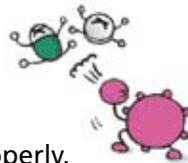
They are spies who collect information of enemy in an unguarded moment..



Viruses which drugs are not effective (drug-resistance viruses)

strength... **drug < viruses**

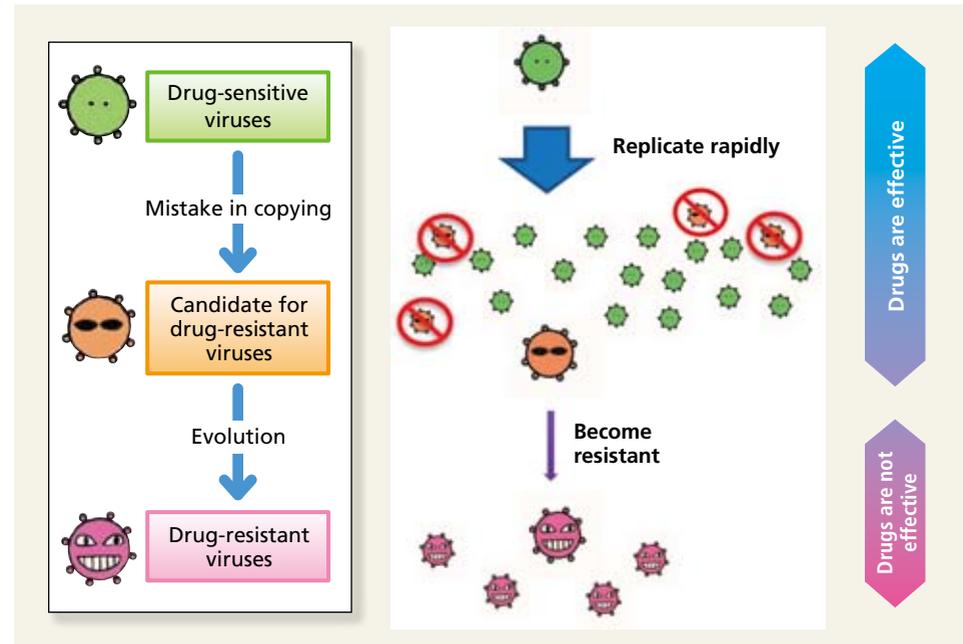
- They have acquired resistance against drugs.
- **Candidate for drug-resistant viruses** evolved into drug-resistant viruses.
- They can replicate even if drugs are administered properly.



They are special units sniping enemies using information strategically

How do the drug-resistant viruses selected ?

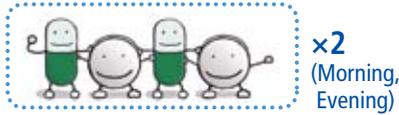
- HIV replicates by making copies of themselves in human body. Anti-HIV drugs can prevent HIV from making copies.
- Since **drug-sensitive viruses** replicate and make many copies, they sometimes produce defective viruses.
- **Candidate for drug-resistant viruses** has an ability to evolve into the **drug-resistant viruses** which drugs are not effective. (Become resistant)
- We can prevent selecting **drug-resistant virus** seeds by taking medicines properly, because anti-HIV drugs are still effective against **drug-sensitive viruses**.



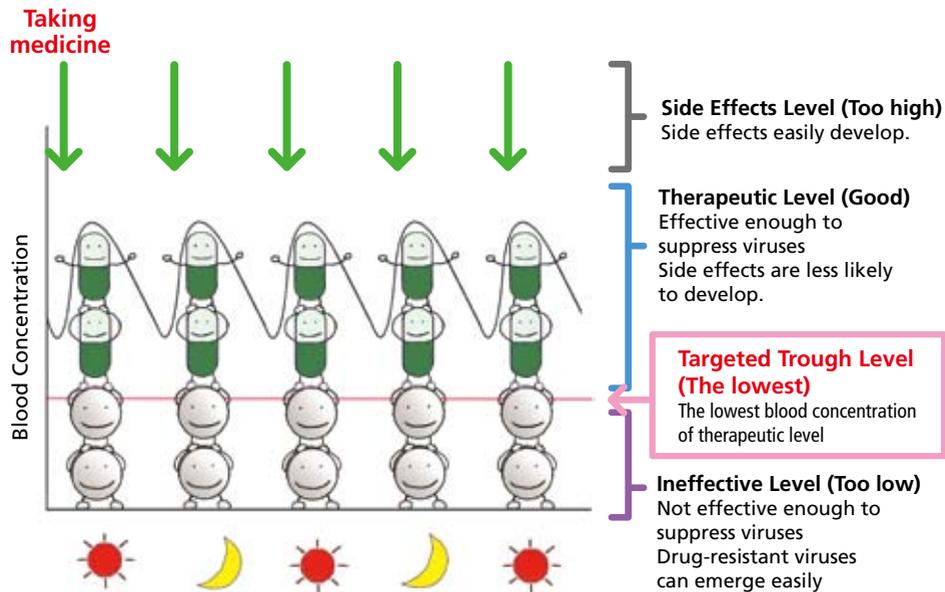
Once drug-resistant viruses emerge, it is difficult to prevent them from replicating even if you take medicines properly.

