January 27, 1984

Deborah A. Boyik
Nuclear Regulatory Commission
Office of Nuclear Regulatory Research
U.S. Nuclear Regulatory Commission
Washington, D.C. 20555

Dear Ms. Boyik:

Enclosed is a request that ^{99m}Tc-Pertechnetate be excepted from the requirements of 10 CFR Part 35, paragraph 35.14 (b) (6) for performance of Dacryocystography. This request is made pursuant to the Final Rule 10 CFR Part 35 as published in the Federal Register, v 48, No 25, Friday, February 4, 1983 pp. 5217. The request has been generated by various members of the American College of Nuclear Physicians. Your attention and help are appreciated.

Sincerely,

G. John Weir, Jr., M.D.
Vice-Chairman Government Affairs Committee
Liason, Nuclear Regulatory Commission

enclosure

cc: Ralph Robinson, M.D.
Schuyler Hilts, M.D.
Robert Henkin, M.D.
Carol Lively
Michael Payne

sjd

ACNP

American College of Nuclear Physicians

Suite 700
1101 Connecticut Avenue, N.W.
Washington, D.C. 20036
(202) 857-1135

REQUEST FOR THE USE OF
^{99m}Tc-PERTECHNETATE FOR
DACRYOCYSTOGRAPHY

REQUEST FOR THE USE OF ^{99m}Tc PERTECHNETATE
FOR DACRYOCYSTOGRAPHY

Table of Contents

REQUEST FOR THE USE OF 99mTc-PERTECHNETATE
FOR DACRYOCYSTOGRAPHY

I. General Information

A. Introductory Comments

This document represents a request for use of 99mTc-Pertechnetate as a diagnostic radiopharmaceutical drug product in patients for certain specific indications and presents specific dosage recommendations for each of these indications.

This request applies to all marketed sources of 99mTc-Pertechnetate that have an approved New Drug Application for other diagnostic purposes, e.g.: brain scan, blood flow studies, etc.

Evidence documenting the SAFETY of 99mTc-Pertechnetate in the performance of diagnostic tests known as Nuclear Dacryocystography includes:

1. The inclusion of this agent in the list of "well established use list" for radiopharmaceuticals (21 CFR Section 310.503) for more invasive use by the intravenous route for brain and other organ scannings.

2. The fact that this agent has been widely used in patients in all age groups for well over ten years without apparent safety problems.

3. No adverse reaction to any patient (adult or child) has been documented in the scientific literature or to the Adverse Reactions Registry of the Society of Nuclear Medicine.

4. Review of adequately controlled studies in scientific literature indicates not only absence of any adverse effect, but superiority over other non-nuclear medicine procedures

5. Radiation dosimetry estimation and calculation have shown that the absorbed radiation doses are within the accepted and conventional limits for diagnostic radiologic and nuclear medicine procedures. (See Appendix).

The evidence of EFFECTIVENESS of 99mTc-Pertechnetate for nuclear dacryocystography in patients of all ages is documented by:

1. The fact that this agent has been widely employed in patients of all ages with tearing problem (epiphora). There is virtually unanimous clinical acceptance of the diagnostic efficacy of the imaging procedures performed with 99mTcPertechnetate.

2. Review of the major scientific literature substantiating through adequately controlled clinical studies that the nuclear-dacryocystography is not only effective, but superior to other diagnostic modalities for the proposed indications.

The proposed DOSAGE RANGE for 99mTc-Pertechnetate is based on:

1. The scientific literature which specifically addresses the problem of the dose range to the critical organ, i.e.: the lens.

2. The review of the major scientific literature indicating that 99mTc-Pertechnetate when employed for these indications at doses within the ranges to be proposed is safe and effective.

3. Retrospective clinical studies indicating that images of satisfactory quality and statistical composition were obtainable in reasonable imaging times when doses within this range were employed.

B. Name of Drug

1. Generic: Technetium 99mTc-Pertechnetate

2. Trade: Pertechnetate Sodium Tc-99m and others

3. Chemical: Na 99mTc04 (Technetium 99m Sodium Pertechnetate)

C. Pharmacologic Category

Diagnostic Radiopharmaceutical Drug Product.

D. Proposed Indications

1. Nasolacrimal System Imaging

2. Functional Imaging of Tear Production and Drainage

E. Dosage Form and Route of Administration

Sterile solution of sodium-pertechnetate administered as eye drop.

F. Related Drugs

None

II. Manufacturing Controls

This information is available in the approved New Drug Applications for currently marketed productes. There are no known problems related to manufacturing which would preclude their use as eye drop.

III. Pharmacology

A. General Considerations

Following an administration of ^{99m}Tc-pertechnetate as eye drop, the agent mixes with tears within the conjunctival space. Within seconds to minutes it leaves the conjunctival space and through the naso-lacrimal drainage system it escapes into the inferior meatus of the nose. During this process the agent passes through the canaliculi, the lacrimal sac and the nasolacrimal duct. In the event of any pathological or functional blockage of the drainage system there will be a back flow resulting in tearing (epiphora), thereby the agent will escape from the conjunctival space by natural tearing process.

While the major part of the agent escapes within a few minutes by normal drainage and tearing, it has been documented that there is some degree of transconjunctival absorption with a fractional turnover rate of 0.015/minute in normal individuals, 0.021/minute in patients without any sac and 0.027/minute in patients with inflamed conjunctivia due to chronic dacryocystitis. Neglecting the relatively small trans-corneal route of disappearance, the values found for technetium dis-appearance could be regarded as representative for transconjunctival transport. The assumption was confirmed by correlating the activity in the blood with the fractional turnover rate. Nonetheless, the total maximum possible absorbed agent will remain below one thousandth of that used in other routine diagnostic procedure, e.g.: brain scanning.

As the study takes only a few minutes to be completed, at the termination of the study blowing the nose and washing the eyes with tap water has been found to clear 95% of the remaining radioactivity.

B. Radiation Dosimetry

Calculation of the radiation dose to lens for ^{99m}Tc-Pertechnetate in dacryocystography has been developed in some detail. The results indicate that the absorbed dose to the germinal epithelium of the lens is 2.2×10^{-5} to 1.4×10^{-4} rad/ Ci (5.9×10^{-12} to 3.8×10^{-11} Gy/Bq) of the agent under normal physiological conditions. With blockage of the lacrimal drainage apparatus, the dose to the lens could increase to 4×10^{-3} rad/ Ci (1×10^{-9} Gy/Bq). The detail method of calculation can be seen in the Appendix.

IV. Clinical Background

Technetium ^{99m}Tc-Pertechnetate has been widely employed for a number of years for brain, salivary gland, thyroid gland and other organ imaging. In addition to these indications, the safety and effectiveness of this agent has also been well demonstrated by its widespread utilization in clinical use for the diagnostic test of nuclear dacryocystography.

The following is a summary of selected literature reports documenting the safety and effectiveness of ^{99m}Tc-Pertechnetate as a diagnostic agent for radionuclide dacryocystography. These reports were selected since they provide the most comprehensive data and represent the most complete and best controlled studies from those available in the literature. Copies of these selected literature reports and additional listings of other published literature are provided in Appendix.

1. Carlton, W.H., Trueblood, J.H., Rossomondo, R.M.: Clinical evaluation of Microscintigraphy of the Lacrimal Drainage Apparatus. J. Nucl. Med. 14: 89-92, 1973.

Lacrimal drainage was studied by sequential imaging ("microscintigraphy") of the orbit after 99mTc was placed in the eyes of 62 patients. Specific criteria of normal drainage were developed from observations in 28 individuals. Thirty-four epiphoric patients in several categories of lacrimal drainage symptomology were studied. This technique of microscintigraphy of the lacrimal apparatus was shown to be a valuable diagnostic tool.

The gamma camera is a widely used diagnostic tool found in more than 1,000 hospitals in the United States. Technetium-99m is a relatively low-dose radioisotope and is extensively used. The development of the micropinhole collimator extends these tools for the use of the ophthalmologist. Microscintigraphy of the lacrimal drainage system is inexpensive, safe, and easy for a nuclear medicine department to perform without patient discomfort. Knowledge of the type of obstruction and location will help in the selection of the best mode of medical or surgical therapy. Microscintigraphy is valuable in assessing the results. Microscintigraphy is the technique of choice to evaluate the dynamics of normal lacrimal drainage. With this technique there is no sampling from the cul de sac and no instrumentation of the patient's canaliculi, thus essentially preserving the normal physiological state.

2. Chadhuri, T.D., Saparoff, G.R., Dolan, K.D., Chadhuri, T.K.: A Comparitave Study of Contrast Dacryocystogram and Nuclear Dacryocystogram. J. Nucl. Med. 16: 605-608, 1975.

A comparative study was run between conventional radiographic contrast dacryocystogram and radioisotope scan of the lacrimal drainage apparatus (henceforth called "nuclear dacryocystogram"). A total of 20 contrast dacryocystograms (DCG), 22 irrigations, and 42 nuclear dacryocystograms (DCG) were performed in 21 patients having symptoms of obstruction in the lacrimal drainage system. The study revealed that there was a good correlation between these two diagnostic techniques and nuclear DCG was, perhaps, superior to contrast DCG.

It has been concluded in this report that the nuclear DCG is superior to contrast DCG both in safety and efficacy because a) it is an atraumatic procedure since no catheterization of the duct is executed, b) it provides better diagnosis of functional and anatomic block, and c) it delivers far les radiation dose to the lens and anterior chamber (4-6 millirads compared to 200-300 milirads delivered from A-P skull X-ray).

3. Saparoff, G.R., Chadhuri, T.K., Chadhuri, T.D., Dolan, K.D., Christie, J.H.: Nuclear Lacrimal Scan vs Dacryocystography. Tr. Am. Acad. Ophth. & Oto. 81: 566-574, 1976.

The lacrimal drainage systems of 78 eyes were studied by technetium scanning at the University of Iowa and, of these, 25 were also subjected to conventional contrast dacryocystography. 26 eyes were asymptomatic for epiphora and normal scans were recorded on all of them. All of the remaining 52 symptomatic eyes had an abnormal lacrimal scan with either a presac or a postsac blockage. In general, there was good correlation with dacryocystography, with the exception of three cases of functional block which had a normal dacryocystogram. Technetium scanning should serve as a valuable tool for diagnosing and localizing lacrimal obstruction.

