

<p style="text-align: center;">WOMEN'S INTERAGENCY HIV STUDY QUESTION BY QUESTION SPECIFICATIONS FORM NP01: BASELINE NEUROPATHY SIGNS AND SYMPTOMS</p>

General Instructions:

1. All dates should be recorded in the MM/DD/YY format.
2. Times should be recorded in HH:MM format.
3. Remember to use leading zeros for the time and severity questions, e.g., 08:00 or 06.
4. Participants should remove shoes and socks.
5. This form should be completed before beginning the physical exam. Remember to verify with the participant the date of her birth. Record the actual time you began **NP01** in **Question A6** "Time Module Began" and the actual time you ended the questionnaire in **Question C8** "Time Module Ended."
6. A participant can refuse at any time. If she refuses a question or test, write "REFUSED" in the margin, initial this notation and any other comments, and then proceed to the next question.
7. If a participant rates a current symptom as "8" or higher, please refer her to her primary care provider or a neurologist for a full evaluation.
8. It is very important that the questions be read to the participant as written and in the correct order. Each participant in the study should hear *exactly* the same question. Using non-standardized language that changes even one or two words can affect the entire meaning of the question and lead to bias. Although some questions could be phrased differently or more simply, every word in the question serves a purpose and is specifically designed to achieve the research goals of the project. In order to combine the responses of all participants and analyze the data, there must be no variations in the way questions are asked.
9. The clinician can and should reconcile factual inconsistencies given by the participant within the context of the interview situation. For example, if the participant indicates that she is taking medication for neuropathy, please confirm that this was reported to the interviewer and recorded on F22MED.
10. If the participant reports multiple episodes of a bothersome symptom, ask her to provide a rating for the symptom when it was at its worst.
11. Be sure to follow-up with the participant after the exam to discuss problems not related to the questions on the form. For example, a participant may want to discuss swelling in her feet, but this should be addressed after the exam.

SECTION B: NEUROPATHY SYMPTOMS

Our goal is to identify pain associated with distal sensory polyneuropathy (DSPN). This kind of pain is bilateral and affects at least the toes. It is described as burning, gnawing, aching, and shooting. Some pain should be present in the toes and/or feet to conclude that DSPN is present. Pain present in the calves or knees that is not also present in the toes and feet is unlikely to be due to DSPN.

In Questions B1 through B6, we are looking to characterize a specific type of pain that starts in the toes and may spread upward to the legs, and always occurs on both sides of the body simultaneously. The severity of pain on each side may differ; however, the pain must happen at the same time, bilaterally. If pain has fluctuated or disappeared at times, the participant should rate the pain when it was at its worst.

There are many types of pain that should be ruled out during the examination. Pain that is only in one side of the body, or spreads from the back down the legs should be excluded. Radicular pain – usually due to a herniated disc in the lumbosacral spine or to bony overgrowth from osteoarthritis in this region (although many other disorders can cause this syndrome) – may be the most difficult to separate from pain due to neuropathy. Radicular pain typically starts in the back and radiates down the leg, but we are not interested in this type of pain. Herniated discs usually cause unilateral pain and the pain is located in the back or at least buttocks. We are also not interested in leg pain due to venous thromboses (blood clots); arthritis in the knee, ankle, or foot; or foot problems due to podiatric causes such as corns and bunions. We are only interested in recording information about neuropathic pain of DSPN, which starts in both toes and feet and may eventually extend into the leg.

HAND PARTICIPANT RESPONSE CARD NP01 TO RATE SEVERITY.

Please note that the symptom questions are structured to ask if the participant has EVER had a type of neuropathy first. After a symptom rating for the EVER question, ask about the same symptom within the last six months. B1, B3, and B5 are EVER questions. B2, B4, and B6 are IN THE LAST SIX MONTHS questions. For example, it is important to stress in Question B1 that you are asking about the participant’s entire life history with pain, aching, or burning in her feet and legs. In Question B2, you would ask about pain, aching, or burning during the last six months. Follow-up administration of neuropathy symptoms will not ask about a participant’s lifetime history.

READ THE INTRODUCTION TO THE PARTICIPANT.

