

**THE ANTIHYPERTENSIVE AND
LIPID-LOWERING TREATMENT
TO PREVENT HEART ATTACK
TRIAL**



Patient Information Brochure

**National Heart, Lung, and
Blood Institute**

National Institutes of Health

**The University of Texas-Houston
School of Public Health**



Patient Information Brochure

What is the ALLHAT Program?

ALLHAT is a nationwide Program that will test the performance of different types of drugs often used to treat high blood pressure and high blood cholesterol. The test will try to determine whether newer blood pressure-lowering drugs, which are more costly than older medicines, are better at reducing the risk of heart attacks. *ALLHAT* will also test whether a newer cholesterol-lowering drug prolongs life.

ALLHAT is being funded by the ***National Heart, Lung, and Blood Institute***, part of the National Institutes of Health. It is being conducted in doctors' offices, medical clinics, and other health care centers throughout the United States. The Program will have two parts: a high blood pressure part and a high cholesterol part. About 40,000 patients will be enrolled in the high blood pressure part. One-half of these patients (20,000) will also be involved in the high cholesterol part of the study. The Program is expected to last until the summer of 2001, unless results call for it to be ended earlier.

This brochure contains information on both parts of *ALLHAT*. Your doctor will discuss with you whether you are eligible for one or both parts.

Who Can Participate?

Men and women aged 55 years or older who have high blood pressure and one or more additional risk factors for heart attack, but who are basically in good health, can participate in the high blood pressure part of *ALLHAT*. In addition, people involved in the blood pressure part who also have moderately high cholesterol and have not been taking a cholesterol-lowering drug for the past two months may participate in the cholesterol part of the Program.

What Drugs Will Be Used In ALLHAT?

The ***blood pressure part*** of *ALLHAT* will test whether treatment with one of three newer types of drugs used to lower blood pressure is better in preventing heart attacks than a standard form of treatment with a diuretic drug. The newer drugs being used are *lisinopril*, *amlodipine*, and *doxazosin*, and the diuretic is called *chlorthalidone*.

Chlorthalidone has been used to treat high blood pressure for more than 25 years and has been proven to reduce the risk of heart attack and stroke in people with high blood pressure. The newer drugs have been used to treat high blood pressure since the 1980s and are known to lower blood pressure as well as *chlorthalidone*. They are even thought by some doctors to have fewer side effects than *chlorthalidone*, but this has not been proven in side-by-side comparisons. Since all these drugs lower blood pressure in slightly different ways (see *How Do the ALLHAT Drugs Work?* on page 11), there may also be differences in their ability to prevent heart attack and stroke, over and above their blood pressure lowering effects. However, this has never been shown in side-by-side comparisons.

Even though much remains to be proven, the newer drugs have been rapidly replacing longstanding treatments, such as chlorthalidone, even though they have not been shown to be more effective. The newer drugs are also very expensive — they can cost up to 30 times as much as the longstanding treatments!

Your doctor and other doctors and scientist working on *ALLHAT* believe that the benefits of these newer drugs must be proven for the welfare of all patients. This is why we are conducting the blood pressure part of *ALLHAT* and are asking you to participate.

For cholesterol part only:

The ***cholesterol part*** of *ALLHAT* will test whether a cholesterol-lowering drug called *pravastatin* will prolong life and reduce the risk of heart attack in men and women aged 55 and older who have moderately high blood cholesterol levels.

Cholesterol in the bloodstream is a major component of the plaques that build up in arteries. These plaques can reduce and sometimes block blood flow. When blood cannot get to the heart, a heart attack results. *Pravastatin* is one of several new drugs that safely and effectively lower high blood cholesterol. This part of *ALLHAT* will involve 20,000 volunteers from among the people who are already in the blood pressure part of the Program.