No adverse effect was noted in these studies. Efficacy over the other diagnostic modalities have been well documented.

4. Chaudhuri, T.K.: Nuclear Dacryocystography. Appl. Radiol. 4: 127-129, 1975.

Nuclear DCG has a good correlation with the conventional contrast DCG. The former is perhaps superior to the latter because of its several advantages: no trauma to the patient since no catheterization of the duct is executed; low radiation dose to the lens (4-6 mrad); and better diagnosis of functional and anatomic block. Nuclear DCG seems to be a reliable and accurate routine screening procedure to evaluate suspected lacrimal block.

No adverse effect was reported.

5. Chadhuri, T.D.: Technical Aspects of Nuclear Dacryocystography. Appl. Rad. 4: 184-187, 1975.

Realizing the widespread use of this diagnostic modality (Nuclear DCG) the author addressed the technical aspects in details with the following summary. "A satisfactory nuclear DCG requires the best possible magnification and resolution of different parts of LDA. For best magnification, the subject's eye must be positioned as close to the pinhole as possible. The best resolution is achieved by using the smallest possible pinhole. Improvising the use of an already existing pinhole collimator provides satisfactory magnification and resolution of LDA at economical cost."

6. Chadhuri, T.K.: Clinical Evaluation of Nuclear Dacryocystography. J. Clin. Nucl. Med. 1: 83-89, 1976.

Using 99mTc-sodium pertechnetate, the radionuclide dacryocystogram (DCG) was employed to help detect obstruction in the lacrimal drainage apparatus. A total of 100 nuclear DCG's were performed in 50 patients who were being studied because of epiphora (tearing). The nuclear DCG was compared to the conventional roentgenographic DCG or an irrigation study in each of these patients. The findings in this report indicate that nuclear DCG is a reliable and dependable method to diagnose and visualize obstruction in the lacrimal drainage apparatus.

A comparison was made between the contrast DCG (using X-ray) and the Nuclear DCG (using 99mTc-Pertechnetate) as follows:

Contrast DCG	Nuclear DCG
1. Traumatic	1. Atraumatic
2. Nonphysiologic test	2. Physiologic test
3. Detects anatomical site of block	3. May detect anatomical site of block
4. High radiation dose to the lens	4. Comparatively low radiation dose to the lens
5. Not applicable in immediate postoperative period	5. Applicable in immediate postoperative period

7. Chaudhuri, T.K.: A Versatile Way of Instilling 99mTc-Pertechnetate for Nuclear Dacryocystography. J. Nucl. Biol. Med. 20: 84, 1976.

   A micropipette system has been described with which one can get a broad spectrum of dose range to be administered as eye drops.

8. Blanksma, L.J., Schweitzer, N.M.J., Beekhuis, H., Piers, D.A.: Testing of Lacrimal Drainage With the Aid of a Gamma-Ray Emmitting Radiopharmaceutical (99mTc04). Docum. Ophth. 42,2: 381-384, 1977.

   99mTc04 is an excellent and harmless indicator in tests of the lacrimal drainage system. The detection instrument resolves the canaliculi, the valves in the lacrimal sac, and the anatomical results of a dacryocystorhinostomy. The pictures are more easily read and are obtained under more physiological conditions than those obtained with the ordinary X-rays, where a radio opaque solution is injected into the lacrimal sac. The latter method also causes more annoyance to the patient. The velocity with which the radioactive substance passes into the sac and from there into the nose appears to be a useable criterion to discern functional deficiencies.

   No adverse reaction has been reported.

9. Baron, J., Hyams, S.W., Schwartz, V.: Application of Nuclear Medicine in Ophthalmology. Docum. Ophth. 43, 1: 151-154, 1977.

   Diagnostic techniques using radioactive isotopes can be used for the investigation of cerebral, orbital, and intraocular tumors and for the dynamic study of tear flow. The value of such techniques in the study of obstruction of the nasolacrymal system (particularly partial and functional obstructions) has been established and the possibility of using Tc99m clearance fo the investigation of dry eyes is being investigated.

10. Amanat, L.A., Wraight, E.P., Watson, P.G., Hawkins, T.D.: Role of Lacrimal Scintigraphy and Subtraction Macrodacryocystography in the Management of Epiphora. Br. J. Ophth. 63: 511-519, 1979.

Fifty-one patients were investigated by subtraction macrodacryocystography (SMDCG, 103 systems) and by lacrimal scintigraphy (LS, 105 systems). It was found that these investigations complemented each other and between them the precise site of obstruction in the lacrimal drainage apparatus could be determined in 80%. The radiation dosage to the lens in SMDCG is significant, and it is therefore recommended that the patients with lacrimal obstruction should: a) have lacrimal puncta dilated with a probe to No. 1 diameter and be forcibly syringed; b) have lacrimal scintigraphy performed; c) if the site of the obstruction is still uncertain, then and only then should SMDCG be performed.

No adverse reaction was reported. The radiation dose to the lens in lacrimal scintigraphy depends to some extent on the degree of retention of tracer in the conjunctival sac. It is usually only a few millirads and does not exceed 20 millirads even in severe obstruction. In contrast the radiation in the area of the lens using the standard techniques of SMDCG, in which the tube distance is very short, is about 2 rads; 200 rads to the lens can produce cataractous changes. Because of this and of the ability of lacrimal scintigraphy to detect the majority of the obstruction, we would recommend that after syringing the tear duct lacrimal scintigraphy is performed. If doubt still remains as to the site of the obstruction, then and only then should macrodacryocystography be performed.

11. Sorensen, T., Jensen, F.T.: Lacrimal Pathology Evaluated by Dynamic Lacrimal Scintigraphy. Acta Ophth. 58: 597-607, 1980.

This study of pathological lacrimal systems demonstrated the usefulness and sensitivity of dynamic lacrimal scintigraphy (dynamic use of computer assisted gamma camera). The method was very sensitive; even small lacrimal obstructions caused a distinct change of the outflow curves. This technique complements other tests in lacrimal assessment especially in patients with epiphora and normal conventional tests.

No adverse reaction was reported.

V. Labelling Review

It is recommended that Technetium 99mTc-Pertechnetate be authorised for use to image the nasolacrimal drainage system.

A. Dosage and Administration

For Nuclear Dacryocystography the 99mTc-Pertechnetate is administered as eye drop. The suggested dose range is 100-250 uCi in one drop for each eye for patients of all ages.

B. Radiation Dosimetry

When used as an eye drop the results indicate that the absorged dose to the germinal epithelium of lens is 2.2×10^{-5} rad/uCi under physiological conditions. With blockage at the lacrimal drainage

apparatus, the dose to the lens could be increased to 4 X 10^{-3} rad/uCi. (See Appendix for details). Washing of eyes at the termination of study will reduce the radiation dose further.

VI. Overall evaulation and conclusions

The information presented in this request is submitted to document the safety and effectiveness of Technetium 99mTc-Pertechnetate when used for the indication of nasolacrimal drainage system imaging (dacryocystography). The evidence presented includes: 1) the fact that this U.S. Pharmacopoeia radiopharmaceutical drug product is included in the list of "well established" radiopharmaceuticals (21 CFR 310.503) for brain imaging, salivary gland imaging, placental localization and blood pool imaging; 2) the fact that this radiopharmaceutical drug product has been widely employed in patients with ophthalmologic disorders with tearing problem (epiphora) for well over ten years with general recognition in the medical community that it is safe and effective; 3) a detailed review of the adequately-controlled studies published in the scientific literature concerning the safety and effectiveness of this diagnostic procedure; and 4) radiation dosimetry studies which indicate that at the doses recommended, 99mTc-Pertechnetate is a satisfactory imaging agent for proposed indications.

It is opined that the evidence presented in this request clearly documents the safety and effectiveness of Technetium 99mTc-Pertechnetate for the use of dacryocystography. The conditions for its use are adequately described.

CLINICAL EVALUATION OF MICROSCINTIGRAPHY OF THE LACRIMAL DRAINAGE APPARATUS

William H. Carlton, Jon H. Trueblood, and Roger M. Rossomondo

Medical College of Georgia, Augusta, Georgia

Lacrimal drainage was studied by sequential imaging ("microscintigraphy") of the orbit after ^{99m}Tc was placed in the eyes of 62 patients. Specific criteria of normal drainage were developed from observations in 28 individuals. Thirty-four epiphoric patients in several categories of lacrimal drainage symptomology were studied. This technique of microscintigraphy of the lacrimal apparatus was shown to be a valuable diagnostic tool.

Many methods have been used to determine the patency of the lacrimal drainage apparatus in man, notably the fluorescein dye test by Jones (*1*), dacryocystography described by Campbell (*2*), Milder and Demorest (*3,4*), and Francois and Neetens (*5*), and the pressure transducer described by Callahan, Forbath, and Besser (*6*). Recently, Rossomondo, et al (*7*), have proposed a procedure called "microscintigraphy" in which a small drop of radioactive water is followed through the lacrimal drainage system with a gamma camera. This test involves no discomfort to the patient. Since the canaliculi are not instrumented and the radioactive material is suspended in a sterile, buffered, normal saline solution, the natural physiologic dynamics of the drainage system are maintained. The radiation dose to the lens of the eye is about 2% of that received in an anteroposterior radiograph. The purpose of this paper is to report on microscintigraphy as a clinical diagnostic tool in the study of the lacrimal drainage system.

MATERIALS AND METHODS

Approximately 100 μCi of ^{99m}Tc was placed in the eye in the form of a 15-μl drop. The patient was positioned in front of the gamma camera and recording was begun approximately 3 sec after the administration of the drop. Two-second exposure frames were recorded with a 35-mm camera for the first 20 sec and 40-sec exposure frames were recorded thereafter. After the first 5-min the patient was allowed to rest and was repositioned for each additional frame. The field of view of each scintiphoto was approximately from the middle of the cornea to the nasal midline.

NORMAL STUDIES

Normal subjects were asymptomatic volunteers with no history of lacrimal drainage problems. A total of 28 individuals, including 12 males and 16 females with ages ranging from 21 to 37, were studied.

Results of a typical normal study can be seen in Fig. 1. Selected frames from the dynamic 35-mm

Received Aug. 25, 1972; original accepted Sept. 25, 1972.

For reprints contact: William H. Carlton, Radiology Dept., Medical College of Georgia, Augusta, Ga. 30902.

