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EXPERIMENTAL STUDIES ON THE SCINTIGRAPHY OF THE PANCREAS IN RATS AND DOGS BY USING ISOTOPE LABELLED DYE

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Indexing Words
pancreatic scintigraphy; ^{131}I-erythrosin B; ^{131}I-rose bengal; intraperitoneal administration; high concentration in pancreas by tetraiodo-dye

Akimasa BANDO. *Experimental Studies on the Scintigraphy of the Pancreas in Rats and Dogs by Using Isotope Labelled Dye.* Kobe J. Med. Sci. 22, 47–62, June 1976–Tetraiodo-dye solutions such as eight per cent erythrosin B solution, ^{131}I-erythrosin B solution and ^{131}I-rose bengal solution were administered to dogs and rats by the intravenous, intraperitoneal or intramuscular routes. ^{131}I-rose bengal, when injected by intraperitoneal route, was found to be accumulated more actively in the pancreas, showing a peak concentration per gram of tissue some fifteen times higher than that of the liver, and also significant intrapancreatic deposit of the dye was long sustained, and yielded pancreatic concentrations approximately four to six times of those usually produced by the conventional intravenous injection of ^{75}Se-selenomethionine.

INTRODUCTION

Pancreatic scintigraphy has been employed for the morphologic diagnosis of diseases of the pancreas. In 1957, an attempt to obtain pancreatic scintigrams was made by Shapiro[11] with the aid of radioactive ^{65}Zn-labelled insulin, based on the principle that pancreatic hormone contains a small amount of zinc. The scanning, however, failed to yield satisfactory scintigrams of the pancreas, since the radioactive substance gained distribution to the surrounding organs including the liver and kidneys. Specificity of accumulation of manganese in the pancreas, though with lower concentration than in the case of zinc, was reported by Meschan.[8] Subsequent pursuit of the studies with radioactive derivatives of such an alkaloid as berberine and of triptophane was carried out, but no evidence of specific intrahepatic accumulation or distribution[2] could be found.

In 1961, Blau and his associates[1] first demonstrated that ^{75}Se-selenomethionine, a methionine with its sulfur replaced by ^{75}Se, behaved in the body virtually in the same manner as methionine. This is due to the fact that free amino acids are taken up by the pancreas from the circulation plasma whereupon enzyme proteins are synthetized and gradually excreted into the duodenal lumen. The radioactive selenomethionine with the structure CH_3-^{75}Se-CH_2-CH_2-CH (NH_2) COOH, and a physical half-life of 127 days, undergoes electron-capture decay (EC) to emit gamma rays. The method thus introduced by

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Blau et al. with success in obtaining pancreatic scintigrams has found wide clinical application.[3,4] The uptake of ^{75}Se-selenomethionine by the pancreas undoubtedly increases to levels higher than those in other organs at 30 minutes and thereafter post-administration, but accumulation of the compound in the liver is active as well, finally to yield greater total radioactivity in the liver than in the pancreas (Fig. 1 and 2). Pancreatic scintigrams are unsatisfactory because of the active accumulation in the liver and the anatomically overlapping position of the two organs. To overcome these disadvantages, various modifications of the technique have been divised, i.e., institution of procedures, postures of patients for scintigraphic scanning, color scintigrams and the use of scintillation cameras. None of these techniques has been much more successful.

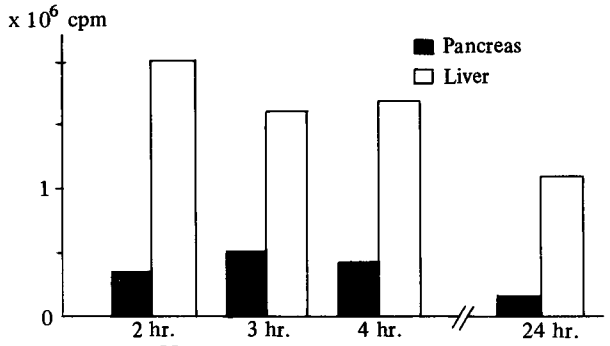

Fig. 1 ^{75}Se-selenomethionine: I. V. inj. total organ.

