Using Clinical Audits and Algorithms in the Scintigraphic Imaging of Infection

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Objective: We describe how using an audit of clinical practice and producing a clinical algorithm can provide a logical approach to using nuclear medicine in a defined group of patients. In this case, patients are undergoing a scintigraphic study for the investigation of focal infection or inflammation.
Methods: A retrospective review was performed on two years of scintigraphic studies used for the localization of infection or inflammation in a community hospital. In each case the indication for the study and the agent used was determined. From this data and a review of current literature, a clinical algorithm was produced which was then applied to all scintigraphic studies over the next year. Changes in the number and pattern of studies performed were then reassessed.
Results: In the first two years of the study a total of 94 scintigraphic studies were performed to localize infection or inflammation. The majority of patients had been studied with ^{67}Ga citrate- or ^{111}In-labeled leukocytes. This gave a mean radiation burden to the patient of 8.1 mSv (0.81 rad) per patient. After application of the algorithm most studies were performed with ^{99m}Tc-labeled leukocytes or ^{99m}Tc human immunoglobulin. This resulted in an increase in use of the service to 82 studies performed in a single year. The mean radiation dose to the patient was reduced to 3.9 mSv (0.39 rad) per patient.
Conclusion: In those areas of nuclear medicine where a choice of agents exists, it is possible to use a combination of clinical audit and algorithm to help decide which is the best agent for each patient, thus providing a better clinical service and, in our case, reducing the mean radiation burden to the patient.
Key Words: clinical algorithm; infection imaging; inflammation imaging; gallium-67; indium-111-WBC; technetium-99m-WBC; technetium-99m-HIG

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Since the 1973 introduction of ^{67}Ga-citrate for imaging infection (*1,2*) nuclear medicine has been able to localize infection and inflammation. Gallium-67 is not ideal as there is excretion into the normal colon which has limited its use in some groups of patients, such as those with inflammatory bowel disease. Leukocytes labeled with ^{111}In-oxine or ^{111}In-tropolone offer a more specific technique. For example, activity in the abdomen only occurs when pathology is present (*3,4*). Leukocyte labeling requires the removal of about 50 mls of the patient's blood and separation of the leukocytes, incubation with the radiopharmaceutical, and reinjection of the cells back into the patient. This labeling can be done in the nuclear medicine laboratory or in a district blood labeling facility.

None of these agents has ideal imaging characteristics and they provide a significant radiation burden to the patient (*5*). Availability of these isotopes can be limited and consequently imaging with them may become uneconomical if they are only ordered occasionally. Gallium-67 and ^{111}In-labeled leukocytes are therefore not ideal for smaller community hospitals.

Scintigraphic imaging of infection and inflammation has been possible with ^{99m}Tc since the introduction of hydroxymethylpropylene amine oxime (HMPAO) (*6*). While cell separation and labeling facilities are still required, the ^{99m}Tc is readily available and HMPAO comes as a standard kit. Another approach has been to use human pooled immunoglobulin G (HIG) labeled with ^{99m}Tc. This can be purchased as a kit or made from commercially available immunoglobulin G (*7,8*).

The availability of these ^{99m}Tc-labeled agents and physical characteristics which suit most commercially available gamma cameras make them more suited for a community hospital. They also provide a significant reduction in radiation burden to the patient (*5,8*) (Table 1).

We have a choice of agents to use in the scintigraphic investigation of patients with suspected infection or inflammation. Choices can however lead to confusion. This may be particularly true when the referring clinician may be unaware of the advantages and disadvantages of each technique.

We therefore used an audit of clinical practice in the scintigraphic investigation of infection and inflammation to construct an algorithm. The chief aims of this algorithm were to:

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TABLE 1
Radiation Burden by Radiopharmaceutical

Radiopharmaceutical	Activity (MBq)	EDE (mSv)	Reference
^{67}Ga-citrate	80	9	5
^{111}In-leukocytes	20	12	5
^{99m}Tc-HMPAO leukocytes	200	3	5
^{99m}Tc-HIG	200	1	8

EDE = Effective dose equivalent.