- B1. Indicate if the participant has ever had pain, aching or burning in both her feet and legs at around the same time. If the participant responds in the negative, then circle “2” and skip to **Question B3**.
- Have the participant use the scale on the *NP01* response card. Ask her to rate the severity of the pain in her right foot and leg where 1 is mild and 10 is severe.
 - Have the participant use the scale on the *NP01* response card. Ask her to rate the severity of the pain in her left foot and leg where 1 is mild and 10 is severe.
- B2. Indicate if the participant has had, in the last 6 months, pain, aching or burning in both her feet and legs at around the same time. If the participant responds in the negative, then circle “2” and skip to **Question B3**.
- Ask the participant to rate the severity of the pain in her right foot and leg.
 - Ask the participant to rate the severity of the pain in her left foot and leg.
- B3. Read the example. Indicate if the participant has ever had “pins and needles” in both her feet and legs at around the same time. If the participant responds in the negative, then circle “2” and skip to **Question B5**. Do not record symptoms due to the example provided. **PROBE:** Do not record “yes” if the participant has experienced “pins and needles” caused simply by sitting too long.
- Ask the participant to rate the severity of the paresthesias in her right foot and leg.
 - Ask the participant to rate the severity of the paresthesias in her left foot and leg.
- B4. Indicate if the participant has had, in the last 6 months, “pins and needles” in both her feet and legs at around the same time. If the participant responds in the negative, then circle “2” and skip to **Question B5**.
- Ask the participant to rate the severity of the paresthesias in her right foot and leg.
 - Ask the participant to rate the severity of the paresthesias in her left foot and leg.

- B5. Read the example. Indicate if the participant has ever had numbness in both her feet and legs at around the same time. If the participant responds in the negative, then circle “2” and skip to **Section C**. Please be sure that the participant understands that the example provided in Question B5 is just an example. Do not record symptoms due to the example provided. **PROBE:** Do not record “yes” if the participant has experienced numbness caused simply by Novocaine or Orajel.
- Ask the participant to rate the severity of the numbness in her right foot and leg.
 - Ask the participant to rate the severity of the numbness in her left foot and leg.
- B6. Indicate if the participant has had, in the last 6 months, numbness in both her feet and legs, at around the same time. If the participant responds in the negative, then circle “2” and skip to **Section C**.
- Ask the participant to rate the severity of the numbness in her right foot and leg.
 - Ask the participant to rate the severity of the numbness in her left foot and leg.

SECTION C: NEUROPATHY SIGNS

Gently assess whether or not simply handling the participant’s feet causes her pain. In these cases, be additionally careful when examining her feet and placing the tuning fork. The tuning fork testing and reflex testing are absolutely painless in participants without neuropathy; however, the examiner should keep in mind that they may be painful in some participants with neuropathy. Some participants may need assistance in removing their socks and shoes.

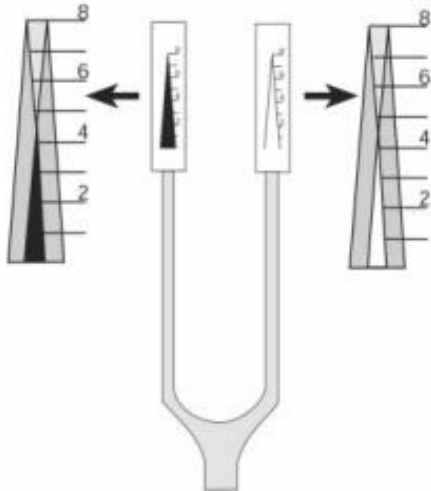
Evaluation of Perception of Vibration: General Principles

Use a Rydel-Seiffer 64/128 Hz tuning fork to conduct the vibration testing.



The Rydel-Seiffer tuning fork is available on AAN on-line store. Catalog number 219118, purchase price \$129 (member price \$109). <https://tools.aan.com/globals/axon/assets/10762.pdf> (see page 3 of the catalog)

To start vibrations, you may either strike the middle of the tuning fork a sharp blow against the side of your hand, or ping the ends of the tuning fork between the thumb and forefinger. When vibrating, two triangles appear on the graduated scale of 0 to 8, in 0.5 increments, that join together as the amplitude decreases. When the participant says she is unable to feel the vibrations, the scale is read at the apex of the single triangle formed from the initial two triangles. Two scales are provided, black and white. They work in the same way and it is largely a matter of user preference as to which one is used.



First set the tuning fork as above and then watch for the black or white triangle to start forming at the bottom of the scale. At this point the tuning fork should be applied to the participant's foot, over the distal interphalangeal joint of the great toe. Refer to the figure below for the correct placement.



If the participant can feel the vibration she is asked to say when she can no longer feel it. As the vibration dies away the triangle enlarges and the tip makes its way to the top of the scale. The scale should then be read off at the point at which the participant can no longer detect the vibration and the value should be recorded, in increments of 0.5. Participants who have neuropathy may not feel the vibration at all, in which case the value should be recorded as "zero."

Do not hold the toe with force or in an area that will dampen the participant's sensation of vibration. If necessary, lightly hold the sides of the participant's toe with your thumb and index finger to stabilize the foot. Some examiners prefer to bend over for the testing, others prefer to use a stool, and a select few prefer to get on the floor on their knees. Use the method that works best for you. The examiner may or may not use gloves. It will not affect the results of the testing.