When you take medicines properly...

- Now imagine you take a set of drugs (4 tablets as shown), twice daily (8 tablets a day).



- When you take medicine, the drug concentration in blood (blood concentration) increases at first, and decreases afterwards while drugs being resolved and metabolized.
- You have to take a next dose punctually to keep the blood concentration around the effective level.

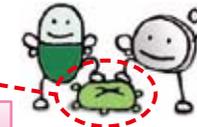


- You must keep your blood concentration higher than the lowest level (Targeted Trough Level) to prevent HIV from multiplying and getting resistance.
- To keep your blood concentration higher than the Targeted Trough Level, you need take medicines regularly and punctually.

When you don't take medicines properly...

When you fail to take anti-HIV drugs, the blood concentration of gets lower than the therapeutic level. Then, how do viruses behave?

Viruses want to replicate
They can't replicate when drugs work effectively
They try to find weakness of the drug to overcome and multiply.



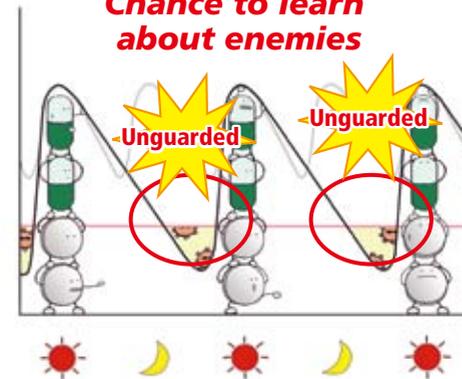
When you take medicines properly...

Enemies (Drugs) are always on their guard and never show their weakness (the graph on the previous page)

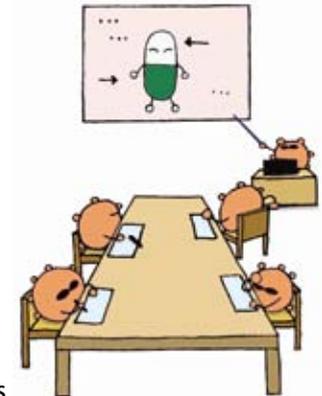
When you don't take medicines properly...

Enemies (Drugs) drop guard : it's a big chance for viruses to learn enemies' characteristics.

**Unguarded :
Chance to learn
about enemies**



~ Special Lecture ~
Be a drug-resistant virus!



Repeated unguarded moments enable viruses to learn drugs weakness, and they acquire the resistance against drugs.