FIG. 1. Normal study of right eye. A shows radioactive material distributed over eye primarily in palpebral fissure 4 sec after administration of drop. B shows radioactivity first seen entering sac at 10 sec. C shows radioactivity first seen at bottom of nasolacrimal duct at 16 sec. D shows complete lacrimal drainage system outlined at 43 sec.

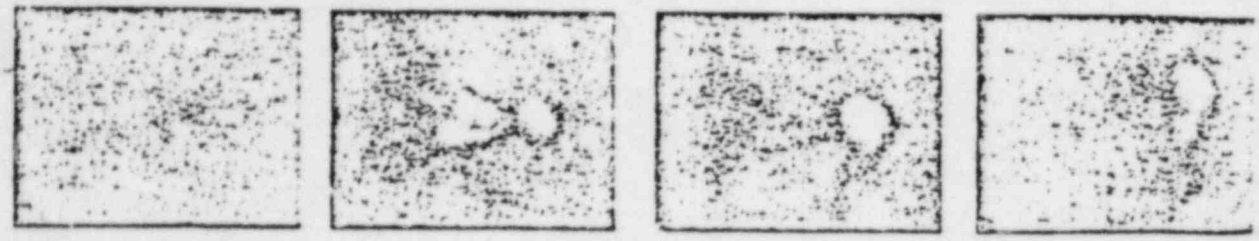

FIG. 2. Apparent obstruction of right eye. In A radioactivity is first seen entering sac at 12 sec. B shows sac filled out at 43 sec. At 3.5 min (C) duct begins filling. D shows radioactivity first seen at bottom of duct at approximately 10 min.

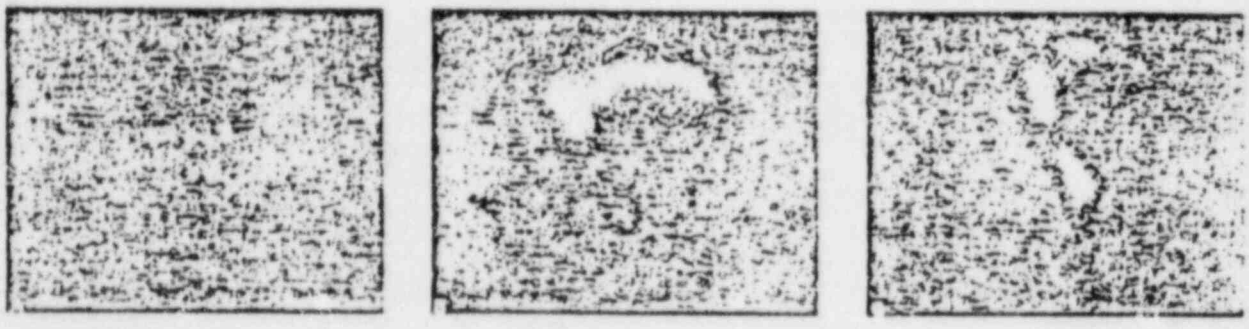

FIG. 3. Apparent obstruction of the left eye in 60-year-old woman with left eye pain and intermittent epiphora. In A radioactive material is first seen in sac at 14 sec. After 2 min (B), radioactive material is first seen at bottom of duct and first suggestion of filling defect in duct appears. C shows filling defect in midportion of nasolacrimal duct clearly seen at 4 min.

recording system are presented. After administration the radioactive material is seen to spread rapidly over the eye, collecting in the palpebral fissure (Fig. 1A). The next frame depicts the radioactive material first entering the lacrimal sac. The time of entry into the sac is one parameter which has been chosen in an attempt to quantify lacrimal drainage dynamics. The next frame shows radioactive material reaching the bottom of the nasolacrimal duct and serves as the second point of reference for measuring transit time. The last frame verifies anatomic definition and clearly illustrates the longer inferior and shorter superior canaliculi. The physiologic clear space previously reported by Rossomondo, et al (7) is clearly seen between the vertex of the canaliculi and the lacrimal sac. The straight nasolacrimal duct is also seen in detail. The increased density of the last frame results from a data collection time of 40 sec rather than the 2-sec exposure times used in the first three frames.

From these initial studies of normal subjects the median transit time from administration of the radioactive material until the material reached the lacrimal sac was determined to be 6 sec with a range from 4 to 43 sec. With the present technique it was not possible to measure a time of less than 4 sec. The median transit time to the bottom of the nasolacrimal duct was 43 sec with a range of 4 to 323 sec. In a future publication more extensive data using computer-assisted imaging and digital analysis will be presented.

ABNORMAL STUDIES

The abnormal patients studied were individuals with a history of clinically significant epiphora. The group of 34 people presented with a history of lacrimal drainage apparatus symptomatology and were arbitrarily divided into three categories: apparent obstruction, injury, and functioning and nonfunctioning post-dacryocystorhinostomies.

Apparent obstructions. Figure 2 shows a study of a 29-year-old white female with a several week history of intermittent epiphora associated with tenderness and swelling in the area of the right lacrimal fossa. This series of scintiphotos demonstrates an apparent obstruction in the area of the valve of Krause. The transit time to the sac is 12 sec. The nasolacrimal duct transit time is approximately 10 min which is considerably longer than the normal median.

Figure 3 shows a study of a 60-year-old black female with a 3-month history of vague left eye pain and intermittent epiphora. A filling defect in the midportion of the nasolacrimal duct is obvious. The sac transit time is 14 sec and the duct transit time is 2 min.

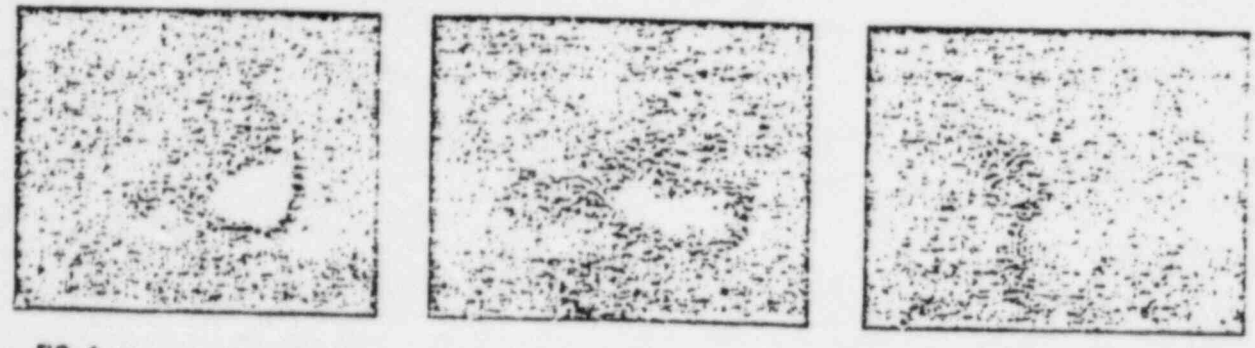

FIG. 4. Injury to medial portion of left lower lid. Radioactivity is first noted in sac after 43 sec (A). At 2 min superior canaliculus is outlined (B). Collection of radioactive material is seen in inferior lacrimal lake. C shows nasolacrimal duct is outlined after 1 hr. Radioactive material has been removed from lacrimal lake with absorbent paper.

Injury. Figure 4 is a study of a 26-year-old black male involved in an industrial accident resulting in the laceration of his left inferior canaliculus. The diagnosis was made by a slit lamp examination. Microscintigraphy done 2 hr post-trauma showed a sac transit time of 43 sec and a duct transit time of approximately 1 hr. The 3-min frame demonstrates a pooling of the radioactive material in the inferior lacrimal lake. The superior canaliculus is clearly outlined but the inferior cannot be visualized.

Post dacryocystorhinostomies. Figure 5 is a study of a 27-year-old white female with a history of chronic dacryocystitis necessitating a left dacryocystorhinostomy for epiphora 3 years before the present study. The patient has not had difficulty with epiphora since the operation. The 6-min frame demonstrates the nasolacrimal duct filled to two thirds of its length. At approximately the midpoint of the duct the radioactive material egresses into the nasal cavity through the surgical ostium and is dissipated in the mucosal lining of the nasopharynx.

Figure 6 shows a study of a 29-year-old black male who had a dacryocystorhinostomy for epiphora 12 years before the present study. Epiphora had persisted during the interval and presently is a major complaint. Figure 6A shows that the radioactive material has collected in the sac but has not progressed down the nasolacrimal duct nor through the surgical ostium. Figure 6B shows no additional progression of the radioactive material after 1½ hr, thus substantiating the clinical impression of a nonfunctioning dacryocystorhinostomy.

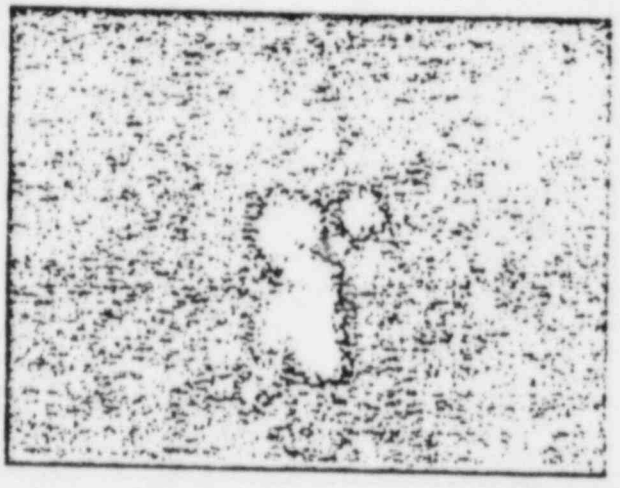

FIG. 5. Post-dacryocystorhinostomy of left eye. Patency of surgical ostium is demonstrated with dissipation of radioactive material onto mucosal lining of nasopharynx. Radioactive material egresses from medial aspect of middle of duct.

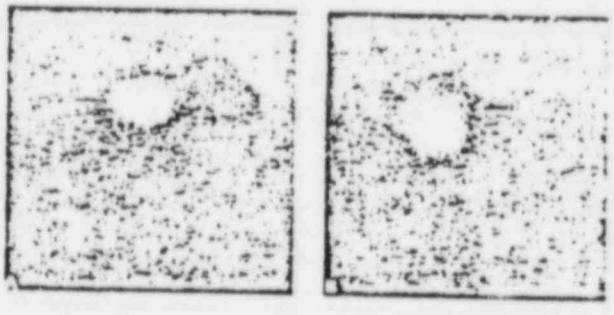

FIG. 6. Post-dacryocystorhinostomy of left eye. Radioactive material enters sac through well outlined canaliculi at 1 min (A). B shows that sac remains filled with no evidence of progression through surgical ostium or down nasolacrimal duct at 90 min.