1. promote a logical approach to the scintigraphic investigation of patients with suspected infection and inflammation;
2. ensure those agents such as ^{67}Ga and ^{111}In-labeled leukocytes, which may not always be available, are reserved for those patients who would benefit most from them; and
3. reduce the mean radiation dose to the patients imaged by using ^{99m}Tc-labeled products where possible. The effectiveness of this approach was then tested by a second clinical audit one year after the algorithm was introduced.

MATERIALS AND METHODS

Demographics

Medway Hospital is a community hospital of 400 acute care beds covering a mixed area of urban, suburban and rural populations. All medical and surgical specialties, except obstetrics, are covered.

Retrospective Review

All scintigraphic studies performed to localize infection or inflammation between January 1, 1991 and December 31, 1992 were reviewed. The clinical problem leading to referral and the type of study performed were noted. This review was performed in the last few days of 1992.

Imaging Protocols

Standard imaging protocols were used for ^{67}Ga with images taken for up to 72 hr postinjection. Indium-111 labeled leukocytes were prepared by the addition of 20 MBq (0.6 mCi) ^{111}In-oxime to leukocytes separated from venous blood. These were then reinjected and images performed over 24 hr. Technetium-99m-HMPAO leukocytes were labeled using the Hammersmith method (*6*) and 200 MBq (6 mCi) reinjected. Images were performed up to 24 hr postinjection, except in the abdomen where images were limited to 1 and 3 hr post-injection. Technetium-99m-HIG was prepared using a commercial kit (Mallinckrodt Medical, Petten, Netherlands). The activity used was 148–222 MBq (4–6 mCi). Images were performed at 1 and 4 hr postinjection.

Clinical Algorithm

The results of the clinical review and additional information from a literature review were used to help build a clinical algorithm using the following guidelines:

1. the number of patients and their presenting clinical problems, as determined by the clinical audit;
2. patients are imaged with the best agent for their particular clinical problem and, if not, consider how this could be achieved;
3. the radiation dose for each patient should be as low as reasonably achievable, without compromising clinical efficacy; and
4. the choice should be practical, in terms of availability of pharmaceutical, camera time and cost.

Additional information was obtained with a literature review. No agent could be used for a particular indication unless its utility had been confirmed by two papers involving at least 10 patients from two different centers. As some agents may not always be available, a first and second choice for each indication was provided. The algorithm was created in the last week of 1992 for application in 1993.

Closing the Audit Cycle

The clinical algorithm was applied on January 1, 1993 and its effectiveness in changing clinical practice was tested using a repeat retrospective review performed to cover the period January 1, 1993 through December 31, 1993. The response of the referring clinicians was monitored objectively by determining if the use of the service had increased after the application of the clinical algorithm. Any reduction in the mean radiation dose to the patient (measured as the effective dose) was tested for significance using an X^2 test.

RESULTS

In the initial study period a total of 94 studies was performed. The number of studies increased from 18 in the first half of 1991 to 33 in the second half of 1992 (Fig. 1). The number of ^{99m}Tc-HMPAO-labeled leukocyte studies increased during this time from 5 in the first half of 1991 to 13 in the second half of 1992. The number of ^{111}In-labeled leukocyte studies remained almost constant during this period and there was a slight increase in the number of ^{67}Ga studies performed.

Technetium-99m-HMPAO leukocyte studies were performed primarily for inflammatory bowel disease (Fig. 2) and patients presenting with fever, particularly if symptoms were acute (Fig. 3). In patients with a chronic history of fever, ^{111}In-labeled leukocytes were chosen. They were also used in inflammatory bowel disease (Fig. 4).

Gallium-67 usage also increased slightly from 4 studies in the first half of 1991 to 8 studies in the second half of 1992. Most of these studies were performed for suspected prosthetic joint infection. The remainder being performed for suspected osteomyelitis.