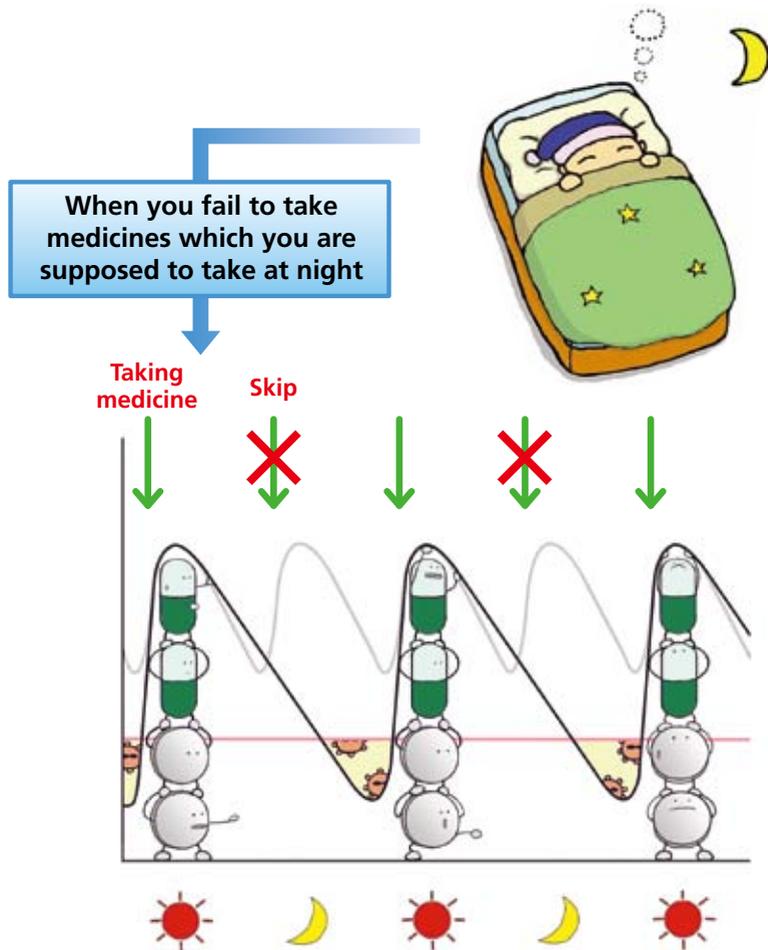
Drug-resistant viruses are no longer defeated by the drugs that you take now.

"Following Properly ? 4 major principles for adherence."

You must take medicine properly
to avoid drug-resistant viruses
What is the exact meaning of taking
medicines properly in the first place ?

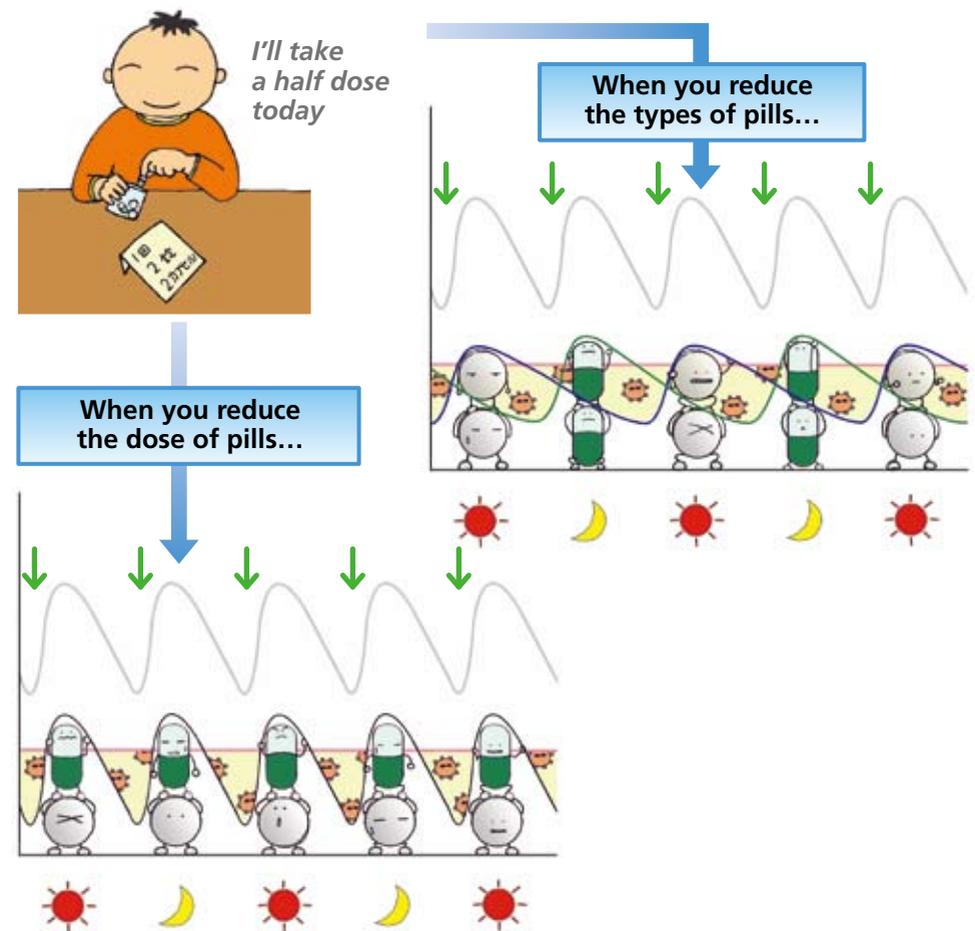
Check! Never forget. Never skip.

