Gallium-67 citrate is used to locate sites of tumor involvement throughout the body. In order to make proper use of this new agent, a knowledge of the normal $^{67}$Ga distribution and physiological variations is necessary. For this report, over 400 whole-body rectilinear scans using 35 $\mu$Ci/kg $^{67}$Ga citrate were reviewed. At 48 hr, normal $^{67}$Ga activity is concentrated in the axial skeleton, liver, spleen, and around the large joints. Foci of uptake are often seen in the salivary, lacrimal, and mammary glands. Activity is also found in the region of the nasopharynx. Under certain physiological conditions, intense localisation may occur within the breast, bowel, and long bones. These variations may mimic malignant tumors. Lymph nodes involved by malignant disease present a distinctive pattern that aids in their identification.

Tumor visualization using $^{67}$Ga photoscanning was first reported by Edwards and Hayes in 1969 (1,2). Since that time, several investigators have confirmed the tumor-specific properties of $^{67}$Ga for a number of epithelial and lymphoreticular neoplasms (3–8).

To date we have scanned over 400 patients with $^{67}$Ga-citrate. The purpose of this communication is to emphasize the special features of our experience that are important to proper interpretation of the $^{67}$Ga photoscan. We will discuss: (A) the normal scan pattern of $^{67}$Ga distribution; (B) problems of interpretation caused by physiologic concentration of radiogallium; and (C) the anatomic distribution and scan appearance of the lymph nodes often involved in neoplastic disorders.

A review of the physiology of $^{67}$Ga uptake is a necessary prerequisite to proper interpretation. The initial studies of $^{67}$Ga distribution were performed by Bruner, Hayes, and Perkinson (9) as part of an attempt to use gallium isotopes for specific therapy of bone tumors (10). Although the primary purpose of these investigators was not achieved, several important observations were made. The distribution of carrier-free $^{67}$Ga was predominantly found within the liver, spleen, kidney, and bone in rats. The addition of stable gallium caused a progressive increase in relative concentration within the skeleton and a relative decrease in soft tissue concentration. As a result of this early work, $^{67}$Ga with a carrier was later evaluated as a bone scanning agent, and it was while scanning the bones of a patient with Hodgkin's disease that the tumor-specific properties of $^{67}$Ga-citrate were discovered (2).

The distribution of $^{67}$Ga in humans has subsequently been studied (11–13). When carrier-free $^{67}$Ga-citrate is injected intravenously, the majority of the isotope is bound to plasma protein, especially transferrin.

During the first day after injection, the kidney excretes about 12% of the administered dose and contains the highest concentration of the nuclide. After this the fecal route of excretion becomes predominant. During the usual scanning period, between 48 and 72 hr, the highest concentrations are seen in the bones, liver, and spleen. About one-third of the isotope is excreted over the first week, and the remaining two-thirds is distributed within the liver (6%)*, spleen (1%), kidney (2%), skeleton (including marrow) (24%), and other soft tissues (34%). Other organs with relatively high concentration include the adrenals, bowel, and lung.

**METHODS**

**Patient population.** Table 1 shows the diagnostic categories and the number of patients scanned during the past 19 months at the National Institutes of Health, Bethesda, Maryland.

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*All percentages in this section refer to percentage of the administered dose of $^{67}$Ga.
Health. All of the patients scanned in this series had documented neoplastic disease or a high suspicion for a malignant disorder. A wide variety of tumor types were represented. Malignant lymphoma and leukemia patients predominated, reflecting the current clinical research emphasis of the National Cancer Institute. A complete statistical evaluation of the scanning results from this series will be presented in another publication as part of the report of the Cooperative Group to Study Localization of Radiopharmaceuticals sponsored by Oak Ridge Associated Universities and the National Cancer Institute. The present communication is intended to review the population of Table 1 with respect to the technical and physiologic factors important to proper interpretation of the photoscans.

**Photoscan technique.** Gallium-67 was obtained in the sterile pyrogen-free form and injected (35 μCi/kg) intravenously 48–72 hr before scanning. Purgatives were administered over the next 2 days to remove gallium from the colon.