In the 12 mo following the application of the algorithm (Fig. 5), 82 studies were performed. An increase of 42% over the previous year. The majority of studies was performed with ^{99m}Tc-labeled agents (Fig. 6). The use of ^{99m}Tc-HMPAO-labeled leukocytes had increased so that it was the most commonly used agent for patients with pyrexia of unknown cause

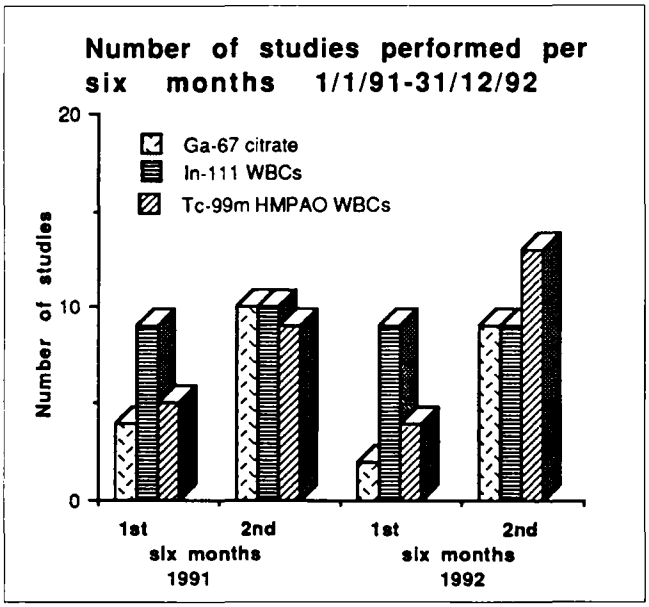

FIGURE 1. Number of scintigraphic studies performed to localize infection between January 1, 1991 and December 31, 1992 per six-month period.

(Fig. 7) and was used exclusively for inflammatory bowel disease.

In patients with suspected prosthetic joint infection or suspected osteomyelitis, ^{99m}Tc-HIG had become the most commonly used agent (Fig. 8).

The mean radiation burden per patient for scintigraphic studies to localize infection or inflammation was 8.1 mSv (0.81 rad) in 1991 and 1992. In 1993 this had been significantly reduced by 51% to 3.9 mSv (0.39 rad) per patient, (X^2 = 270, v = 1, $p < 0.01$).

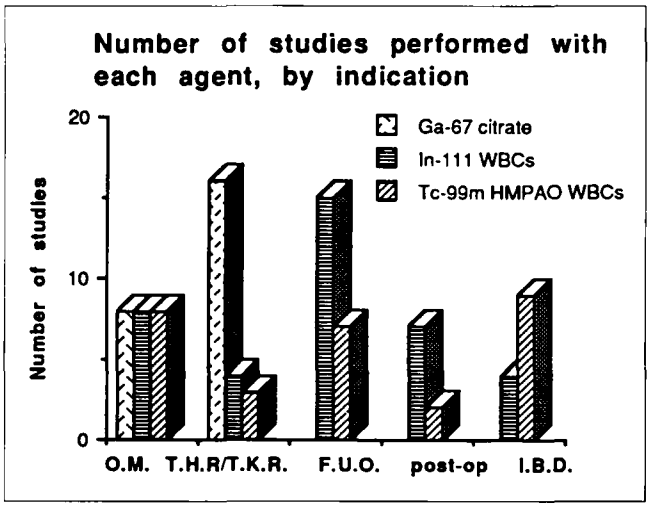

FIGURE 2. Number of studies performed with either ^{67}Ga-citrate, ^{111}In-labeled leukocytes (WBCs) or ^{99m}Tc-labeled leukocytes (WBCs) in 1991/1992 for each indication. Legend: OM = osteomyelitis; THR/TKR = total hip or knee replacement; FUO = fever of undetermined origin; Postop = postoperative fever; and IBD = inflammatory bowel disease.