- When you fail to take anti-HIV drugs as prescribed, the blood concentration of drugs easily gets lower than the therapeutic level, which means drug-resistant viruses can emerge.



Check! Don't spare your pills!

- If you reduce the dose or the types of anti-HIV drugs on your decision for reasons such as side effects or shortage of the drugs, the blood concentration gets lower than the therapeutic level easily. Then drug-resistant viruses can emerge.

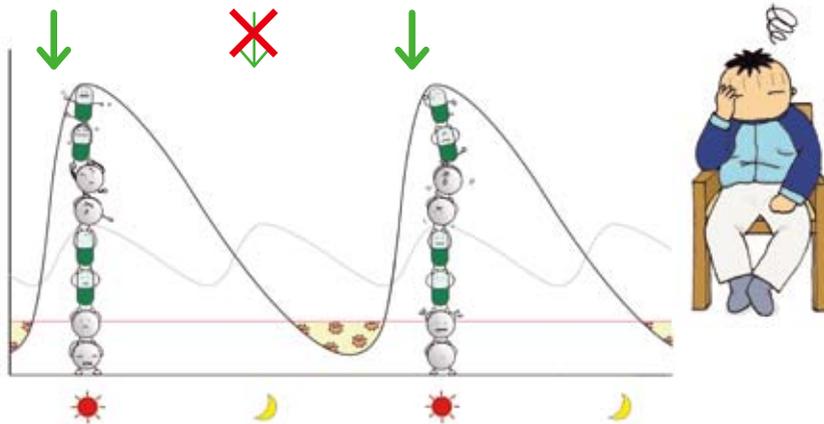




Remind Drug-drug interaction

Check! Never take too much. Never take a several dose at a time.

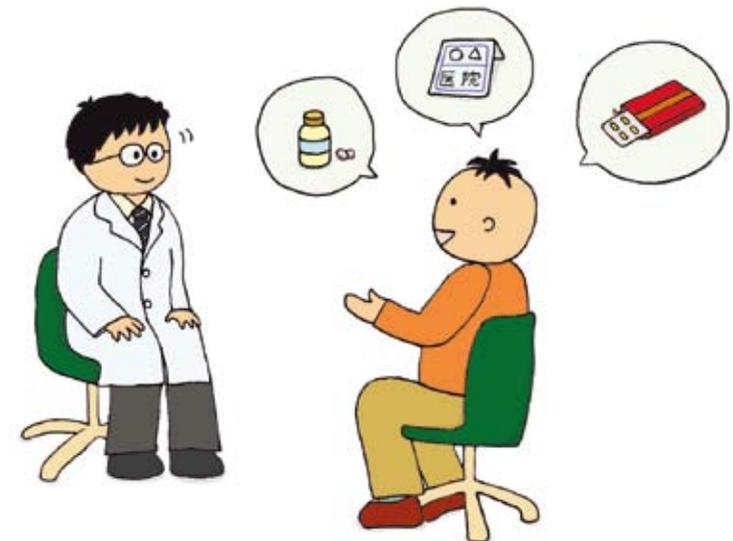
- When you take the drugs at once which are supposed to be taken in several times in a day, or take a double dose of a medicines to make up for a missed dose, the blood concentration of drug gets higher than the Side Effects Level.
- It is dangerous because the higher blood concentration leads side effects easily.
- Taking too much medicines at once doesn't result in higher effectiveness.
- Some types of drugs which are supposed to be taken several times a day are metabolized in shorter time.
Even if you take several dose at once, their efficacy doesn't last longer.



Check! Never quit, but continue.