Doctors know that lowering high cholesterol in the bloodstream in middle-aged people, especially in men, reduces their risk of having heart attacks and other kinds of heart disease. What doctors do not know is whether older people, especially women, obtain the same benefits from cholesterol-lowering as

younger people. Since the changes in blood vessels that lead to heart attacks can take many years to develop, it is possible that starting treatment after age 55 might have no effect on the length of life or on heart disease at all. It is also possible that any decrease in heart disease might be balanced by an increase in other diseases, so that treatment does not prolong life.

ALLHAT will try to answer these important questions and so could influence treatments given to patients in the future. This is why we are doing the cholesterol part of *ALLHAT* and are asking those of you with moderately high cholesterol levels to participate.

What Happens in the Study?

Once you and your doctor have discussed the Program and you have agreed to participate in *ALLHAT*, you will be examined by your doctor to be sure you are eligible for the study. This examination may require more than one visit to the doctor or medical clinic to measure your blood pressure. The examination may also require that you have an electrocardiogram (ECG) tracing of your heartbeat and some other blood tests. During this brief time, you may also be asked to cut down or stop taking some of the blood pressure drugs you are now taking, so that your body can be ready to switch over to the *ALLHAT* blood pressure drugs. Your doctor will check your blood pressure closely and be sure you get any treatment you need to keep it under control.

Once your doctor decides that you are eligible for the high blood pressure part of the Program, and you agree to sign up, one of the four *ALLHAT* blood pressure drugs

will be chosen for you by chance — like the flip of a coin. This medicine will be given to you by your doctor at no cost to you for the length of the Program. All of these drugs are commonly used to lower blood pressure and the way they work is described in the section called *How Do the ALLHAT Drugs Work?* (page 11). Of every five patients who volunteer for the Program, one will be assigned by chance to receive the drug *lisinopril*, one to receive *amlodipine*, and one to receive *doxazosin*. The remaining two of every five patients will be assigned to the standard drug, *chlorthalidone*. All of the *ALLHAT* drugs will look alike, and neither you nor your doctor will know which drug you are taking. It is important that neither of you know which drug you are on because sometimes knowing that can affect the way you are treated or even the way you report on your health. In an emergency, your doctor can easily find out what drug you are taking.

The four *ALLHAT* blood pressure drugs are **not new or experimental drugs**, but they will not look like the tablets commonly supplied by a pharmacy or drug store. This is because the four drugs being used in *ALLHAT* will all be put into the same kind of capsules to make them look alike. Since these *ALLHAT* medicines look different than those given out at a pharmacy, the FDA (Food and Drug Administration) requires that the message *Caution: New Drug—Limited by Federal (USA) Law to Investigational Use* be placed on the drug bottle labels for these medicines. But, they are not new drugs; they will only look new.

As a participant in *ALLHAT*, you will be asked to see your doctor for regular blood pressure check-ups at least every three months during the first year and every four months for the next four to six years, or as long as *ALLHAT* lasts (see *How Long Will the Program Last?*, on page 7). These check-ups will be like your usual visits

for treatment of your high blood pressure, except for two things: first, your doctor will send some information about your health to the *ALLHAT* Center in Houston, Texas, and second, you will be asked to take one of the *ALLHAT* blood pressure medications instead of being given your prescription for the pharmacy. Other than that, your treatment will be just the same as it would be without your being involved in *ALLHAT*.

It is very important that you continue to take the *ALLHAT* drugs for as long as the Program lasts and that you see your doctor regularly for treatment of your high blood pressure.

For cholesterol part only:

If you would like to be in the cholesterol part of *ALLHAT* and give your consent to do so, your doctor will examine you to see if you are eligible. If your cholesterol level is very high or you are already taking a cholesterol-lowering drug, you will not be eligible for this part of the Program since most doctors agree that, even in older people, treatment for very high cholesterol levels probably **does** reduce the risk of heart attack. It would not be wise to include you in a study where your cholesterol might not get special treatment.