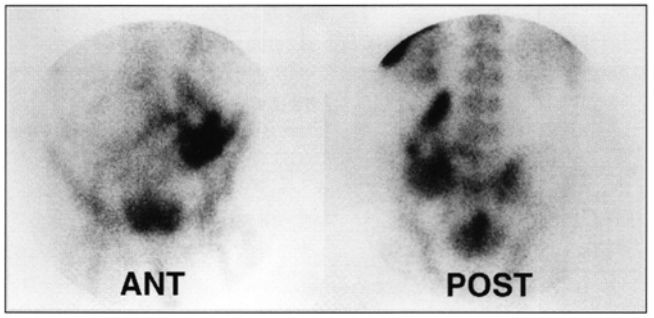

FIGURE 3. Seventy-four-year old male presenting with fever and groin tenderness 10 days after placement of a left aortic iliac bypass graft. Technetium-99m-HMPAO-labeled leukocyte images three hours postinjection clearly show a collection of white cells in the distal end of the graft. During surgery a large staphyloccocal abcess surrounding the distal anastomosis was found.

DISCUSSION

It is possible to use a review of clinical practice and a clinical algorithm to produce a more logical approach to imaging infection. This resulted in more patients being studied and a fall in the mean radiation burden to the patient. One factor

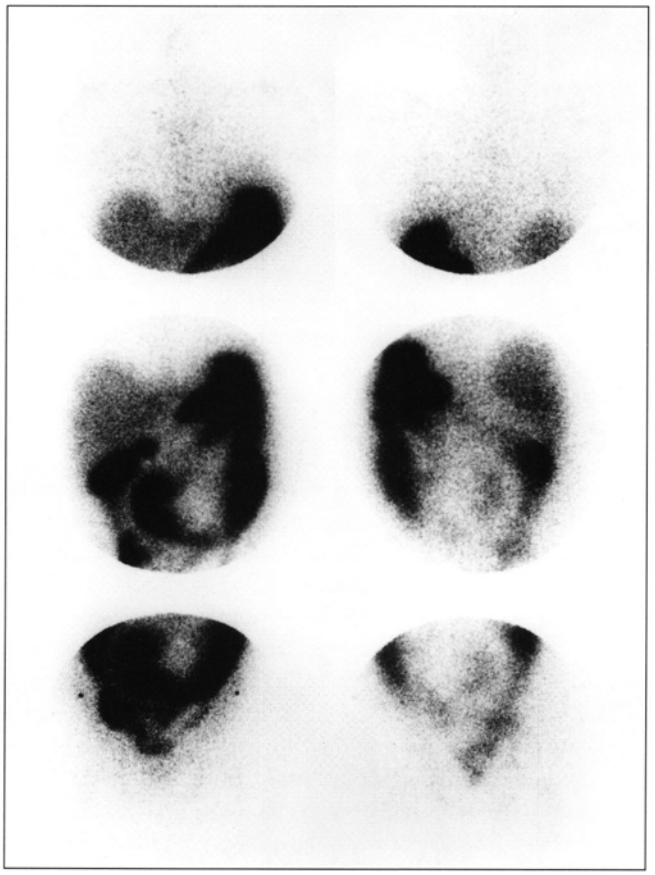

FIGURE 4. Thirty-two-year old male patient with six-month history of abdominal discomfort and diarrhea. An initial barium enema examination was normal but ^{111}In-oxime-labeled leukocytes performed 24 hr postinjection show multiple noncontinuous areas of small and large bowel inflammation characteristic of Crohn's disease. This was confirmed on biopsy of the colonic mucosa.