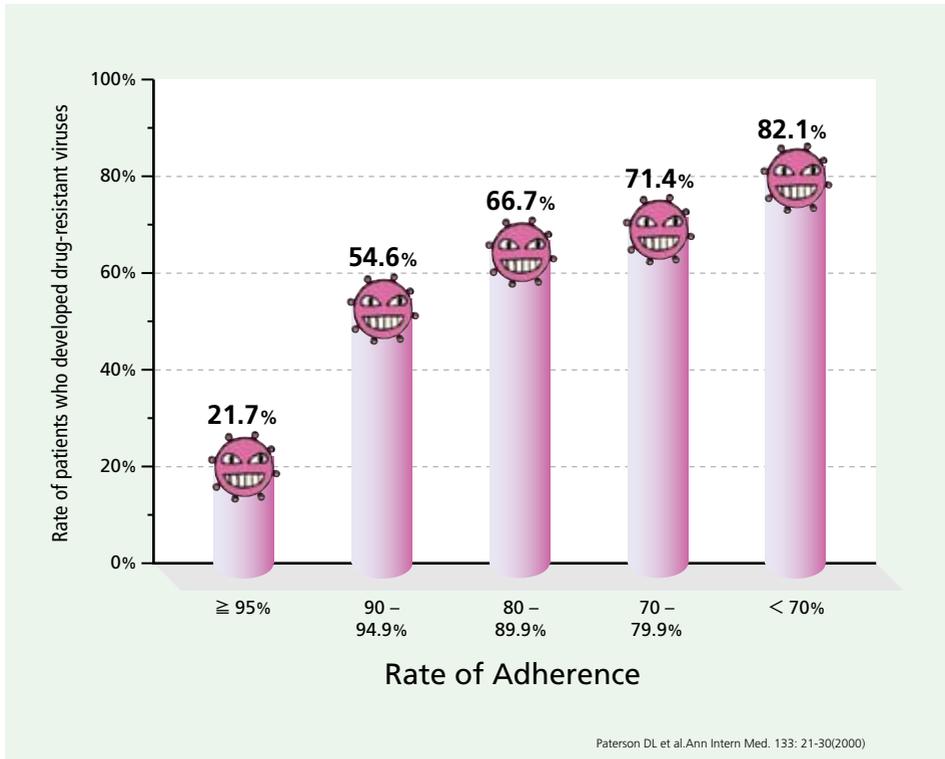
- It is necessary to take anti-HIV drugs for life. You may not quit taking them even if your symptoms or the result of medical test are improved.
- When you feel uncomfortable to take medicines because of possible side effects or mood change, you should inform health care providers first. It is dangerous to quit (or interrupt) taking anti-HIV medicines on your decision.
- To keep all your medical appointments is important to keep an eye our for any change of you physical condition.

- When taking two or more drugs regularly, matter of chemistry (**Drug-drug interaction**) must be considered.
- Unfavorable drug interaction may result in less effectiveness or side effects.
- Not only drugs prescribed by a doctor, but also some over-the-counter drugs or supplements which are sold at a pharmacy or a convenience store could cause the drug interaction.
- Some of the major anti-HIV drugs have strong drug-drug interactions with various drugs.
- You should inform health care providers to check the drug-drug interaction if you take medicines or supplements regularly or intend to start taking them.



The goal is 100%, which means..

- "Proper" means >95% adherence!
- The study showed that more drug resistant viruses were selected with bad adherence less than 95% (ref)



**It is important to take 100% of doses
to avoid emerge of drug-resistant viruses.**

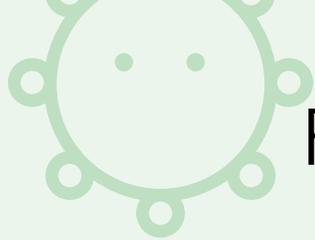
How properly should patients take medicines to avoid drug-resistant viruses.

How many missed doses in a month (30 days) could be allowed to keep "95%" adherence ?

- ◆ Those who are prescribed once-daily regimen take 30 times a month.
If...
you forget once, it means taking medicines 29 times a month ($29 \div 30 = 96.6\%$).
you forget twice, it means taking medicines 28 times a month ($28 \div 30 = 93.3\%$).
Therefore, forgetting only twice makes the adherence less than 95%.
- ◆ Those who are prescribed twice-daily regimen take 60 times a month.
If...
you forget once, it means taking medicines 59 times a month ($59 \div 60 = 98.3\%$).
you forget twice, it means taking medicines 58 times a month ($58 \div 60 = 96.6\%$).
you forget three, it means taking medicines 57 times a month ($57 \div 60 = 95\%$).
Therefore, forgetting 3 times still keeps the adherence more than 95%.