ASYMPTOMATIC VARIANT

Figure 7 shows a study of an asymptomatic, 22-year-old white female with an entirely negative ophthamologic history and physical examination. The radioactive material rapidly entered the sac in 4 sec and progressed in a counter-clockwise direction forming an unusual C-configuration. Figure 7D shows the sac and canaliculi to be clearly outlined. Figure 7E shows the nasolacrimal apparatus completely outlined. This interesting configuration is thought to represent a congenital variant.

COMMENTS

The gamma camera is a widely used diagnostic tool found in more than 1,000 hospitals in the

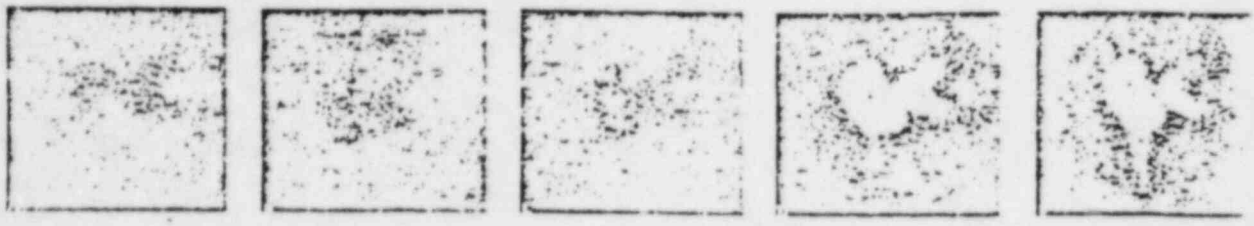

FIG. 7. Asymptomatic variant left eye. In A, B and C radioactive material is seen rapidly entering sac and progressing in counterclockwise direction at 4, 6, and 8 sec. In D canaliculi and sac are well outlined at 40 sec. At 2.5 min (E) nasolacrimal apparatus is completely outlined. Interesting configuration is thought to represent congenital variant.

United States. Technetium-99m is a relatively low-dose radioisotope and is extensively used. The development of the micropinhole collimator extends these tools for the use of the ophthalmologist. Microscintigraphy of the lacrimal drainage system is inexpensive, safe, and easy for a nuclear medicine department to perform without patient discomfort. Knowledge of the type of obstruction and location will help in the selection of the best mode of medical or surgical therapy. Microscintigraphy is valuable in assessing the results.

Microscintigraphy is the technique of choice to evaluate the dynamics of normal lacrimal drainage. With this technique there is no sampling from the cul de sac and no instrumentation of the patient's canaliculi, thus essentially preserving the normal physiological state.

ACKNOWLEDGMENTS

We wish to thank Dave Rigby for his help in the preparation of this manuscript. We also wish to thank Mark Brown and Louis A. Wilson for their valuable criticisms and suggestions.

REFERENCES

1. JONES LT, BOYDEN GL: *Oculoryngology*. Hagerstown MD Prior, 1955, pp 5–28

2. CAMPBELL W: The radiology of the lacrimal system. *Brit J Radiol* 37: 1–26, 1964

3. MILDER B, DESMOREST BH: Dacryocystography. I. The normal lacrimal apparatus. *Arch Ophthal* 51: 180–195, 195

4. DESMOREST BH, MILDER B: Dacryocystography. I The pathologic lacrimal apparatus. *Arch Ophthal* 54: 410 421, 1955

5. FRANCOIS J, NEETENS A: Dacryocystographie. *Ar Ocul(Paris)* 200: 778–785, 196

6. CALLIAN WP, FORBATH PG, BESSER WDS: A meth of determining the patency of the nasolacrimal apparatu *Amer J Ophthal* 60: 476–481, 1965

7. ROSSOMONDO RM, CARLTON WH, TRUEBLOOD, et a A new method of evaluating lacrimal drainage. *Arch Op to be published*

A COMPARATIVE STUDY OF CONTRAST DACRYOCYSTOGRAM AND NUCLEAR DACRYOCYSTOGRAM

Tapan K. Chaudhuri, Gerald R. Saparoff, Kenneth D. Dolan, and Tuhin K. Chaudhuri

Eastern Virginia Medical School and V.A. Hospital, Hampton, Virginia and University of Iowa Hospital, Iowa City, Iowa

A comparative study was run between conventional radiographic contrast dacryocystogram and radioisotope scan of the lacrimal drainage apparatus (henceforth called "nuclear dacryocystogram"). A total of 20 contrast dacryocystograms (DCG), 22 irrigations, and 42 nuclear dacryocystograms (DCG) were performed in 21 patients having symptoms of obstruction in the lacrimal drainage system. The study revealed that there was a good correlation between these two diagnostic techniques and nuclear DCG was, perhaps, superior to contrast DCG.

The conventional radiographic procedure called dacryocystography (*1*) is at present the technique of choice for evaluating obstruction in the lacrimal drainage apparatus. The purpose of this paper is to present a comparative study of contrast dacryocystogram (DCG) and a recently introduced radioisotope or nuclear dacryocystogram (DCG) in order to assess the diagnostic accuracy of the latter procedure.

MATERIALS AND METHODS

A total of 21 patients having symptoms of blockage in the lacrimal drainage apparatus were studied using both contrast and nuclear DCGs. All patients had nuclear studies bilaterally, a majority of them had had unilateral contrast studies with a few having bilateral contrast studies, and a small group had no contrast studies but had irrigation tests instead. Thus, a total of 20 contrast DCGs and 42 nuclear DCGs were performed in this group of patients.

About 200 μCi of ^{99m}Tc-pertechnetate in 0.01–0.05 ml sterile normal saline vehicle was used as an eye drop for each eye and the patient was immediately positioned upright in front of a scintillation camera face (Fig. 1). Care was taken not to spill technetium outside the eye because of resulting artifacts in the scintiscan. The collimator used in this study was a 0.04-in. diam pinhole. This helps in getting higher magnification and resolution of the different parts of the lacrimal drainage system such as the canaliculi, the sac, and the nasolacrimal duct. Patients were properly positioned so that their eyes were at the level of the pinhole. The distance between the pinhole and the patient's eye varied between 0.5 to 3 in. depending on whether or not one or both eyes were scanned. Following instillation of the radioisotope in the conjunctival sac, the patients' eyes were scanned sequentially at 0, 5, 10, and 15 min after instillation. Both Polaroid and conventional x-ray films were exposed. At the end of the study, both contrast and nuclear studies were read independently by different physicians unbiased by the other study.

FIG. 1. Position of patient for nuclear dacryocystography. (A) Collimator base; (B) pinhole insert.

Received Dec. 17, 1974; revision accepted Jan. 30, 1975.

For reprints contact: Tapan K. Chaudhuri, Nuclear Medicine, Eastern Virginia Medical School and V.A. Center, Hampton, Va. 23667.

Reprinted from the JOURNAL OF NUCLEAR MEDICINE, July, 1975, Volume 16, Number 7, Pages 605-608.

FIG. 2. Anterior nuclear DCG on left eye showing normal flow. Note visualization of sac in immediate scan and duct in subsequent scans.

FIG. 3. (A) Contrast DCG showing obstruction (horizontal arrow) on right eye distal to dilated sac. (Curved arrow points to contrast dye along lid margin.) (B) Nuclear DCG reveals no flow on right eye distal to sac up to 15 min. Note normal drainage on left eye (C) at same time.

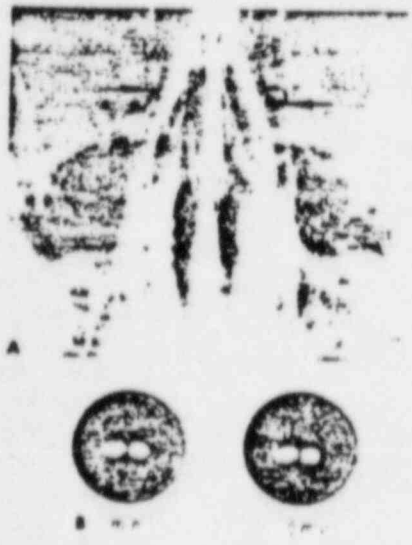

FIG. 4. (A) Contrast DCG discloses no flow of dye distal (arrows) to sac bilaterally. (B) Anterior nuclear DCG also demonstrates no activity distal to sacs bilaterally.

RESULTS

Twelve studies demonstrated obstruction in the lacrimal drainage system in both contrast DCG and nuclear DCG. Seven had unilateral obstruction; five had bilateral obstruction. Five patients underwent dacryocystorhinostomy (DCR) and a postoperative scan was also obtained in this group of patients. Studies on three of them demonstrated patency of dacryocystorhinostomy while in two other patients, postoperative DCG still revealed "no flow" indicating an unsuccessful operation which fitted well with the results of the fluorescein dye test. Two studies were normal in contrast DCG and irrigation but abnormal in nuclear DCG (functional block). Two studies demonstrated anatomic discontinuity of canaliculus.

We will illustrate studies of one patient from each group. Figure 2 represents a case with normal nuclear DCG on left eye. Figure 3A, B, and C shows obstruction on the right eye demonstrated in both studies. Figure 4A and B depicts bilateral obstruction demonstrated in both contrast and isotope studies. Figure 5 is the study of a patient with functional block, i.e., normal contrast DCG but abnormal nuclear DCG on the left eye. Figure 6A represents the preoperative contrast study showing obstruction on the right eye distal to the sac. Figure 6B depicts the nuclear studies demonstrating "no flow" preoperatively and return of flow postoperatively indicating successful surgery. Figure 7 represents the postoperative scan of a patient who had DCR on the right eye. The scan demonstrates "no flow" on the right eye indicating unsuccessful surgery. This patient continued to have epiphora postoperatively and a fluorescein dye test also disclosed failure of surgery indicating good correlation with the isotope study. Figure 8 represents the scan of a patient who had complete transection of the right lower canaliculus due to laceration resulting from a dog bite. Note the ragged distribution of activity along the right lower canaliculus while the right upper canaliculus and the left upper and lower canaliculi have a smooth outline of activity.

