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Localization of Deep Abscesses with Radioactive Isotopes

An Experimental Study

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Life-endangering effects of deep abscesses make early and precise identification and localization important to permit adequate surgical drainage. An experiment was undertaken to study the feasibility of detecting abscesses by using leucocytes tagged with radioactive isotopes. For the labeling, 51chromium appeared preferable to 131jodine or 99technetium. Leucocytes so labelled will concentrate sufficiently in abscesses to permit identification of abscesses by scintillation scanning. For clinical application, techniques require further simplification and refinement to eliminate interference by collection of radioactive isotopes in the liver and spleen.

HE precise identification and localization of abscesses in deep-seated locations, particularly in the peritoneal cavity and retroperitoneal regions, is critical for early, direct and adequate surgical drainage. Patients with abscesses in these locations are seriously ill and require surgical drainage with minimal operative trauma to save their lives. Sawyer and associates¹ report a 43% mortality for retroperitoneal abscesses.

We undertook a study to localize deep abscesses experimentally by using leucocytes tagged with radioactive materials which would be identified by scintillation scanning. Efforts consisted of the development of a reliable technique for the experimental production of abscesses, in vitro manipulations to incorporate radioactive isotopes in viable leucocytes, and finally determining practical techniques to identify the abscesses by means of tagged leucocytes. We found it possible to detect abscesses by these techniques, but their localization is not sufficiently precise, and the procedures are too cumbersome to permit their clinical use at this time.

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We used three materials to produce abscesses in dogs: 5% phenol solution,

Allen, Berguer, DuSault and Block

suspensions of coagulase positive staphylococcus organisms, and suspensions of feces. The concentration of the staphylococcus aureus organisms was 1 x 108 per cubic millimeter. The phenol solution and staphylococcus suspension were injected into the animals subcutaneously in 1 cc volumes. Success was inconsistent. Quite frequently the injection of phenol will produce a local burn which is resolved with scar formation unless it became secondarily infected. There was also an inconsistent response to the production of abscesses with staphylococcus organisms. This was probably related to the fact that some of the animals, when initially brought to the hospital laboratory, were routinely treated with high doses of penicillin, and no abscess would be produced. On the other hand, certain animals - in a debilitated state with respiratory infection — would develop an overwhelming sepsis with the injection of staphyloccus. They would succumb within 48 hours before a well demarcated abscess could develop. Our greatest success was with the suspension of dog feces. This was placed in a gelatin capsule with a small amount of USP barium sulfate in order to serve as a radio-opaque marker for the implantation site. The dog was anesthetized and the left lower quadrant was shaved and prepared with merthiolate. A 15 mm transverse skin incision was made over the left lower quadrant. The external oblique muscle was opened and the capsule implanted between the external and internal oblique muscles of the abdominal wall. The defect in the muscles was closed with fine catgut suture, as was the skin. Invariably, within 48 hours, an area of abscess and surrounding cellulitis developed. If the abscess was left undrained or untreated, it frequently proved fatal within one week's time.

Labeling of Leucocytes with Radioactive Isotopes

One of our objectives was to achieve

a pure collection of autogenous leucocytes which could be labeled by uptake of a radioactive isotope and yet retain a high degree of viability. Previous work in this area had obtained leucocyte preparation rich in viable leucocytes by the technique of a peritoneal lavage². We felt this method did not have application to human medical practice, and it was discarded. Other workers made white blood cell enriched preparations with sedimentation of anticoagulated whole blood and progressive centrifugation to separate the buffy coat3. While this method produces a high white blood cell count, its main drawback is again the many residual red cells in the preparation. With the aid of Dr. Hajime Hayashi of the Department of Pathology, we employed a technique similar to the last described. In addition, an effort was made to remove the high number of red blood cells remaining in the preparation.

The procedure ultimately developed for production of leucocytes requires the removal of 120 cc of whole blood from the dog with the abscess. The blood is divided into 20 cc aliquots, each containing 1.5 cc of heparin (10,000 units per cc) and 2 cc of dextran solution (molecular weight approximately 200,000) for sedimentation of red blood cells. This sedimentation is permitted to occur for 30 minutes, after which the supernate, rich in white blood cells, is removed from each aliquot, and all are combined for centrifugation at 800 revolutions per minute for 5 minutes. This provides a button consisting of equal volumes of leucocytes and erythrocytes. This "red button" measures about 1.5 cc, and is resuspended in 2 cc of 9.5% saline at 4° C. Adding 5 cc of distilled water at 4° and agitating for 30 seconds lysed the erythrocytes in this collection. After adding 1.5 cc of 5% sodium chloride solution. the resulting suspension was centrifused for two minutes at 800 revolutions per minute. The supernatant fluid containing the hemolyzed red corpuscles is dis-