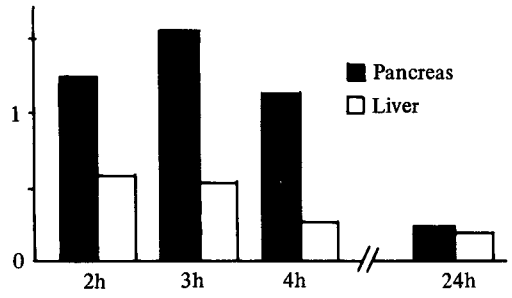

Fig. 2 ^{75}Se-selenomethionine: I. V. inj. g tissue.

Because of this, the history of study of pancreatic parencymotous radiography was carefully reviewed once again in an attempt to seek more appropriate nuclides than ^{75}Se-selenomethionine.

Ingraham[5] in 1935 described secretion from the pancreatic duct of intravenously

injected aniline dyes. Pancreatography was tried in laboratory animals by White[13] in 1959 by using iodinated aniline dyes, but all the tests failed because of the toxicity and insolubility of the dyes. In 1956, Nardi[9] reported on his observation that the pancreas alone emitted a bright yellow fluorescence characteristic of berberine upon exposure of the visceral organs to ultraviolet light following administration of the alkaloid to rats by intravenous route. Despite the observation of Nardi, a series of radioactive derivatives of berberine prepared by Blau in 1960 utterly failed to show any significant pancreatotropic specificity. Further observation of the mechanism of intrapancreatic ^{65}Zn-insulin metabolism was attempted by Shapiro to obtain parenchymatous pancreatograms by using halogenated derivatives of radioactive insulin. However, this experiment failed to produce satisfactory results because of toxicity of the halogens and the heavy metal. Based on the experimental studies on the specific selective ability of alloxan to destroy the pancreatic Langerhans' cells, Peskin[10] performed parenchymatous pancreatography in 1965, using this diabetogenic mesoxalyl urea, but the experiments failed to reveal the pancreatogram, since Langerhans' cells actually occupy only two per cent of the parenchyma.

In 1964, Ledoux-Lebard and co-workers,[6] demonstrating affinity of the pancreas to pigments and the physiologic mechanism involved, carried out pancreatography, using the tetraiodo-dye erythrosin B (iodeosin B)[7]: pancreatic parenchymatograms were obtained one hour after intravenous injection of erythrosin B in adult dogs.

The study herein to be described represents an attempt at scintigraphic scanning of the pancreas with ^{131}I-erythrosin B–an erythrosin B with its iodine substituted by radioactive ^{131}I. Pancreatic scintigrams were obtained in laboratory animals by using ^{131}I-erythrosin B, and the dose for intrahepatic accumulation of the radioactive tetraiodo-dye was determined, as well as with ^{131}I-rose bengal which is a chemically homologous dye, much more readily obtainable and much easier to handle. Parallel studies to determine the route of dye uptake by the pancreas and drugs effective in promoting the uptake and appropriate dosages were also pursued.

MATERIALS AND METHODS

A. Materials

1. Animals.

Adult dogs (mongrel, male) ranging in weight from 7 to 8 kgs and rats of the Donrhu strain with a weight range from 150 to 200 gm were used. The animals were maintained in animal care rooms for a minimum of 14 days during which parameters of normal behavior and physical condition were carefully followed prior to admission to study.

2. Dye Solutions.

a. Erythrosin B (Iodeosin B).

Tetraiodo-2, 5, 7-flourescein, a red dye of the tetraiodo series which dissolves to 11.10 per cent in water at 26° C was used. An eight per cent solution in water, pH 1.0,

$NaO\text{-}(C_6H_{12}O)_2C\text{-}C_6H_4COONa$, was applied.

b. ^{131}I-erythrosin B.

The dye is an RI-labelled erythrosin B with its iodine substituted by ^{131}I (Fig. 3).

c. ^{131}I-Rose bengal.