The patient was scanned using a dual-probe 5-in. NaI(Tl) Ohio-Nuclear whole-body scanner with 5:1 minification. Anterior and posterior projections were simultaneously obtained. When the anteroposterior scans were equivocal, lateral scans were performed.

**REGIONAL PHOTOSCAN INTERPRETATION**

A normal whole-body $^{67}$Ga photoscan is shown in Fig. 1 with the anterior view on the left and the posterior on the right. For each region of the body the major normal localizations and physiologic variants will be presented and contrasted with similar pathologic lesions.

**Head and neck.** Reference to Fig. 1 shows the

<table>
<thead>
<tr>
<th>TABLE 1. $^{67}$Ga WHOLE-BODY SCANS (APR. 1971–SEPT. 1972)</th>
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<tbody>
<tr>
<td>Diagnosis</td>
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<tr>
<td>------------------------------------------------------------</td>
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<tr>
<td>Lymphomas</td>
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<tr>
<td>Hodgkin’s disease</td>
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<tr>
<td>Leukemia</td>
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<tr>
<td>Lung cancers</td>
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<td>Head and neck cancers</td>
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<td>Melanomas</td>
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<td>Breast cancers</td>
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<td>Soft tissue sarcomas</td>
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<td>Uterine cancers</td>
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<tr>
<td>Primary bone cancers</td>
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<tr>
<td>Pancreatic cancers</td>
</tr>
<tr>
<td>Central nervous system tumors</td>
</tr>
<tr>
<td>Ovarian cancers</td>
</tr>
<tr>
<td>Hepatomas</td>
</tr>
<tr>
<td>Miscellaneous neoplasms</td>
</tr>
<tr>
<td>Unknown malignancies</td>
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<td><strong>Total</strong></td>
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**FIG. 1.** Normal whole-body $^{67}$Ga scan in 44-year-old woman. Anterior view is on left and posterior view is on right.

**FIG. 2.** Anterior $^{67}$Ga scan of 15-year-old female with acute myelogenous leukemia. Myeloblastomas are shown in nasopharynx (arrow) and left breast.
within the bony thorax, spine, and scapulae. These structures may occasionally cause interpretation problems.

On the anterior view, concentration of $^{67}$Ga in the sternum may be so prominent as to mimic tumor uptake. The triangular shape of the manubrium with the apex pointed downward (Fig. 4) and the superior orientation are of some benefit in differentiating the sternum from enlarged hilar or peritracheal lymph nodes. These structures can be separated by a lateral view of the chest.

On the posterior view, the lower ends of the scapulae often show a prominent concentration near the lateral chest wall (Fig. 1). This must be differentiated from rib lesions or tumors in axillary or lateral thoracic nodes. Again, lateral views may be of help.

Occasionally, uptake occurs in the breasts, which is particularly prominent when the breasts are under the physiologic stimulus of the menarche, cyclic estrogenic and progesterational agents, or pregnancy (14).

Figure 3 is a photoscan of a woman with Hodgkin’s disease who was scanned 3 weeks postpartum. The patient was not nursing her infant, but she was

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**FIG. 3.** Anterior $^{67}$Ga scan of 25-year-old woman performed at 6 weeks postpartum. Intense $^{67}$Ga uptake in both breasts was confirmed by finding of high activity in breast milk.

nuclide normally distributed throughout the soft tissues of the scalp, the osseous structure and marrow cavity of the skull, and the soft tissues of the neck. The most active concentration is normally seen in the region of the nose on the anterior projection and the marrow containing spaces of the occiput on the posterior projection. The lacrimal glands concentrate $^{67}$Ga to a variable extent and may be strikingly prominent on the anterior projection (Fig. 1). In addition, the salivary glands can also be observed.

Pathologic concentration near the nasal antrum may be masked by the normal uptake in this region. Figure 2 is a whole-body scan of a patient with acute myeloblastic leukemia whose biopsy revealed myeloblastoma in the region of the posterior nasopharynx and tonsils (arrow). Initially, this scan was interpreted as normal in this region, and it was only after treatment had ablated uptake that an abnormality was appreciated. In retrospect, this region concentrates the isotope more extensively than usual in cases of physiologic uptake in the region of the mouth (see Fig. 1).