Localization of Deep Abscesses with Isotopes

carded, leaving a "white button" of leucocytes. These leucocytes are then resuspended in 20 cc of Hartman's solution and incubated in an agitator bath with the radioactive isotope at 37° C for 45 minutes. Following this, the leucocytes were washed in 9.5% saline usually for three times. The cells are resuspended in 20 cc of buffered Ringer's solution containing glucose, heparin and high molecular weight dextran. The level of radioactivity in the cell suspension is checked and the material is then injected intravenously for localization of an abscess in the dog.

We found that a number of radioactive isotopes will concentrate in leucocytes. The percent uptake by leucocytes depended in part upon the washings carried out after incubations. Uptakes obtained were 4-12% for ⁹⁹Te, 2-21% for ¹³¹I and 2-6% for ⁵¹Cr.

The technique for preparing leucocytes has yielded approximately 60% viable cells in final suspension. Viability was judged by cell motility and pseudopod formation and moist slide preparations, appearance of morphology on Wright stained smears, and by the ability to incorporate vital stains. This percentage of viability is somewhat lower than reported by other authors, and probably is indicative of the cell trauma of the many manipulations performed.

Serious disadvantages are inherent with all of the radioactive isotopes used to label leucocytes. The associated labeling of protein by ¹³¹iodine resulted in interference due to collection of the isotope in the spleen and liver. The short half-life (approximately 6 hours) of ⁹⁹technetium, given as technetium 99m pertechnetate, is clinically advantageous by permitting higher concentrations and safety. However, this time interval is too short for the procedures used in this study. Also, since these isotopes appar-

ently function as intracellular rather than membrane tags, labeled cellular debris as well as free isotopes are caught by the reticuloendothelial system, producing unwanted visualization of the spleen and liver. The use of 99technetium-labeled diethylamine penticillic acid, a chelating agent excreted only by the kidney. appeared promising. But, its rapid excretion prevented adequate concentrations in abscesses. The 51chromium concentrates well in leucocytes but has the disadvantageous characteristic of also concentrating in erythrocytes. It is essential to remove the supernatant protein material, as well as contaminating red blood corpuscles, from the labeled leucocytes.

Early in the study we found that the yield of white blood cells from the infected animals varied greatly. The average white cell count in the infected animals was 19,400 per cubic mm with a range of 7,200 to 31,000 per cubic mm. The white blood cell count in the cell suspensions that were reinjected into the animals averaged 3,300 per cubic mm with a range of 300 to 6,300 per cubic mm, in a total volume of 20 cc. This gives a projected total number of viable autogenous white corpuscles at approximately 6.3 x 108.

Concentration of Labeled Leucocytes in Abscesses

Initial exercises were performed using 300 microcuries of 51 Cr for labeling of autogenous leucocytes. These were injected intravenously into dogs with abscesses. Single crystal scintillation counter probes were placed over each of three sites: In the left lower extremity containing an experimental abscess, in the right lower extremity as a control, and in the heart as a measure of circulating isotope. The tracing of this information gave a qualitative estimate of the radioactivity in the three locations. The radioactive isotope did concentrate in

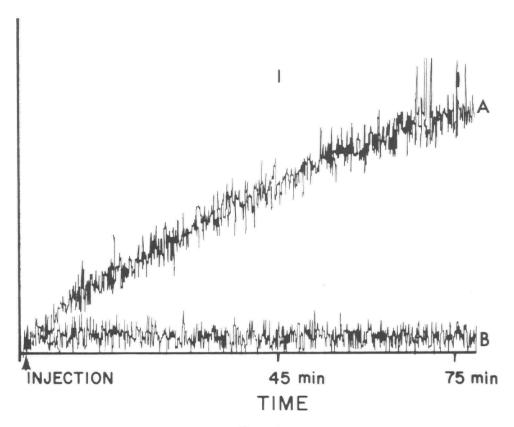


Figure 1
Tracing demonstrating increasing activity in abscess (A) and background activity (B).

the experimental abscesses. Activity present at 45 minutes following the injection was considerably different as compared with the peak of activity of the isotope in the abscess which occurred at approximately 75 minutes (Figure 1). The control probe remained at background levels of radioactivity.