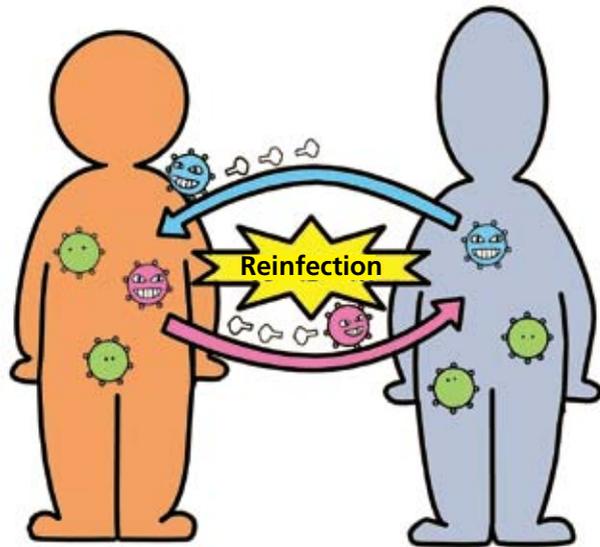
- Roughly speaking, the less times you take medicines a day, the easier the adherence gets lower.
- It is more and more important to take medicines properly as more once-daily medicines are available, which are basically easy and better medications.





Reinfection.

- Reinfection means being infected by HIV again. However properly you take medicine, anti-HIV drugs can entirely lose effectiveness, when the infected viruses are drug-resistant.
- Even if you take medicines, you have possibility to be reinfected and to infect others.



Try not to take risky actions putting others and yourselves in danger of infection and reinfection.

You have to:

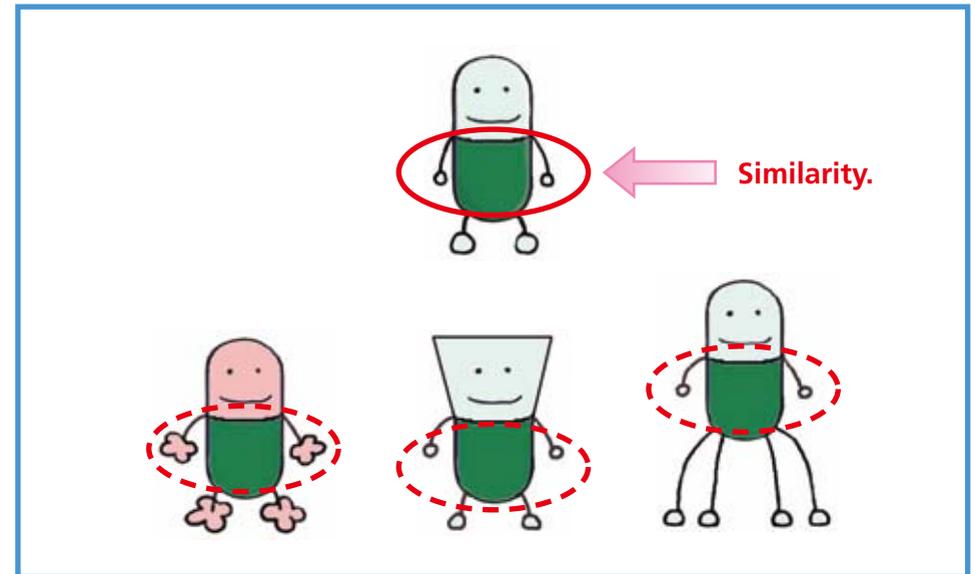
- **avoid having bareback sex without condoms**
- **avoid having random sex with many and unspecified people**
- **avoid sharing needles and syringes**
- **avoid touching a lot of others' blood**
- **avoid donating blood**

etc.

Cross-resistance



- You have to change medicines if one of the drugs loses effectiveness because of drug-resistant viruses.
- Usually the new drug is effective against the drug-resistant viruses but if it has the similar characteristics to the previous drug, it might not work effectively.
- In other words, some of drug-resistant viruses show resistance against drugs you have never taken and it is called "**Cross-Resistance**".