Reference values for normal health controls have been published in the *Journal of Neurology, Neurosurgery and Psychiatry* 1998;65(5):743-7.

Normal Reference Values for Lower Extremities

Age	Value
≤40	≥4.5
41-60	≥4.0
61-85	≥3.5
>85	≥3.0

It is very important to establish a vibration control for every participant. This allows the participant to understand what you mean by “vibration.” Demonstrate first on her wrist and ask, “What do you feel?” It is important to consistently ask this exact question and see if the participant feels the sensation we are expecting. She should describe the feeling as a buzzing or tingling, not merely pressure. She may also imitate the sound of the sensation. Do not bias the participant by asking the question differently, e.g., “Do you feel the buzzing?” This type of question wording gives away the answer. The participant should tell you that the vibration stops when you remove the tuning fork. There is a little art to this as some participants will “tune out” and forget to tell you when they stop feeling the vibration. This may lead you to infer that they still feel the buzzing. One should test this at the wrist by purposely withdrawing the tuning fork after a few seconds. If the participant correctly stated that the buzzing stopped, repeat at the wrist and time how long she feels the vibration.

C1a & C1b. Indicate the number in increments of 0.5 (0 to 8) at which the participant can no longer feel the vibration in her right (C1a) and left (C1b) great toe at the distal interphalangeal joint.

Instructions for Evaluation of Perception of Vibration

1. Establish a vibration control. Inform the participant that the tuning fork will make a loud, clanging sound, but that is normal.
 - a. Place the stem of the tuning fork on the participant’s wrist.
 - b. Ask the participant, “What do you feel?”
 - c. If the participant tells you that she feels vibration, then go on to test the great toes.
 - d. If the participant doesn’t tell you that she feels vibration, ask her, “Do you feel a vibration?” on her forehead.
 - e. Proceed when participant feels vibration.
2. Testing vibration in the toes.
 - a. Place the vibration fork stem against the distal interphalangeal joint of the great right tow.
 - b. Record the result in Question C1a for the right toe.
 - c. Repeat for the left toe and record the result in Question C1b.
3. If you do not think the participant understood you the first time, repeat the test and record the new numbers.
4. If unable to evaluate the vibration for any reason, record “-9.”

Evaluation of Deep Tendon Reflexes: General Principles

Use a large Queen's Square hammer to conduct the deep tendon reflex testing. Knee reflexes and ankle reflexes will be tested. The participant should be seated on the examining table so that her feet do not touch the floor and her legs can swing freely at the knees.





Hold the hammer about two-thirds of the way down the handle, near the red plastic tip.

The examiner should practice until a “swinging” movement of the hammer is mastered. Use your wrist to start the motion and then loosen your grip slightly so that the weight of the hammer leads the motion. If you loosen too much, you may lose control of the hammer. The movement of the hammer is stopped when the hammer strikes the participant's tendon; the examiner does not provide the braking of the hammer. Never strike the participant with excessive force and be mindful that, for some participants, any amount of contact with their feet is painful. Gloves are optional and their use will not affect results.

Assessing Knee Jerk

Before striking the patellar tendon, palpate the knee cap. The patellar tendon can be felt immediately distal to the bony knee cap. It is the patellar tendon that is struck with the reflex hammer. If using the Queen's Square hammer, one can strike the tendon in one of two ways. Use the method that is the most comfortable for you.

METHOD A	METHOD B
<p>Hold the hammer parallel to the thigh with the examiner's hand above the knee cap. This usually works best if the examiner stands to the side and slightly behind the subject.</p> 	<p>Strike the tendon from the side with the axis of the hammer perpendicular to the thigh.</p> 

Striking the tendon with the hammer stretches the tendon, causing the quadriceps muscle (the large muscle in the front of the thigh) to contract, leading to extension of the leg at the knee. You can also observe the quadriceps contract. There should be a slight delay from the time the tendon is struck until the time the muscle contracts. The most common reason for not eliciting the reflex is bad aim, and it is perfectly acceptable to repeat the procedure making sure you are hitting the tendon and not the kneecap.

Assessing Ankle Jerk

Be sure that the participant is seated and that you are seated or otherwise in a stable, balanced position. Hold the foot slightly away from the examining table if you need room to swing the hammer. Test that the participant is relaxed by letting her foot fall and seeing if it dangles loosely. You can also tap the bottom of her foot gently to see if she is tensing her foot. Encourage the participant to relax. Many people will remain in control of their reflexes and will not relax.

The examiner dorsiflexes the ankle from its passive position to a 90-degree angle between the foot and ankle before striking the tendon with the hammer.