**Thorax.** In the thorax, $^{67}$Ga is normally distributed

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**FIG. 4.** Anterior $^{67}$Ga scan in 22-year-old man showing marked localization of activity in colon obscuring abdominal detail. In addition, manubrium is prominent and must be distinguished from mediastinal disease.
able to manually express a small amount of milk from both breasts. Concentration of $^{67}$Ga was measured at 90 and 120 hr after injection and found to be approximately 70 nCi/ml, indicating that $^{67}$Ga in appreciable amounts was being excreted in the milk.

The breast is also a common site of myeloblastomas, which may mimic physiologic uptake. The uptake of gallium in the left breast of the patient in Fig. 2 was a result of myeloblastoma. Involvement of this degree should not be confused with physiologic uptake in the stimulated breast, which is usually symmetrical even when less prominent.

**Abdomen.** Gallium-$^{67}$ is normally concentrated within the liver and spleen, but other intra-abdominal structures are normally not seen (Fig. 1). On the posterior view the spine and sacrum are prominent.

The most common problem of photoscan interpretation in the abdomen is the presence of $^{67}$Ga within the bowel. Figure 4 shows the abdomen of a patient in whom accumulation of $^{67}$Ga was so dense that no interpretation was possible in the region of the abdomen. The entire outline of the colon can be seen including cecum, ascending, transverse, and descending portions. If the cleansing of the bowel has been inadequate, interpretation of any abnormality in the abdomen should be made with great care.

The physiologic concentration of gallium in the liver may interfere with the diagnosis of malignant involvement of the liver. Figure 5 shows the $^{99m}$Tc-sulfur colloid liver scan with a large filling defect because of hepatoma in the right lobe. The $^{67}$Ga scan of the liver appears to be entirely normal with homogeneous distribution of the radiogallium throughout its substance. In the right neck, however, there is a previously undiagnosed metastatic node (arrow) in the deep cervical lymph node chain, which is the only abnormality on the gallium photoscan. The hepatoma actively concentrates $^{67}$Ga in the liver and the neck, but the hepatic primary could not be diagnosed because the normal liver tissue also accumulates activity as seen in Fig. 1. Suzuki and others have reported that tumor uptake of $^{67}$Ga was indistinguishable from normal liver uptake in 8 out of 19 cases of hepatic neoplasm with satisfactory scans (15).

The kidneys have the greatest activity in the body during the first day after a gallium injection; by the time of scanning, concentration has fallen greatly (13). Hayes had shown excellent visualization of the kidneys in a rat scanned at 1 hr with $^{68}$Ga (16). However, the kidneys normally do not appear on the 47–72-hr human scan.

We have observed definite renal activity in malignant involvement of the kidneys as well as acute

FIG. 5. $^{99m}$Tc-sulfur colloid liver scan on left shows large mass lesion in patient with hepatoma. Anterior $^{67}$Ga scan on right shows uniform uptake in liver and tumor. In neck metastasis also takes up gallium (arrow).

FIG. 6. Posterior $^{67}$Ga scan of 54-year-old male with Hodgkin's disease involving both kidneys as well as bones, liver, and widespread lymph nodes.
involvement (arrows) was noted after the $^{67}$Ga scan showed uptake in these regions. This must be differentiated from activity in the site of $^{67}$Ga injection.

**LYMPH NODE CORRELATION**

An understanding of the regional distribution and scan appearance of lymph node groups is of significant importance to $^{67}$Ga whole-body scanning in lymphoma and leukemia. Figure 9 is an anterior photoscan of a patient with lymphosarcoma and widespread involvement of many lymph node chains. Particularly well shown in this patient is the left infraclavicular chain which is contiguous medially with the left peritracheal and supraclavicular lymph node groups. Laterally, the infraclavicular group blends into the axillary lymph nodes. Although in this case the peritracheal and para-aortic lymph node chains are distorted by considerable enlargement, it is still possible to see the characteristic left and right orientation of these lymph node groups. In the abdomen, the right para-aortic lymph node chain sends a branch across the midline to form the left common iliac lymph node chain. Involvement of the external iliac, femoral, and inguinal lymph nodes is also seen in this patient. Care must be taken to insure adequate

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**FIG. 7**. Normal and abnormal $^{67}$Ga uptake in epiphyses of long bones is shown by these scans. On right is scan of 12-year-old patient with Ewing's sarcoma and physiologic uptake in bones due to rapid growth. On left is scan of 53-year-old patient with leukemia showing similar localization.