Once your doctor decides that you are eligible for the cholesterol part of *ALLHAT*, and you agree to sign up, you will be assigned to one of two groups by chance, like flipping a coin. One group will be given the cholesterol-lowering drug *pravastatin*; the other group, called the usual care group, will not be given *pravastatin* through *ALLHAT*. If you are assigned to the *pravastatin* group, your doctor will give you

pravastatin at no cost to you, and will check some blood tests from time to time (about every 6-8 months) to be sure the drug is not giving you any side effects. If you are chosen for the usual care group, your doctor will be free to prescribe any other cholesterol-lowering treatment he or she feels might be necessary to reduce your risk of heart attack. Participants in both groups will be advised to follow a special low-fat diet.

How Long will the Study Last?

ALLHAT is expected to end in the summer of 2001. If clear answers about the value of newer drugs to lower blood pressure, or the importance of lowering blood cholesterol in older persons, are obtained before then, *ALLHAT* may be ended sooner.

What is Expected of Participants?

By agreeing to participate in *ALLHAT*, you agree to follow two important rules:

- You must take the drugs prescribed through *ALLHAT* every day for as long as the Program lasts.
- You must see your doctor regularly for treatment of your high blood pressure.

You will have check-up visits every three months during the first year of *ALLHAT* and every four months after that. At the beginning, you may need to see your doctor every month or so to adjust your blood pressure medication. This is important to make sure the *ALLHAT* medicine lowers your blood pressure to the right level

and that you are not having any problems with it. You may want to look at the section *How Do the ALLHAT Drugs Work?*, on page 11, for more facts about the drugs.

For cholesterol part only:

If you are also in the cholesterol part of *ALLHAT*, you will need to continue to follow the low-fat diet given to you at the beginning of the study. If you are assigned to receive *pravastatin*, you will need to take this medicine every day. In the first few months of *ALLHAT*, and every one or two years after that, your doctor will check your cholesterol level to make sure you are getting the right amount of *pravastatin*. You may be asked to increase or decrease the amount of *pravastatin* you are taking so that your cholesterol doesn't go too high or too low.

You should not worry if your doctor is treating you for other health problems besides high blood pressure or high cholesterol. Your treatments will continue. But, any tests or drugs taken for these other health problems will not be paid for by *ALLHAT*.

ALLHAT Check-up Visits

At each *ALLHAT* check-up, these following things will be done:

1. Your blood pressure will be measured.
2. You will be asked if you have stayed in a hospital overnight since your last visit, and if so, where and when.

3. You will be asked if you have had any of six major health problems since your last visit.
4. You will be asked how much of your *ALLHAT* medicine you have taken, and the doctor or nurse will collect all unused medications.
5. You will be given enough *ALLHAT* medicine to last until your next doctor's visit.

You may have noticed that many of these are things that usually happen when you see your doctor for treatment of your blood pressure. The only differences are some of the questions that you will be asked will be worded in a standard way, so that answers to the these questions can be collected in the same way from all 40,000 patients in *ALLHAT*.

If your doctor finds that your blood pressure has not been adequately lowered by your assigned *ALLHAT* drug, he or she may decide to increase the dose of the drug. If your blood pressure stays high, you may be given a second or even a third drug to lower it to the desired level. Your doctor will be given a supply of four additional drugs commonly used to treat high blood pressure and can give you any of these drugs at no cost to you. Unlike your assigned *ALLHAT* drug, both you and your doctor will know the names of any other blood pressure drugs prescribed for you.

If your blood pressure is still not low enough, or if for some reason you cannot take these drugs, your doctor is free to choose other drugs for your blood pressure, but these will not be paid for by *ALLHAT*.