You have limited treatment options once drug-resistant viruses to a certain drug emerge, because some drugs which have similar characteristics become ineffective as well.



Q1 Will drugs lose effectiveness when I take them for a long time ?

A No. Drugs remain effective even though you take for a long time, unless drug-resistant viruses appear.

Q2 My doctor recommended me to change my medicines to better ones with fewer side effects, but I'm worried that once I change current medicines, I will lose future treatment options when drug-resistant viruses appear.

A You won't lose your options. The number of options will not decrease when you change your medicines for reasons of side effects, size of tablets, or frequency of taking medicine.

Q3 Can I change back to previous drugs when the new drugs result in severer side effects ?

A Yes, you can. Previous drugs remain effective if the reason of change is not because of drug-resistant viruses. Since you have to take side effects into account in the long-term treatment, it is important to discuss with your doctor.

Q4 How can I find out whether I have drug-resistant viruses or not ?

A A blood examination called "Drug Resistance Test" reveals the emergence of drug-resistant viruses. This test can be covered by health insurance.

Q5 In the case that my current drugs lose effectiveness, does any drug I've never taken is effective against HIV ?

A Not always. Anti-HIV drugs with the similar characteristics to the ones which lose effectiveness are You can find out which drugs are effective by drug resistance tests.

Q6 What if I realize that I forget to take medicines ?

A There are several ways to handle depending on the time you realize it.

① If you have still some time before the next pills (when you realize just after the previous turn)

- Take medicines as soon as possible
- Take your next dose as scheduled
- You don't have to delay the next dose.

② If the next turn is coming soon (you were late in recognizing that you forgot)

- Skip the dose you forget.
- Take your next dose as scheduled
- Do not take a double dose.
- Inform your doctor how many times you fail to take medicine, when you see the doctor next time.

If you have any questions, let's ask health care providers.

Q7 What if I'm running out of medicines because of natural disasters or troubles during travels.

A In emergency, the ways of coping are different depending on the drugs. Be prepared in advance to handle the situation properly even in emergency.

For emergency

- Ask health care providers in advance the ways of coping and contact information in emergency.
- Keep a several-day backup supply of your medicines with you always.
- Remember names and amount of drugs. It is recommended to write down these information on a piece of paper and put it in your wallet.
- Write down phone numbers of the hospital on a piece of paper in case your mobile phone gets out of work.

Do not forget to confirm with your health care providers the way of coping every time you change or add medicines.



Which type are you in ? Tips to avoid forgetting to take medicines



A variety of strategies to maintain adherence according to your type.

Type A: who forgets to take medicines carelessly

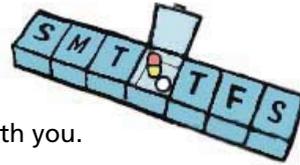
- Use alarm function of mobile phones and other electronic devices.
- Use an app of smartphones which reminds taking medicines.
→ You can find some apps with words "medicines Reminder"
- Use email tool that avoid forgetting.

Don't to forget mail (忘れちゃだメール)

<http://www.da-mail.jp/>

Provided by the Ministry of Health, Labor and Welfare
/ free of charge/ anonymous

- Ask your household members to remind you to take medicines at the scheduled time.



Type B who forgets to carry medicines.

- Put your medicines in a pill box and bring it with you.
- Keep a backup supply of medicines at work.

Type C: who forgets whether you took medicines or not.

- Use a 7-day pill box.
→ It is useful that you can tell by just looking.

Type D: who falls asleep without taking medicines and realizes in the morning.

- Confirm with your health care providers the way of coping in advance.

Type E: who couldn't take medicines because he couldn't eat anything. who couldn't take medicines because the time of meal has changed so much. (medicines which should be taken with food)

- Ask and confirm how much food you should eat when you take medicines with your health care providers in advance.
- Ask and confirm how late you can take medicines after meal with your health care providers.

"Taking anti-HIV medicines properly" means
taking everyday,
taking exact dosage,
types of medicines,
taking exact types, and keep taking.

Any of them can't be missed.



We appreciate all the patients and health care providers who gave us numerous supports to make this booklet.

「きちんとのおむ」ってどんなこと? <英語訳>

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