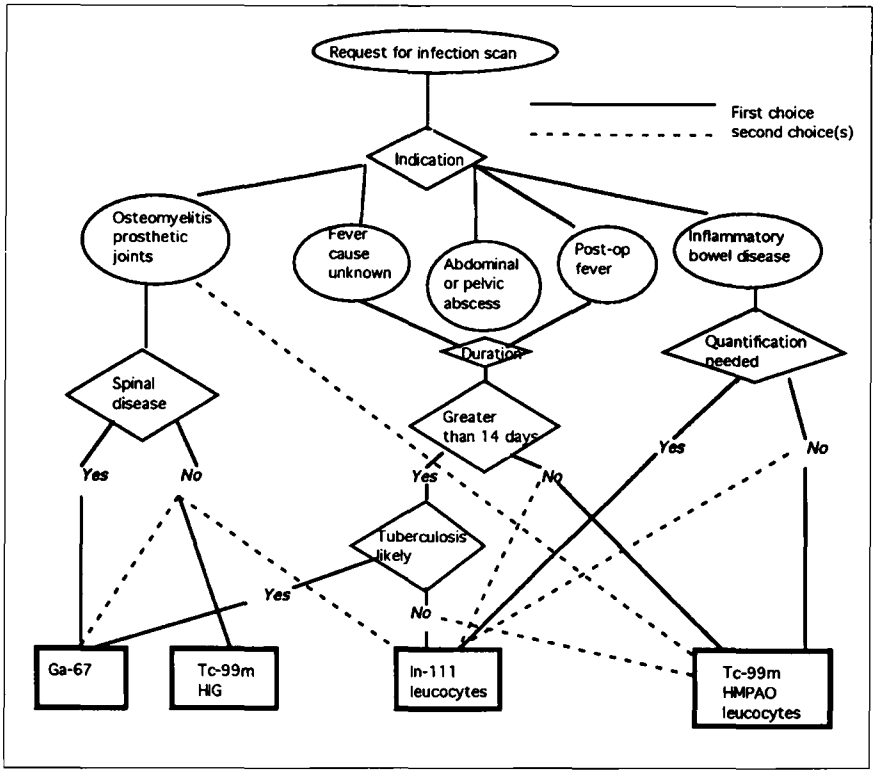

FIGURE 5. Clinical algorithm for the scintigraphic detection of focal infection.

which improved throughput was the adoption of one- and three-hour imaging protocols for acutely ill patients imaged with ^{99m}Tc-HMPAO-labeled leukocytes (*9*). Results were therefore available on the day of request.

Technetium-99m-HMPAO-labeled leukocytes were used for inflammatory bowel disease primarily to reduce the radiation burden to these patients, often young adults, who over time may need multiple studies. The accuracy of ^{99m}Tc-HMPAO-labeled leukocyte imaging is similar to that of ^{111}In-labeled leukocytes (*6,10,11*).

The use of ^{99m}Tc-HIG in patients with orthopedic infections is more controversial as this is a relatively new agent. There are good data to indicate that it has a high sensitivity and specificity in both osteomyelitis and infected prosthetic joints (*7,8,12*) (Fig. 8). If this agent is not available it can be replaced, in most cases, by ^{99m}Tc-HMPAO-labeled leukocytes. Technetium-99m-HIG comes in multidose kit form and is used ideally when three to four patients can be imaged on the same day. This is normally the case in patients with suspected orthopedic infections which are chronic and indolent.

The algorithm acted as a guide to help logical decision making, tailored for each patient's clinical need. This resulted

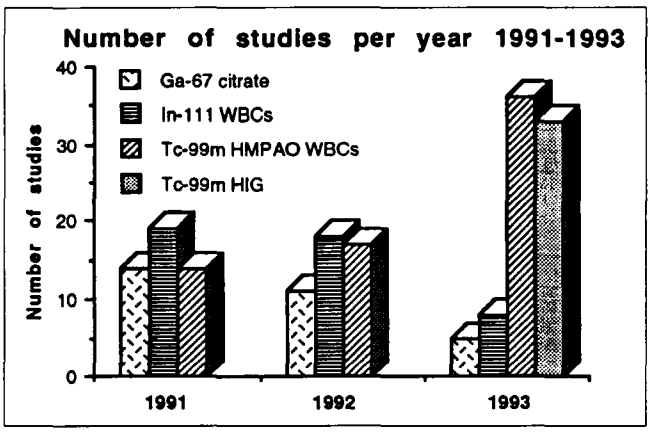

FIGURE 6. Number of studies performed with agent over the period January 1, 1991 through December 31, 1993.