Pyelonephritis and nephrolithiasis. Figure 6 shows the 48-hr scan of a patient with proven Hodgkin's disease involving the kidneys. Intense localization occurs in both kidneys.

**Extremities.** The concentration of $^{67}$Ga is normally greatest in the epiphyseal region of the long bones, appearing in the shoulders, elbows, and knees. This may be particularly prominent in children with rapidly growing bones as shown by the scan on the right in Fig. 7 of a 12-year-old girl with Ewing's sarcoma of the right ilium. Occasionally such normal concentration may be confused with the increased concentration around the knees and distal extremities seen in the patient with leukemia. Figure 7, on the left, shows a 53-year-old man with chronic myelogenous leukemia in blast crisis. The increase in radionuclide is not confined to the epiphyses but occupies the entire distal femur and proximal tibia. The reason for this concentration in such patients is not known, but it does appear to correspond to the most active site of the functioning marrow in such patients (17).

A pattern of specific concentration of radionuclide is seen in malignant involvement of the epitrochlear nodes. Figure 8 shows a 53-year-old obese woman with lymphosarcoma whose bilateral epitrochlear

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**FIG. 8**. Posterior $^{67}$Ga scan of 27-year-old woman with Hodgkin's disease involving epitrochlear nodes. There is also normal uptake in tips of both scapulae.
bowel cleansing when interpreting pelvic nodes. The epitrochlear node group, not seen on this patient, is shown in Fig. 8.

In a number of cases we have observed gallium localization in mediastinal and epigastric lymph nodes before radiographic evidence of disease. These findings were subsequently supported by histologic or radiographic findings or response to therapy.

**DISCUSSION**

Brief reports of the "normal" appearance of the gallium scan have appeared in the literature (18,19). However, as described in this report, there are many variations on the normal pattern. These may appear in the absence of disease under the influence of various physiologic phenomena such as lactation and puberty. Neoplastic and inflammatory lesions may cause gallium uptake that closely resembles these normal patterns.

A thorough knowledge of all the usual and variant localizations of gallium is necessary for the most reliable interpretation. In normal patients, $^{67}\text{Ga}$-citrate acts as a bone scanning agent similar to $^{18}\text{F}$ and $^{88}\text{Sr}$ with localization in the axial skeleton and the epiphyses of the long bones. The normal $^{67}\text{Ga}$ scan differs from other bone scans in showing more soft tissue background and less distal long bones. In contrast to $^{18}\text{F}$, the bladder is not seen as a route of excretion, but various other secretory organs—such as the lacrimal, salivary, and mammary glands—may be seen.

Familiarity with the scan projection of the various lymph node groups, as described here, is also important. The lymph nodes are normally not visualized on $^{67}\text{Ga}$ scans; their appearance is an indication of disease. In this series lymph node visualization did not occur with benign reactive hyperplasia. Uptake in lymph node areas was from a tumor in most cases and suppurrative infection in a few.

It is often impossible to differentiate neoplastic from inflammatory lesions on the scan alone. This requires correlation with the patient's history and other diagnostic studies. We have not observed gallium uptake in benign tumors.

When there is uncertainty about a focus of activity, lateral views will frequently help separate the normal structures from lymph node groups. Other sources of data are also required. These include the patient's history, particularly the age, hormonal status, localizing symptoms, and bowel movements before scan. Physical examination may confirm palpable nodes or masses seen. Correlation with radiographs is also of help. However, it should be remembered that the gallium scan may provide the first evidence of a malignant lesion before it is detected by physical examination or radiography. A suspected lesion that cannot be shown to be a normal variant should be an indication for further study to include plain x-rays, tomography, and other radioisotopic procedures.

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