DISCUSSION

The procedure commonly employed at present to diagnose blockage in the lacrimal drainage apparatus is radiographic contrast dacryocystography (DCG) (*1*). The major disadvantage of this technique, however, is that the study requires catheterization of the canaliculi thus traumatizing the patient.

More recently a radioisotopic method has been introduced (*2*). To date, however, there is no detail report in the literature of a comparative study between these two techniques to determine how they compare in diagnostic accuracy. We have made a

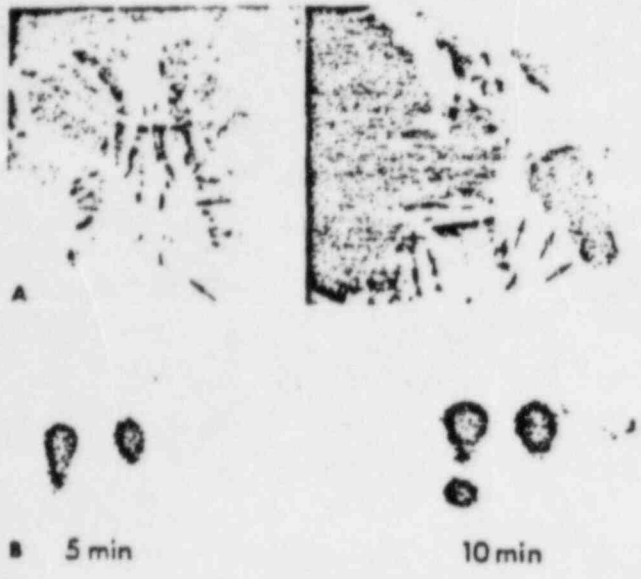

FIG. 5. (A) Contrast DCG (anteroposterior and lateral views) reveals normal flow of dye (arrows) on left eye. (B) Nuclear DCG shows block on left eye distal to sac. (Note, however, normal drainage on right eye.)

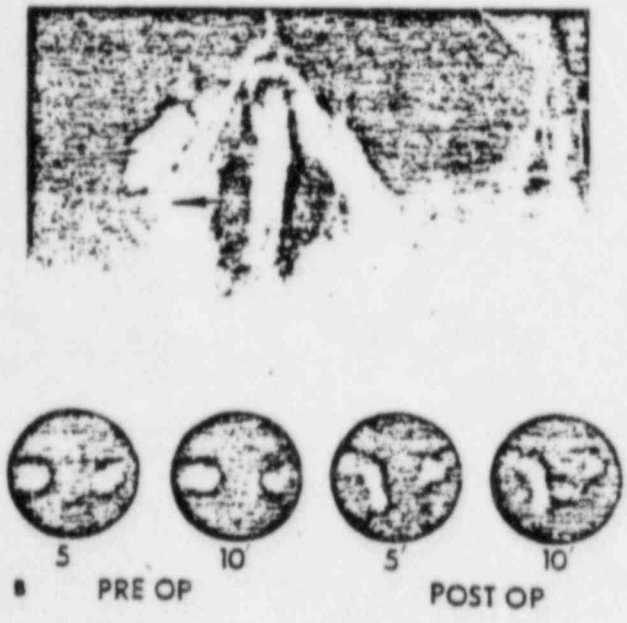

FIG. 6. (A) Preoperative contrast DCG showing obstruction distal (arrow) to dilated sac on right eye. Left eye also had symptoms of obstruction and positive irrigation test. (B) Nuclear DCG. Preoperative scans show bilateral obstruction distal to sac. Postoperative scans demonstrate successful operation.

comparative study of these two diagnostic tests and concluded that the isotope technique is superior to x-ray DCG.

We would like to propose a nomenclature for the radioisotope procedure—"nuclear dacryocystography" to conform with the style of naming other nuclear medicine procedures such as nuclear angiocardiography, nuclear venography, nuclear angiography, etc.

We used a conventional Searle Radiographics pinhole collimator with our specially designed and assembled (*3*) insert having an aperture diameter of 0.04 in. This way, one gets higher magnification and resolution of different parts of the lacrimal drainage system, namely the canaliculi, sac, and the nasolacrimal ducts.

It is difficult to determine the $T_{1/2}$ of tear drainage because it varies so much from one patient to another because of emotional factors, irritation to the eye, and the pre-existing conjuctivitis, etc. However, whatever the variables are, one should visualize activity in the nose within 8–10 min. More than 10 min indicates delayed drainage or blockage. We concluded this from our experience with 21 patients.

We observed a good correlation between these two techniques in all studies. In none of these cases did we observe abnormal contrast DCG but normal nuclear DCG. In two studies there was a discrepancy, namely, normal contrast DCG but abnormal nuclear DCG. The reason for this discrepancy is that the contrast DCG is performed under manual injection pressure while nuclear DCG is a physiologic study mimicking the normal state of tear drainage. With contrast DCG, normal and extreme pathologic obstruction can be demonstrated. In functional block, however, such as in abnormal "lacrimal pump" or partial stenosis of the nasolacrimal duct where the system irrigates freely but does not permit free passage of tears under normal circumstances, the nuclear DCG would be abnormal whereas the contrast DCG would be normal since the latter is performed with catheterization and under manual injection pressure. Thus, contrast DCG which employs direct catheterization of the canaliculi and injection under pressure could create a false passage or open up physiologic or anatomic blocks, thus erroneously implying nor-

FIG. 7. Post-DCR anterior scan of patient taken at 15 min shows unsuccessful operation on right. Patient still had symptom postoperatively. (Left eye demonstrates normal flow.)

FIG. 8. Anterior nuclear DCG at 5 min of patient who had complete transection of right lower canaliculus resulting from dog bite.

mality. Nuclear DCG should obviate both these problems.

The absorbed radiation dose to the lens in nuclear DCG would range from 4–6 mrads compared with 200–300 mrads delivered from an anteroposterior skull x-ray.

Nuclear DCG would also help the ophthalmologist decide whether or not dacryocystorhinostomy (DCR) should be performed in a patient with a suspected lacrimal block. Thus, DCR is indicated if nuclear DCG shows evidence of obstruction, if the system does not irrigate, and if the patient remains symptomatic.

A temporary block of the system by mucus plug, concretion, or other debris or a block due to anomalous valve of Krause or valve of Taillefer in the nasolacrimal duct would go undetected by either irrigation or contrast DCG. These types of anatomic block, however, can often be detected by nuclear DCG.

We, therefore, think nuclear DCG is superior to contrast DCG because (A) it is an atraumatic procedure since no catheterization of the duct is executed, (B) it provides better diagnosis of functional and anatomic block, and (C) it delivers smaller radiation dose to the lens and anterior chamber.

In conclusion, nuclear DCG should be a routine screening procedure to evaluate suspected lacrimal block preoperatively. A postoperative nuclear DCG would also be a valuable tool in assessing the success of DCR.

ACKNOWLEDGMENT

The authors wish to thank Paula S. Fyne and Darlene Marshall for typing the manuscript. Thanks are also due to Larry C. Gaskins and I. W. Reeves for their help with the photography.

REFERENCES

1. PETTIT TH, COIN CG: Dacryocystography. *Radiol Clin North Am* 10: 129–142, 1972

2. CARLTON WH, TRUEBLOOD JH, ROSSOMONDO RM: Clinical evaluation of microscintigraphy of the lacrimal drainage apparatus. *J Nucl Med* 14: 89–92, 1973

3. CHAUDHURI TK: Technical aspects of nuclear dacryocystography. Unpublished.

Nuclear Dacryocystography

TAPAN K. CHAUDHURI

Nuclear physicians are at present frequently called upon by ophthalmologists and plastic surgeons to diagnose and define the site of obstruction in the lacrimal drainage apparatus (LDA). Thus the scintiscanning of LDA (nuclear dacryocystography) is becoming more popular as a simple and reliable diagnostic tool for the diagnosis of blockage in LDA. Scintiscans of several varieties of blocks are illustrated to demonstrate the usefulness of this nuclear medicine procedure.

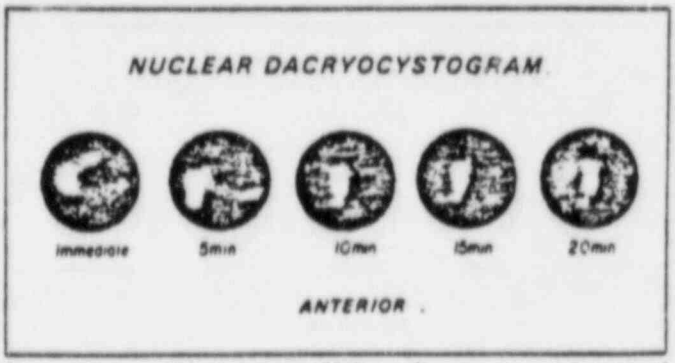

Figure 1: Sequential scintigrams of left eye showing normal drainage of radioactive tear. One can visualize the sac in the immediate scan, and the proximal duct in 5-min scan. At 10-min scan, the radioactivity is seen in the inferior meatus of the nose.