At the beginning of the study and about every two years after that, an electrocardiogram (ECG) and blood tests will be done. The ECG is a painless procedure that is done while you rest quietly on a couch. It monitors your heart beat for a few minutes to see if it is beating

normally. You will have about two tablespoons of blood drawn from your arm for the blood tests. One of the blood tests will be to check your potassium level, which can be affected by blood pressure medicines. If your potassium level is low, your doctor will give you **potassium pills** to take at no cost to you. The ECGs and blood tests done as part of *ALLHAT* will be sent to a central laboratory for measurement at no cost to you.

For cholesterol part only:

In addition to the blood tests every two years, patients who are taking *pravastatin* will have blood drawn at each check-up (every three months) for the first year and about every eight months after that. These tests will help your doctor be sure that the *pravastatin* is not causing any side effects or problems with your muscles, which have been reported in a few people who take this drug.

This is all there is to being part of *ALLHAT*. Most of the things that will happen in *ALLHAT* are things that doctors usually do for patients with high blood pressure and high cholesterol, except that the medications and some tests will be given to you at no cost and facts about your health will be collected in a standardized way. If you are like many older people, your doctor will probably be treating you for other problems not related to *ALLHAT*, and may advise you to have other tests or take other medicines for these problems. These tests and other medicines will not be paid for as part of *ALLHAT*, but it is important for your health that you follow your doctor's advice.

How do the ALLHAT Drugs Work?

Four different kinds of drugs that lower blood pressure will be used in *ALLHAT*, and each of them works in different ways. It might help to think about the pressure of blood in a blood vessel as being like water flowing through a pipe under pressure. One way to lower the pressure is to let some of the fluid out of the pipe, which is basically the way that ***diuretics***, or water pills, work. The diuretic that will be used in *ALLHAT* is called *chlorthalidone*.

Another way to lower the pressure is to make the pipes, or the blood vessels, wider. Normal blood vessels can get wider, or dilate, and get narrower, or constrict, in reaction to things like exercise, heat, or cold. Sometimes, blood vessels can become too narrow, or over-constricted, and stay that way, causing high blood pressure. ***Calcium blocking drugs*** keep calcium from causing the walls of the blood vessels to constrict, and are used in this way to lower blood pressure. The calcium blocking drug that will be used in *ALLHAT* is called *amlodipine*. ***Alpha-blocking drugs*** keep the nerves in the walls of the blood vessels from causing them to constrict, and this effect also lowers blood pressure. The alpha-blocking drug that will be used in *ALLHAT* is called *doxazosin*. Another class of drugs, called ***ACE (angiotensin converting enzyme) inhibitors***, act by preventing a substance that is released by the kidney from constricting the blood vessels. The ACE inhibitor that will be used in *ALLHAT* is called *lisinopril*.

You will be taking one of these drugs every day. Like all medicines, they may produce some unwanted ***side effects*** which are rarely serious but can be troublesome. You could have such side effects as drowsiness, tiredness, weakness, impotence, headache, dizziness and

cough which might be related to the medicines. Most people who take these drugs do not have any side effects at all, but if they do occur, your doctor will decide whether the drug you are taking should be changed or stopped.

Other risks and discomforts which might occur include bruising, bleeding, and a slight risk of infection from drawing blood. In addition, while your blood pressure medicines are being adjusted or decreased, your blood pressure may increase. During this period, you will be monitored closely and treated if your blood pressure increases high enough to put you in any danger.

For cholesterol part only:

Pravastatin lowers cholesterol in the blood by slowing down the speed at which the body makes cholesterol. *Pravastatin* is usually taken once a day.

Sometimes, though not often, people taking *pravastatin* may get stomach upset, tiredness, or muscle pains. If you have these or other problems while taking *pravastatin*, you should let your doctor know right away. *Pravastatin* can also cause mild liver trouble. Your doctor and the study doctors will be checking your liver functions by means of the blood tests. If this occurs, your doctor may reduce or stop the *pravastatin*.

How Will Patients be Protected?

Participants in the *ALLHAT* Program will be protected in several ways.