Some participants will have a very obvious, brisk reflex. Others will have more subtle reflexes. A normal response is for the ankle to plantar flex downward after a short delay and the muscle (gastrocnemius) in the posterior of the calf will contract. The biggest problem is when no or very little reflex is elicited. If you are not sure whether you are getting a reflex, you can put your hand over the calf when you strike the reflex and feel for the contraction. If you don't find a reflex, it could be because the reflex was absent or decreased or because the technique used to conduct the reflex testing is inadequate. The examiner should check her technique by eliciting a knee, elbow, or forearm reflex. Most of the time with DSPN, the ankle reflex is lost, but other reflexes are present. By eliciting a knee reflex and not eliciting an ankle reflex, one gains confidence that bad technique is not the cause of the absent reflex.

Instructions for Evaluation of Knee and Ankle Deep Tendon Reflexes

C2a & C2b. Before striking the patellar tendon, palpate the knee cap. Strike the tendon from above or from the side using the method that works most reliably for you. The most common reason for not eliciting the reflex is bad aim, and it is perfectly acceptable to repeat the procedure making sure you are hitting the tendon and not the kneecap. Indicate the results of the knee reflex in the right (C2a) and left (C2b) knees.

- 0 Absent reflex
- 1 Hypoactive reflex
- 2 Normal, Increased, or Clonus reflex
- 9 Unable to evaluate

If the participant has, for example, one knee in a cast, then record and initial this information in the margin. Circle “-9” for that knee. If you cannot obtain a reflex even after multiple attempts, circle “0.” Some individuals do not have a reflex, but this is not necessarily an indication of a neurologic problem.

C3. Based on the results in **Questions C2a** and **C2b**, indicate if both the right and left knee reflexes are equal to 2, i.e., normal, increased or clonus. If both the left and right are normal, then circle “1” and skip to **Question C5**. If no, meaning that the participant had at least one knee reflex measured as absent (“0”), hypoactive (“1”), or the clinician could not assess an knee reflex (“-9”), then circle “2” and go to **Question C4**.

C4a & C4b. If you must proceed to Question C4, demonstrate how the participant should hold her hands (see below figure). Tell her that on the count of three she should close her eyes, bite down, and pull tightly. Count to three and when you are sure that she is tensing her hands, swing the hammer. If the participant has long fingernails and cannot lock her fingers, she can clasp opposite forearms with her hands. Encourage the participant to pull hard while you swing the hammer. Indicate the results of the knee reflex test for the right (C4a) and left (C4b) knees.



Jendrassik maneuver: If no reflex is elicited, have the participant interlace her fingers as shown, and tell the participant that on the count of three, she should pull outwards. Strike the tendon when she is pulling outwards. The Jendrassik Maneuver need only be conducted on the side where the reflex was <2.

C5a & C5b. Swing the reflex hammer behind the foot so that it directly strikes the Achilles tendon above the heel, making sure you are hitting the tendon and not the heel. Observe the calf muscle for a contraction. A true reflex manifests as a slight delay then a jump downward led by the ball of the foot. You may repeat this a second time to confirm the presence or absence of the reflex. Indicate the results of the ankle reflex test in the right (C5a) and left (C5b) knees.

- 0 Absent reflex
- 1 Hypoactive reflex
- 2 Normal, Increased, or Clonus reflex
- 9 Unable to evaluate

If the participant has, for example, one foot in a cast or an amputated foot, then record and initial this information in the margin. Circle “-9” for that ankle. If you cannot obtain a reflex even after multiple attempts, circle “0.” Some individuals do not have a reflex, but this is not necessarily an indication of a neurologic problem.

C6. Based on the results in **Questions C5a** and **C5b**, indicate if both the right and left ankle reflexes are equal to 2, i.e., normal, increased or clonus. If both the left and right are normal, then circle “1” and skip to **Question C8**. If no, meaning that the participant had at least one ankle reflex measured as absent (“0”), hypoactive (“1”), or the clinician could

not assess an reflex (“-9”), then circle “2” and go to **Question C7**. If the participant had a normal, increased, or clonus reflex for *both* ankles, then proceed to **Question C8**. If the participant had an absent or hypoactive reflex in one or both ankles, proceed to **Question C7** and repeat the reflex test while the participant performs the **Jendrassik maneuver**. You should repeat the reflex test for both the right and left ankles even if only one ankle had a normal reflex *without* the Jendrassik maneuver.

- C7a & C7b. If you must proceed to Question C7, demonstrate how the participant should hold her hands (see above figure). Tell her that on the count of three she should close her eyes, bite down, and pull tightly. Count to three and when you are sure that she is tensing her hands, swing the hammer. If the participant has long fingernails and cannot lock her fingers, she can clasp opposite forearms with her hands. Encourage the participant to pull hard while you swing the hammer. Indicate the results of the ankle reflex test for the right (C7a) and left (C7b) knees.
- C8. Record the time that the neuropathy questions and measurements in *NP01* were completed.