REPRINTED FROM APPLIED RADIOLOGY/NUCLEAR MEDICINE MAY/JUNE 1975

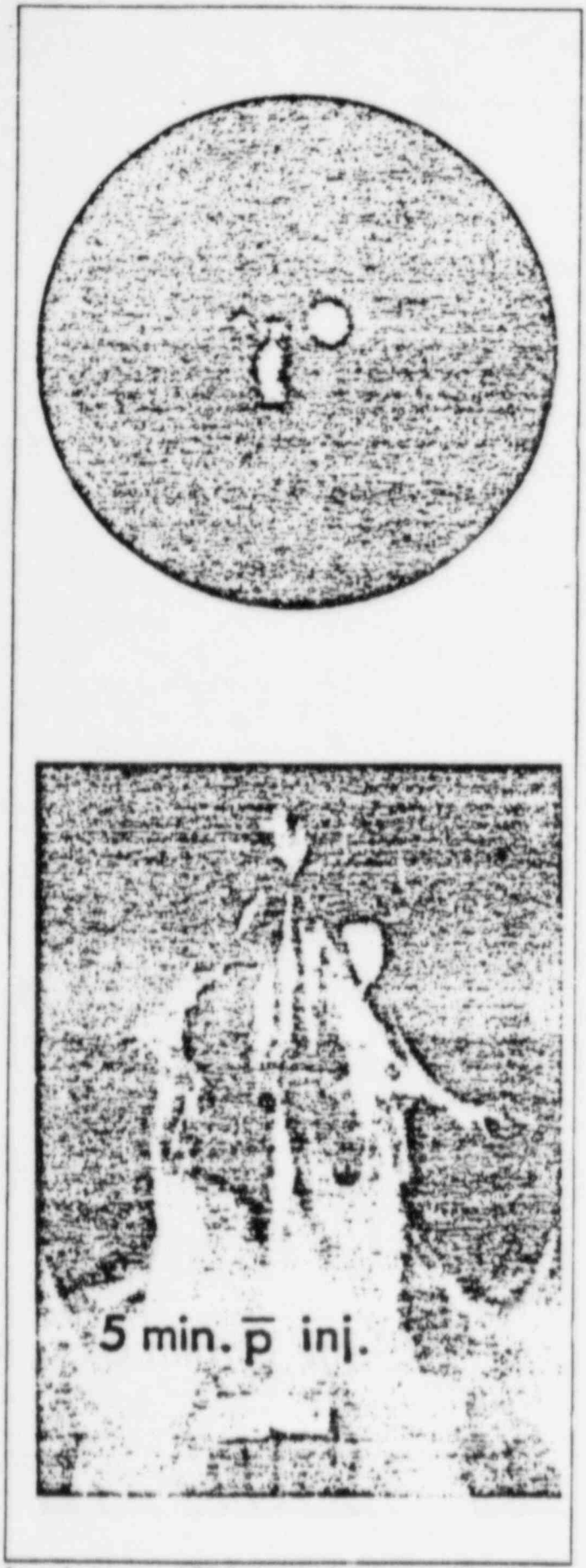

Figure 2: a) Nuclear DCG (both eyes) showing normal flow OD and block OS distal to the sac. b) Contrast DCG of the same patient also showing block distal to the sac (OS).

A total of 25 patients with symptoms of epiphora were referred by ophthalmologists and plastic surgeons to our nuclear medicine laboratory for performing nuclear dacryocystography (DCG). All patients had nuclear studies (a total pf 50 nuclear DCGs) bilaterally, and a majority had simultaneous correlation with conventional radiographic contrast DCG. All nuclear DCGs were performed with ^{99m}Tc-pertechnetate and a gamma camera using a 0.04-in.-diameter pinhole collimator. About 200 μCi of ^{99m}Tc-pertechnetate in 0.01 ml eluate was instilled in the conjunctival sac after upright positioning of the patient in front of the gamma camera face so that the eyes were at the level of the pinhole. Sequential scintiphotos were obtained either in Polaroids or in x-ray films. The conventional radiographic contrast DCGs were performed using standard technique.

Only a few studies revealed normal flow; the majority had abnormal studies which fell into the following categories: (1) unilateral block; and (2) bilateral block. The most common site of block was at the sac-duct junction. Only one typical example from each group is shown here as an illustrative case.

Figure 1 represents a normal study (OS). Figure 2a demonstrates a block on OS (distal to the sac) which correlates well with the contrast DCG (Figure 2b). Figure 3a depicts the nuclear DCG of a patient with bilateral block distal to the sacs. Figure 3b shows the same patient's contrast DCG, also revealing bilateral block distal to the sac.

Discussion

One of the most common causes of epiphora (tearing) is blockage in LDA. The presently available techniques to diagnose an obstruction in LDA are: (1) irrigation; (2) fluorescein dye test; (3) sodium saccharin test; and (4) dacryocystography. All of these procedures have one or more drawbacks.

The idea of contrast DCG had its roots in a study by Ewing,[1] who first used a suspension of bismuth subnitrate to demonstrate lacrimal abscess cavity. Milder and Demorest[2,3] later laid down the techniques and interpretation of normal and abnormal dacryocystograms. More recently, Pettit and Coin[4] made a vivid review of this radingraphic procedure for the diagnosis of lacrimal block. However, this study is traumatic to the patient, and pressure injection of the contrast dye may lead to tissue extravasation, possible iodine hypersensitivity and nonfunctioning atonic sac. Finally, the test is not physiologic, and the absorbed radiation dose to the lens (target organ) is high (300-400 mrads per AP skull film).

Rossomondo *et al.*[5] introduced a physiologic technique (lacrimal microscintigraphy) for studying LDA. Later on, Chaudhuri *et al.*[6] ran a comparative study between conventional radiographic DCG and radioisotope DCG. They also coined the term "nuclear dacryocystography."

This new procedure not only has the value of preoperative diagnosis of lacrimal block, but also is a useful tool in assessing the success of surgery (dacryocystorhinostomy, etc.). The exact definition of the site of block by scintiscan also helps the surgeon to select the type of surgery (Jones tube, Canaliculorhinostomy, dacryocystorhinostomy, etc.) to be performed in the particular patient.

Temporary anatomical block of LDA, such as by mucus plug, concretion, debris, anomalous valve of Krause or Valve of Taillefer, would be missed by contrast DCG because the pressure injection would open up such blocks; however, a nuclear DCG would detect such abnormalities. Moreover, a functional or physiologic block (e.g., malfunctioning of "lacrimal pump") would also go undetected by contrast DCG because this procedure bypasses the "lacrimal pump."

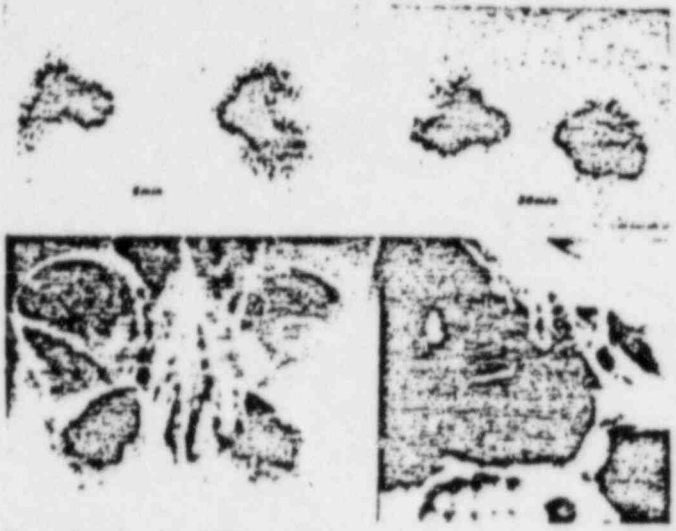

Figure 3: a) Nuclear DCG reveals bilateral block distal to the sac even up to 30 min. b) Contrast DCG (AP and left lateral views) demonstrate no flow of the dye distal to the sacs bilaterally.

Summary

Nuclear DCG has a good correlation with the conventional contrast DCG. The former is perhaps superior to the latter because of its several advantages: (a) no trauma to the patient since no catheterization of the duct is executed; (b) low radiation dose to the lens (4-6 mrad); and (c) better diagnosis of functional and anatomic block.[7] Nuclear DCG seems to be a reliable and accurate routine screening procedure to evaluate suspected lacrimal block.

Acknowledgment

The author wishes to thank Mrs. Paula S. Fyne for typing the manuscript. Thanks are also due to Mr. Larry C. Gaskins and Mr. I.W. Reeves for their help in photography.

References

1. A.E. Ewing, "Roentgen Ray Demonstrations of the Lacrimal Abscess Cavity," *Amer. J. Ophth.*, Vol. 26, 1909, pp. 1-4
2. B. Milder and B.H. Demorest, "Dacryocystography: I. The Normal Lacrimal Apparatus," *Arch. Ophth.*, Vol. 51, 1954, pp. 180-195
3. B.H. Demorest and B. Milder, "Dacryocystography: II. The Pathologic Lacrimal Apparatus," *Arch. Ophth.*, Vol. 54, 1955, pp. 410-421
4. T.H. Pettit and C.G. Coin, "Dacryocystography," *Radiol. Clinic of N. Amer.*, Vol. 10, 1972, pp. 129-142
5. R.M. Rossomondo, W.H. Carlton, J.H. Trueblood, *et al.*, "A New Method of Evaluating Lacrimal Drainage," *Arch. Ophth.*, Vol. 88, 1972, pp. 523-525
6. T.K. Chaudhuri, G.R. Saparoff, K.D. Dolan, *et al.*, "A Comparative Study of Contrast Dacryocystogram and Nuclear Dacryocystogram," *J. Nucl. Med.*, Vol. 15, 1974, p. 482
7. T.K. Chaudhuri, "Nuclear Ophthalmology — Current Clinical Status and Future Direction," in *Current Concepts in Nuclear Medicine*, E. James Potchen, ed., St. Louis: C.V. Mosby Co., 1975

■

Tapan K. Chaudhuri, MD, is Associate Professor and Chief, Nuclear Medicine Section, Eastern Virginia Medical School and the Veterans Administration Center, Hampton, Va.

APPENDIX-1

BIBLIOGRAPHY

Articles summarized in Section IV (Copies Included).

1. Carlton, W.H., Trueblood, J.H., Rossomondo, R.M.: Clinical Evaluation of Microscintigraphy of the Lacrimal Drainage Apparatus. J. Nucl. Med. 14: 89-92, 1973.

2. Chaudhuri, T.K., Saparoff, G.R., Dolan, K.D., Chaudhuri, T.K.: A Comparative Study of Contrast Dacryocystogram and Nuclear Dacryocystogram. J. Nucl. Med. 16: 605-608, 1975.

3. Saparoff, G.R., Chaudhuri, T.K., Chaudhuri, T.K, Dolan, K.D., Christie, J.H.: Nuclear Lacrimal Scan Vs Dacryocystography. Tr. Am. Acad. Ophth. & Oto. 81: 566-574, 1976.

4. Chaudhuri, T.K.: Nuclear Dacryocystography. Appl. Radiol. 4: 127-129, 1975.

5. Chaudhuri, T.K.: Technical Aspects of Nuclear Dacryocystography. Appl. Rad. 4: 184-187, 1975.

6. Chaudhuri, T.K.: Clinical Evaluation of Nuclear Dacryocystography. J. Clin. Nucl. Med. 1: 83-89, 1976.

7. Chaudhuri, T.K.: A Versatile Way of Instilling ^{99m}Tc-Pertechnetate for Nuclear Dacryocystography. J. Nucl. Biol. Med. 20: 84, 1976.