1. Patients whose doctors believe that they may have a bad reaction to the *ALLHAT* drugs will not be entered into the Program.
2. All patients in the Program will begin their drugs in small doses so that they can be closely watched. If a problem develops, it will be treated, and the *ALLHAT* medication will be cut back or stopped as needed.
3. Your own doctor and other doctors working in the Program will watch carefully for any problem that might be caused by the *ALLHAT* drugs.
4. A national committee of experts who are not directly working in *ALLHAT* will carefully review all the *ALLHAT* results every six months or more often if needed. If the results show great benefit or harm from one of the drugs, the Program will be stopped right away and patients and doctors will be told of the results.

We believe that the benefits of the *ALLHAT* Program for you and for society far outweigh any chance of harm to you, but this is a judgement you and your doctor should make together.

What Are the Benefits of Participating?

1. In addition to your regular medical care, the information given by you at each visit will be looked at by other doctors working on this Program. Special laboratories will do your blood tests and look at your ECGs using the most up-to-date methods.

2. Many services related to the Program are provided to you at no cost. You will not be charged for your *ALLHAT* drugs or laboratory tests.
3. This is a chance for you to join in a national research effort which could help people like you with high blood pressure or high cholesterol live more productive and longer lives.
4. The results of this Program may help your doctor choose the best treatment for your high blood pressure or high cholesterol.

Why Get Involved?

Only patients who have high blood pressure or high cholesterol can participate in this Program and provide the answers we need; so we turn to people like you. Perhaps, that is how it should be because we are trying to prevent future heart attacks and prolong life among people like yourself. You can help us. We in turn will make every effort to safeguard your welfare and provide the best possible care for your high blood pressure and high cholesterol. We promise to place your best interests ahead of our own interests in *ALLHAT*.

Where Can I Get More Facts?

This brochure tells the basic facts about the *ALLHAT* Program. Your doctor, nurse, or physician's assistant can provide you with further information about the Program. We urge you to ask any question you may have about the Program, its purpose, its design, and what it involves.

The success of the Program depends on the participation and cooperation of patients like yourself. Before

you agree to join us, please be sure that you understand the Program and that all your questions have been answered.

For more information about *ALLHAT*, your rights as a Program participant, and what to do if you have research-related injuries, you may contact any of the following people.

_____	_____
Name	Telephone number
_____	_____
Name	Telephone number
_____	_____
Name	Telephone number

I have reviewed this brochure with the participant and fully explained to the participant the nature and purpose of the procedures it describes and such risks as are involved in carrying them out.

_____	_____
Signature of Person Obtaining Consent	Date

Patient's Initials: _____

Consent Form for ALLHAT Cholesterol-Lowering Treatment Study

The ALLHAT cholesterol-lowering treatment study at _____ has been explained to me, and I have read the *ALLHAT Patient Information Brochure*. I know that I have the opportunity to ask any questions that I may have. I understand that, if I am eligible, I will be invited to take part in the cholesterol-lowering study and that I will be expected to participate until the summer of the year 2001.

The purpose of this research study, the procedures to be followed, possible discomforts and risks, and expected benefits have been described to me. It has been explained to me that high blood cholesterol is a common condition and that persons with high blood cholesterol are more likely to have a heart attack than those who have low cholesterol. It has been explained to me that I do not have to participate in this study in order to receive treatment for my high cholesterol. I further understand that as a participant in this study:

- 1) My cholesterol and its effect on my body will be measured by standard medical tests. I will be eligible for the study if my cholesterol levels are moderately, but not extremely, high and I am **not** already on drug treatment for high cholesterol.
- 2) There are several drugs which lower high cholesterol. One of these drugs, *pravastatin*, has been chosen for this research study because it is commonly used by doctors when treating patients with high cholesterol. Doctors do not know whether lowering cholesterol levels like mine with *pravastatin* will reduce my chance of having a heart attack. Whether I receive *pravastatin* or not will be assigned by chance, like flipping a coin, rather than by my doctor.
- 3) If I am assigned to receive *pravastatin*, my doctor may adjust the dosage or even prescribe an additional drug to lower my cholesterol to a satisfactory level. If I am not assigned to receive *pravastatin*, my doctor may later decide to prescribe a cholesterol-lowering drug if my cholesterol rises or my clinical condition otherwise requires it. In either case, I will continue to receive encouragement to follow the recommended heart-healthy diet. I understand that the ALLHAT study will not provide non-study medicines. If other medications are prescribed, my doctor will explain to me any side effects they might have. No new or "experimental" medicines will be used in this study.
- 4) There may be side effects from *pravastatin*, such as muscle pains or trouble sleeping, other allergic reactions, and other side effects. Inflammation of the liver may occur in a small number (about 1%) of patients taking *pravastatin*. If I receive this drug, I will be tested for this complication at regular intervals throughout the study. My doctor may perform additional tests to confirm this, and may stop my study drug. Inflammation of the liver disappears when the drug is stopped. The possible side effects that may occur have been explained to me as well as the fact that I can ask any questions about these possible side effects and any other aspect of the study that I do not understand. The doctor, therapist, nurses and others involved in my treatment under this study will watch closely for such side effects. If necessary, they will stop the medication which appears to be causing such side effects and will give me different medication if I need it.
- 5) All information about me, including my medical history, laboratory data and findings of physical examinations, will be kept confidential to the extent permitted by law. My research records, just

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Participant's Initials _____

like hospital records, may be subpoenaed by court order. In certain instances, representatives from the National Heart, Lung, and Blood Institute or the FDA (Food and Drug Administration) may need to see my records in order to verify the study data. Study results may be published; however, my identity will not be revealed. At the end of the study, all paper forms with my name or other identifying information will be kept in locked rooms for a period of five years and then will be destroyed.

- 6) The *ALLHAT* researchers are requesting my Social Security Number under Public Health Service Act 42 USC 285a. I understand that my name and Social Security or Medicare Number will be used to help the *ALLHAT* researchers locate me in the future if I cannot be located at my home address by my doctor; they may be used to help *ALLHAT* researchers know if I am hospitalized; and they may be used to search vital status records in a follow-up study conducted in the future. I understand that providing this information is voluntary, that I may still participate in *ALLHAT* even if I refuse to provide this information, and that I will not be denied any federal right, benefit, or privilege by my refusal to provide this information.
- 7) My name, Social Security Number, Medicare Number, and any other publicly identifying information will be kept in computerized records separate from my *ALLHAT* medical data. These records will be kept indefinitely in a locked place and only used for the purposes stated in (7) above.
- 8) All medical information about me will be kept in computerized records for analysis with such data from all other participants, but these records will **not** contain my name or Social Security Number or Medicare Number, or any other publicly identifying information. These computerized medical records will be kept indefinitely for future use by authorized researchers.

I understand that my participation in this study is entirely voluntary. I am free to withdraw my consent and to discontinue participation in this study at any time. No penalty or loss of benefits will occur if I refuse to participate or if I withdraw from the study. If I refuse to participate in the cholesterol-lowering trial, or if I withdraw from the cholesterol-lowering trial later, I can still participate in the blood pressure part of this study and I can still receive treatment for high blood cholesterol from my doctor if I need it. I have been given the names and telephone numbers of persons whom I may contact for answers to questions about the study, my rights as a research subject, and what to do if I have research-related injuries. The above points have all been explained to me to my satisfaction and, understanding them fully, I hereby give my consent to enter this treatment study. I will be given a copy of this informed consent form.

Printed Name of Participant

Signature of Participant

Date

I have reviewed the patient brochure with the participant and fully explained to the participant the nature and purpose of the procedures described above and in the brochure and such risks as are involved in carrying them out.

Date

Signature of Person Obtaining Consent

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Participant's Initials _____