A total of 57 animals was prepared subsequently and studied in greater detail using varying techniques. The scans of abscesses were made at intervals using a 5-inch Picker color scan or a Dynapix scintillation scanner. Table 1 shows the various isotopes and number of animals used in each group. The last column depicts the percentage of success with each isotope. We had the greatest number of runs using ¹³¹I, and here our success rate was the poorest. Because this was the initial isotope used, many failures were related to our gaining skill

Table I

ISOTOPE	NUMBER OF DOGS	ABSCESS IDENTIFIED	PERCENTAGE SUCCESS RATE
⁵¹ Cr	19	15	78%
131	27	5	18%
⁹⁹ Te	6	2	33%
DPTA	3	1	33%

Localization of Deep Abscesses with Isotopes

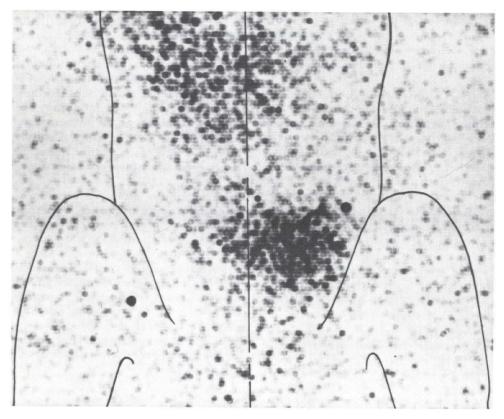


Figure 2
Abdominal scan of dog with concentration of isotope in left lower quadrant abscess, and activity in liver area.

in the manipulation of the cells. Other failures were also related to the poor abscess development in the animal, and to equipment breakdown. Thus, percentages shown in the table do not quantitate the desirability of choice of a given isotope. Although our criteria for success was the demonstration of the abscess on a scan, this is a subjective matter. We were able to produce a positive scan with each isotope at least one time. However, our greatest success and reproducibility came with the use of 51Cr (Figure 2). Advantages of this isotope are the ease of tagging the leucocytes and ready removal of the free 51Cr in solution with ascorbic acid, eliminating the need for repeated washing of the leucocytes. The

major disadvantages with the 51Cr is that the preparation must be totally free of red blood cells. Although lysis of red cells by distilled water was effective, it killed off some white blood cells. We postulated that these injured white cells and red cell envelopes secondarily tagged were removed by the reticuloendothelial system. Therefore, interference by a collection of the isotope in the liver and spleen was never entirely eliminated.

Our study demonstrated the feasibility of identification and localization of abscesses which are labeled by autogenous leucocytes, tagged with radioactive isotopes, and detected by scintillation scanning. However, the procedure lacks

Allen, Berguer, Du Sault and Block

facility for clinical use since interference by collection of the isotopes in major organs remains a problem, the procedure is cumbersome, and safety of the technique has not yet been established.

Others have utilized various techniques in experimental studies to achieve detection of deep abscesses. Labeling of protein by radioactive isotopes has not been sufficiently specific4. Winkelman and associates3 have demonstrated the efficacy of 51Cr labeled leucocytes in delineating experimental abscesses located in the extremities. Devsine and associates2 have harvested erythrocyte-free leucocytes from the peritoneal cavity experimentally in order to eliminate the problem of contamination by erythrocytes labeled with 51Cr. However, this technique does not appear to be applicable clinically.

Available radiologic techniques provide some aid in the detection of abscesses. These include liver scans, liver-lung scans, the use of subtraction scans, and the use of a variety of other multiple organ scans. Combinations of organ scans, arteriography, intravenous pyelograms, and standard radiologic studies of the gastrointestinal tract with radio-opaque media can provide diagnostic aid but are time-consuming and are frequently excessively rigorous for

critically ill patients. Although echograms are reportedly capable of identifying deep abscesses, we have found accuracy affected by the gas and fluid-containing gastrointestinal tract and confusion due to the similarity of interfaces of some tumors with those of abscesses. Furthermore, none of these techniques are specific for abscesses or inflammation. A technique is needed which positively identifies abscesses, rather than one which provides evidence for exclusion.

The abscesses produced experimentally were acute in nature. Whether leucocytes tagged with radioactive isotopes collect satisfactorily in chronic abscesses was not determined. Also, a comparison was not made between cellulitis and abscesses relative to the collection of labeled leucocytes. Other variables requiring study include the minimum size of an abscess to be detectable, number of labeled leucocytes needed for detection, and radiation safety factors.

Acknowledgments

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