8. Blanksma, L.J., Schweitzer, N.M.J., Seekhuis, H., Piers, D.A.: Testing of Lacrimal Drainage With the Aid of a Gamma-Ray Emitting Radiopharmaceutical (^{99m}TcO4). Docum. Ophth. 42,2: 381-384, 1977.

9. Baron, J., Hyams, S.W., Schwartz, V.: Application of Nuclear Medicine in Ophthalmology. Docum. Ophth. 43,1: 151-154, 1977.

10. Amanat, L.A., Wraight, E.P., Watson, P.G., Hawkins, T.D.: Role of Lacrimal Scintigraphy and Subtraction Macrodacryocystography in the Management of Epiphora. Br. J. Ophth. 63: 511-519, 1979.

11. Sorensen, T., Jensen, F.T.: Lacrimal Pathology Evaluated by Dynamic Lacrimal Scintigraphy. Acta Ophth. 58: 597-607, 1980.

Articles not summarized.

Rossomondo, R.M., Carlton, W.H., Trueblood, J.H., Thomas, R.P.: A New Method of Evaluating Lacrimal Drainage. Arch. Ophth. 88: 523-525, 1977.

Chaudhuri, T.K.: Nuclear Ophthalmology: Current Clinical Status and Future Direction. Appl. Radio. 7: -, 1977.

Gabriel, I., Hernady, T. Follmann, P.: Experiences WithIsotope Diagnosis of the Lacrimal Ducts. Buch Augenarzt, 1981, (84) p30-4.

Von Denffer, H., Gullotta, U., Dressler, J.: Dacryocystography and Radionuclide Dacryocystography. Buch Augenarzt, 1981, (84) P19-29.

Pohjanpelto, P., Vorne, M., Vahatalo, S., Unto, E.: Gamma Imaging of the Lacrimal Apparatus. Duodecim, 1980, 96 (15) p1015-20.

Muto, P., Capuano, S., Criscuolo, A., DeRosa, C., Calabro, S., Salvatore, M.: Scintigraphy of the Lacrimal Ducts in Childhood. Radiol. Med., Nov, 1980, 66 (11) p839.

Tesler, Z., Friedman, L., Peisajovich, A., Siverman, C.,: Radioactive Dacryocystography. Harefuah, Jul, 1979, 97 (1-2) p4-5.

Sorensen, T., Jensen, F.T.,: Conjunctival Transport of Technetium-99m Pertechnetate. Acta Ophth., Aug, 1979, 57 (4) p691-9.

Robertson, J.S., Brown, M.L., Colvard, D.M.: Radiation Absorbed Dose to the Lens in Dacryoscintigraphy With 99mTcO4-. Radiology, Dec 1979, 133 (3 pt 1) p 747-50.

Laflamme, P., Lamoureux, J.: Isotopic Dacryocystography: A Technic Used in the Evaluation of the Function of Lacrimal Ducts. Un. Med. Can. 1978, 107 (1) p47-50.

Von Denffer, H., Dressler, J., Gullotta, U.: Comparative Nuclear Medical and Radiological Studies in Disorders of the Lacrimal Ducts. Ber Dtsch. Ophth. Ges., 1977, 74 p592-7.

Aflalo, G., Robert, J.: Isotope Examination of the Lacrimal Duct. Preliminary Study. Bull Soc. Opht. Fr., Jul-Aug, 1976, 76 (7-8) p611-4.

Denffer, H., Dressler, J.: Radionuclide Dacryography in Clinical Practice and Research. Klin Monatsbl Augen., Jul 1976, 169 (1) p66072.

Hurwitz, J.J., Welham, R.A., Maisey, M.N.: Intubation Macrodacryocystography and Quantitative Scintillography: the "Complete" Lacrimal Assessment. Trans Am. Acad. Ophth. Oto., Jul-Aug, 1976. 81 (4 pt 1) pOP575-82.

Pink, V., Gliem, H.: Examination of Function by Scintillography After Dacryocystorhinostomy. Klin Monatsbl Augen., Dec 1975, 167 (6) p830-5.

Meyer, P.B., Dausch, D.: Clinical Experiences With Radionuclide Dacryocystography. Klin Monatsbl Augen., Sep, 1975, 167 (3) p421-6.

Murai, Y.: Study of Tear Flow Using Radioactive Isotope. Acta Soc. Ophth., Oct, 1975, 79 (10) p1405-13.

Von Denffer, H., Dressler, J.: Radionuclide Dacryocystography for Demonstrating Obstructions of the Lacrimal Drainage Apparatus. Albrecht Von Graefes Arch. Klin Ophth., 1974, 191 (4) p321-8.

APPENDIX-2

RADIATION DOSIMETRY

Radiation Absorbed Dose to the Lens in Dacryoscintigraphy with $^{99m}TcO_4^-$ 1

James S. Robertson, M.D., Ph.D., Manuel L. Brown, M.D., and D. Michael Colvard, M.D.[2]

Calculations of the radiation dose to the lens for $^{99m}TcO_4^-$ in dacryoscintigraphy are developed in some detail. The results indicate that the absorbed dose to the germinal epithelium of the lens is 2.2×10^{-5} to 1.4×10^{-4} rad/μCi (5.9×10^{-12} to 3.8×10^{-11} Gy/Bq) $^{99m}TcO_4^-$ under physiological conditions. With blockage of the lacrimal drainage apparatus, the dose to the lens could increase to 1×10^{-3} rad/μCi (1×10^{-8} Gy/Bq).

INDEX TERMS: Diagnostic radiology, radiation dose • Dosimetry, radionuclide • Eyes • Lacrimal gland and duct, radionuclide studies, 2[23].1299 • Lens

Radiology 133:747–750, December 1979

A METHOD for using $^{99m}TcO_4^-$ ion in studies of the lacrimal drainage apparatus was introduced by Rossomondo *et al.* (1) and has been used by others (2–5). In this procedure a drop of 50 to 200 μCi (1.85 to 7.4 MBq) $^{99m}TcO_4^-$ is placed near the center of the cornea, after which lacrimal fluid flushes the tracer into the drainage system. Some of the anatomical relationships involved are shown in Figure 1A, and the distribution of radioactivity 1–5 minutes later is shown in Figure 1B. It has been stated that the radiation dose to the lens for this procedure is approximately 4 mrad (0.04 mGy) if a half-life of 1 minute is assumed (1) or simply (without stating the assumptions) as "approximately 10 millirads" (0.1 mGy) (2), but details of the dosimetry are not well documented. The following exposition addresses this problem.

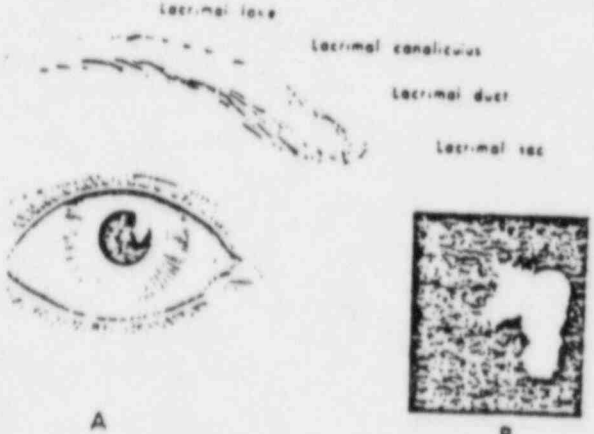

Fig. 1. A. Anatomical relationship of the lacrimal drainage apparatus and the eye.
B. Scintigram of the lacrimal drainage apparatus 1–5 minutes after administration of 100 μCi (3.7 MBq) $^{99m}TcO_4^-$ as a drop on the cornea.

ANATOMY AND PHYSIOLOGY

Charles and Brown (6) have given a detailed analysis of the shape and position of the lens in various states of accommodation and have reviewed data on the variations of several dimensions of the eye as a function of age. If data from Reference Man are used (7), the adult human eyeball is a spheroid having average sagittal, transverse, and vertical diameters of 24.4, 23.8, and 23.5 mm, respectively. The total weight of both eyes is 15 g. The cornea has the shape of a spherical segment with a surface area of 1.3 cm^2, a radius of curvature of 7.86 mm, and a specific gravity of 1.076. Its thickness is about 0.6 mm. The lens is a biconvex semisolid body with a specific gravity of 1.079–1.121. Its weight increases with age from an average of 153 mg at 10–20 years to 258 mg at 80–90 years. The anteroposterior diameter of the lens increases from 3.5 mm at 20 years to 4.2 mm at 80 years. Its transverse or equatorial diameter is 9–10 mm. (The dimensions vary slightly with visual accommodation.) The distance between the anterior poles of the lens and cornea varies between 3 and 4 mm. The germinal area of the lens, which seems to be the principal area involved in the production of cataracts by ionizing radiation (6, 8), is located in the anterior pre-equatorial region of the lens and in the adult lies 2–4 mm below the surface of the eye. The lens is avascular but has been shown to have metabolic activity associated with its epithelial layer (9, 10).

The radiation dose from radioactivity introduced into the tear system is strongly dependent on the turnover rate of the lacrimal fluid. This turnover rate and the rate of tear secretion have been studied by several methods including (*a*) the rate of fluorescein dye washout (11), (*b*) the rate of appearance and the concentration of desquamated cells (12), and (*c*) the rate of disappearance of the $^{99m}TcO_4^-$ ion

From the Nuclear Medicine Section (J.S.R., M.L.B.) and the Department of Ophthalmology (D.M.C.), Mayo Clinic/Foundation, Rochester, MN 55901. Presented at the Work-in-Progress Session of the Sixty-fourth Scientific Assembly and Annual Meeting of the Radiological Society of North America, Chicago, IL, Nov. 26–Dec. 1, 1978. Received May 15, 1979, and accepted June 5.
[2] Present address: 10192 North Coggins Dr., Sun City, AZ 85351.

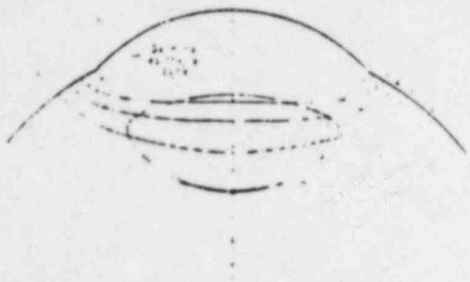

Fig. 2. Isodose contours intersecting the lens for 100 μCi (3.7 MBq) ^{99m}Tc uniformly distributed on the corneal surface are shown. The numbers at the right indicate the dose rates in mrad/min. The units used were chosen to relate the results to the activity level used in practice. The gradations on the optic axis indicate the distance from the corneal surface in millimeters.