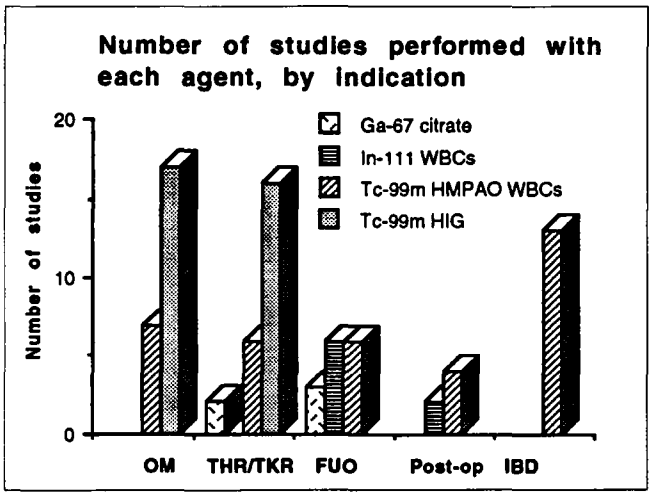

FIGURE 7. Number of studies performed with either ^{67}Ga-citrate, ^{111}In-labeled leukocytes (WBCs), ^{99m}Tc-labeled leukocytes (WBCs) or ^{99m}Tc-HIG in 1993 for each indication. Legend: OM = osteomyelitis; THR/TKR = total hip or knee replacement; FUO = fever of undetermined origin; Postop = postoperative fever; and IBD = inflammatory bowel disease.

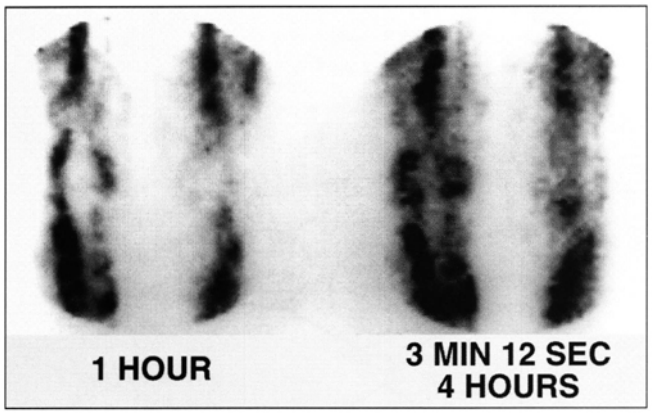

FIGURE 8. Patient with infected prosthetic knee replacement showing increased uptake of ^{99m}Tc-HIG at one and four hours.

in a reduced need for ^{67}Ga-citrate and ^{111}In-labeled leukocytes, which were directed toward more chronic soft tissue infections and suspected spinal osteomyelitis where labeled leukocytes are not applicable (*13*). After application of the algorithm there was an 82% increase in the use of the nuclear medicine service for the investigation of patients with infection and inflammation. Increased use is a better objective measure of the satisfaction of referring clinicians than is the use of subjective questionaires and surveys.

Caution may be needed, however, in applying the algorithm to other nuclear medicine departments, as it has been formed by local circumstances and needs. Local versions should be constructed for each department, taking into account published data, clinical practice and the requirements of the referring clinicians (Table 2). After application of any clinical algorithm, its effectiveness should be measured after an appropriate time interval. Doing this can ensure that we are providing the optimum study for our patients.

TABLE 2
Algorithm Guidelines for the Scintigraphic Investigation of Infection and Inflammation

Review present patterns of use of nuclear medicine procedures for imaging infection and inflammation.
Determine if local patterns of disease dictate that certain studies be done more commonly than others (e.g., ^{67}Ga in patients with AIDS).
Cost and availability of relevant radiopharmaceuticals and cell-labeling facilities.
Determine how radiation dose to each patient can be kept as low as reasonably achievable.
Determine if there are any patient groups which would benefit from a nuclear medicine evaluation for infection and inflammation who are not being studied currently. Can this be changed using the algorithm?
Obtain feedback and let the algorithm evolve.

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