(13). The average normal rate of tear flow is about 1.2 μl/min with a turnover rate of about 16%/min (11). However, slight stimuli produce appreciable changes so that the turnover rate may exceed 80%/min without being noticed by the subject and may readily exceed 100%/min. The turnover rate is decreased in certain disease states or as a physiological result of advanced age (14).

METHOD

The radiation absorbed dose is calculated by first determining a point-source dose-rate function, then integrating this function over the area or volume of distribution of the radiotracer, and multiplying by the residence time.

Dose-Rate Function

The ^{99m}Tc conversion electrons and Auger electrons have maximal ranges of less than 1 mm in water and so were disregarded for these calculations, since the sensitive area of the lens lies at least 2 mm from the surface of the cornea (6). Point-source dose-rate data using values of the specific absorbed fraction Φ based on Table 6 of MIRD Pamphlet No. 2 (15) and the dose-rate constant Δ, for ^{99m}Tc from MIRD Pamphlet No. 10 (16) were used. Within the distance range of interest, the absorbed dose rates are very closely fitted by the following equation, which will be used as the point-source dose-rate function:

$$\dot{D}(P, \text{point source}) = 0.0012A/s^2 \quad \text{rad/min} \qquad (1)$$

where $\dot{D}$ is the radiation absorbed dose rate in rad/min, P is the point of interest, A is activity in μCi, and s is the distance from the source to P in mm.

Dose Rates

The dose rate at any point of interest from ^{99m}Tc uniformly distributed in a thin layer, such as the lacrimal fluid on the surface of the eye, is obtained by substituting the areal concentration, A/S, for A in Equation 1 and integrating the resulting function over the area of distribution, S:

$$\dot{D}_P = 0.0012\,\frac{A}{S}\int_S \frac{dS}{s^2} \quad \text{rad/min} \qquad (2$$

Three distributions of the source activity will be considered.

1) ^{99m}Tc on the corneal surface (Fig. 2),
2) ^{99m}Tc in the lacrimal lake (Fig. 1), and
3) ^{99m}Tc in the lacrimal drainage apparatus (Fig. 1).

Since the cornea and the sclera both have spherical surfaces, although with different radii, the integrations for the first two phases were achieved by regarding these surfaces as spherical segments. The lacrimal drainage apparatus is far enough from the lens to be approximated as a disk source.

For the spherical segments, Equation 2 was integrated by taking the elements of surface area dS to be circles isodistant from the point of interest. The distance s, was expressed in terms of the sphere radius R, the distance of the point of interest from the center of the sphere αR, and the angle θ between the radius through the point of interest and the radius through the element of surface. Thus

$$s^2 = R^2(1 + \alpha^2 - 2\alpha\cos\theta) \quad \text{and}$$

$$dS = 2\pi R^2 \sin\theta\, d\theta$$

Integrating Equation 2 between the limits $\theta = 0$ and $\theta = \psi'$ leads to the expression:

$$\dot{D}_P = \frac{0.0012A}{\alpha R^2(1-\cos\psi')}\log_e\left[\frac{s(\psi')}{s(0)}\right] \quad \text{rad/min} \qquad (3$$

where the notation $s(\psi')$ indicates the distance s when θ equals the upper limit ψ', and $s(0)$ indicates the distance s when $\theta = 0$. This expression may be compared with that for the dose rate along the axis of a disk source (17,18):

$$\dot{D}_P = \frac{0.0012A}{r^2}\log_e\frac{r^2+h^2}{h^2} \quad \text{rad/min} \qquad (4$$

where r is the radius of the disk ($r = R\sin\psi'$) and h the distance from P to the center of the disk. For comparison with the spherical segment formula, note that $(r^2 + h^2) = s(\psi')^2$, but $s(0) > h$. For off-axis points, the use of the disk approximation permits use of the further simplification that the isodose curves are ellipses with their foci at the ends of the disk's diameter (17).

Returning to the spherical segment source, for those values of θ that cause the isodistant circles to intersect the boundary of the segment, the integration using $2\pi R$ becomes inappropriate. Instead, the circular arc $2\Psi' R$ was used, where Ψ' is a solid angle derived by using the cosine law for spherical triangles and which expresses the arc subtended within the segment boundary. For these cases, Equation 2 is not readily integrated in closed form, and numerical integration was used. Incremental values of θ

qual to 0.02, 0.05, or 0.1 radian were selected as needed achieve three-place accuracy.

Dose Rates from ^{99m}Tc on the Cornea: For these alculations the values R = 7.9 mm, S = 130 mm^2, and = 46° (0.84 radian) were used. Figure 2 shows the ose curves for this phase superimposed on a drawing the horizontal section through the eye. For ^{99m}Tc uniformly distributed on the corneal surface, the dose rates the lens range between 2 × 10^{-5} and 5 × 10^{-5} rad/Ci·min) (5 × 10^{-12} to 14 × 10^{-12} Gy/[Bq·min]), with the se rate to the germinal epithelium of the lens being about × 10^{-5} to 3.5 × 10^{-5} rad/(μCi·min) (8 × 10^{-12} to 9.5 10^{-12} Gy/[Bq·min]). Since both the lens and the source e symmetrical about the optic axis, the dose rate to the rminal epithelium of the lens is uniform within fairly rrow limits.

Dose Rates from ^{99m}Tc in the Lacrimal Lake: The rface of the lacrimal lake (Fig. 1) was assumed to be proximated by a spherical segment with ζ = 14° (0.24 dian), corresponding to an area of 28 mm^2 when the dius of the sclera R = 12.2 mm. As shown in Figure 3, the germinal epithelium of the lens and in the lens as a hole, these assumptions lead to dose rates ranging from × 10^{-5} rad/(μCi·min) (19 × 10^{-12} Gy/[Bq·min]) for the ar points to 8 × 10^{-6} rad/(μCi·min) (2.2 × 10^{-12} Gy/q·min]) or less for the more distant points.

Dose Rates from ^{99m}Tc in the Lacrimal Drainage Apratus: As indicated in Figure 1, these structures are at ast 12 mm from the limbus and thus are about the same stance from the nearest point of the lens and 20 mm or re from the distant points. The dose rates for this range e calculated from Equation 4. Using r = 5 mm, the dose es range from 2.9 × 10^{-6} to 7.7 × 10^{-6} rad/(μCi·n(7.8 × 10^{-13} to 21 × 10^{-13} Gy/[Bq·min]) for ^{99m}Tc he lacrimal sac.

Absorbed Doses

To obtain the radiation absorbed dose it is necessary know the residence time τ for the activity in each of the ee phases. As has been indicated, the overall turnover e of the lacrimal fluid varies within wide limits. For a siological turnover rate of 16 %/min (11), the total τ 4.25 min. Assuming that the time is divided into 1 min. he cornea, 1 min. in the lacrimal lake, and 4.25 min. e lacrimal system, the total dose to the near point of lens is

$$(\times 3.5) + (1 \times 7.0) + (4.25 \times 0.77)] \times 10^{-5}$$
$$= 1.4 \times 10^{-4} \text{ rad}/\mu\text{Ci } ^{99m}\text{Tc}$$
$$(\text{or } 3.8 \times 10^{-11} \text{ Gy/Bq } ^{99m}\text{Tc}).$$

e constant for the rate of lacrimal fluid turnover is inased to 100 %/min., and the residence time for the ee phases is divided in the same proportions, the abed dose is reduced to 2.2 × 10^{-5} rad/μCi (5.9 × $^{-12}$ Gy/Bq). If, however, the lacrimal drainage system ocked, the absorbed dose is increased. Using disappearance by physical decay only (half-life 6.03 hr.), the maximum absorbed dose to the near point of the lens from ^{99m}Tc in the sac of the lacrimal drainage apparatus is 4.02 × 10^{-3} rad/μCi (1.09 × 10^{-9} Gy/Bq) ^{99m}Tc administered.

Fig. 3. Isodose contours intersecting the lens for 100 μCi (3.7 MBq) ^{99m}Tc in the lacrimal lake are shown. Numbers at the right indicate the dose rate in mrad/min.

CONCLUSION

For the usual administered doses of 100–150 μCi (3.7–5.5 MBq) ^{99m}Tc in dacryoscintigraphy, these calculations indicate that in normal subjects the radiation absorbed dose to the medial portion of the germinal epithelium of the lens is 0.014–0.021 rad (0.14–0.21 mGy). With complete blockage of the lacrimal drainage apparatus, the maximal theoretical dose is 0.402–0.603 rad (4.02–6.03 mGy). The contralateral lens is 50 mm or more from the lacrimal sac and receives a dose of 0.025–0.037 rad (0.25–0.37 mGy) with complete blockage, and a negligible dose in normal subjects.

REFERENCES

1. Rossomondo RM, Carlton WH, Trueblood JH, et al.: A new method of evaluating lacrimal drainage. Arch Ophthalmol 88:523–525, Nov 1972
2. Brizel HE, Sheils WC, Brown M: The effects of radiotherapy on the nasolacrimal system as evaluated by dacryoscintigraphy. Radiology 116:373–381, Aug 1975
3. Saparoff GR, Chaudhuri TK, Chaudhuri T, et al.: Nuclear lacrimal scan vs dacryocystography. Trans Am Acad Ophthalmol Otolaryngol 81:566–574, Jul–Aug 1976
4. Chaudhuri TK: Clinical evaluation of nuclear dacryocystography. Clin Nucl Med 1:83–89, Jul 1976
5. Chaudhuri TK: Technical aspects of nuclear dacryocystography. Appl Radiol Nucl Med 4:184–187, Nov–Dec 1975
6. Charles MW, Brown N: Dimensions of the human eye relevant to radiation protection. Phys Med Biol 20:202–218, Mar 1975
7. International Commission on Radiological Protection: Report of the task group on reference man. ICRP Publ. No. 23. New York, Pergamon Press, 1975
8. Hanna C, O'Brien JE: Lens epithelial cell proliferation and migration in radiation cataracts. Radiat Res 19:1–11, May 1963