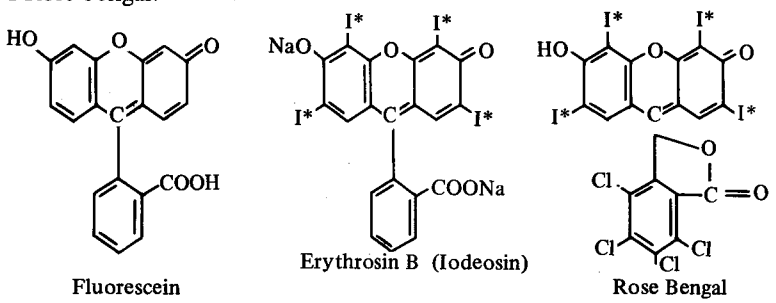

Fig. 3 Tetraiodo-dye solutions.

3. Esberiven.

The preparation contains as its principal active ingredients melilot extract from Melilotus officinale (or Melilotus altissimus) and rutin (a vitamin P-like substance) which is known to act as a capillary stabilizer and to normalize peripheral vascular permeability. Esberiven improves and increases the arterial and venous blood flows, and that of the lymph as well, perhaps partly due to its ability to affect the arterial and venous systems with indirect increase in the amount of lymph, and also partly due to its direct action upon the lymphatic system, augmenting its function. Intravenously administered esberiven has been shown to produce increments of lumph flow by a maximum of 263 per cent, or by 177 per cent on the average.

4. Gascon.

The active principle of the drug is dimethylpolysiloxane (20 mg per ml), an organic silicon compound, with the chemical structure shown in Figure 4, which occurs as an oily substance. It possesses a profound surfactant activity; concentrations of approximately 10 ppm usually suffice. The compound has been described to be chemically quite stable and physiologically inactive and to exert little effect on the enzyme system in the body. Its actions being basically physical, studies published demonstrate lack of absorption from the gastrointestinal tract following oral administration or from the skin.

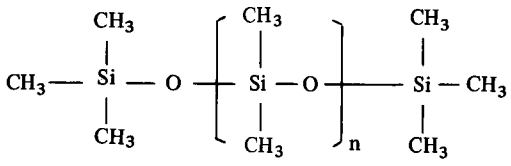

Fig. 4 Gascon.

B. Methods

Tetraiodo-dye solutions such as eight per cent erythrosin B solution (8% iodeosin B, referred to hereinafter as 8% EB), ^{131}I-erythrosin B solution (^{131}I-EB) and ^{131}I-rose bengal solution (^{131}I-RB) were administered to dogs and rats by the intravenous, intraperitoneal or intramuscular routes. Macroscopic observation was carried out concerning the intrapancreatic accumulation of the dye and also roentgenologic examination was performed for the pancreatic dye uptake in two groups of animals receiving 8% EB. Scintigraphic examination for detecting the distribution of radioactive ^{131}I-EB and ^{131}I-RB in various cardinal organs including the pancreas was carried out in several groups of animals divided according to routes of administration. Evaluation of effectiveness of drugs (esberiven and gascon) as to the specific affinity to the pancreas was made in a few groups of animals. The dogs and modes of administration of these dye solutions were as follows:

1. 8% EB Dosage Group.
   i) Intravenous administration, 20 ml, followed by X-ray examination (Adult dogs).
   Serial roentgenograms of the abdomen were taken following intravenous injection of 8% EB via sublingual vein beginning immediately after the injection and continuing over the ensuing 24 hours.
   ii) Intravenous administration, 0.1 ml, followed by macroscopic observation (Rats).
   After an intravenous injection with 8% EB via the coccygeal vein, subgoups of rats were killed by exanguination at given intervals (the same in all cases of rat experiments) of 0, 5, 10, 30, 60 and 120 minites, and 24 hours post-administration, to obtain gastrointestinal tracts along with the pancreas (Fig: 5). The rat specimens thus resected were cleaned of contents and examined grossly for intensity and extent of pigmentation of the organs.
2. ^{131}I-EB Dosage Group (Rats).
   i) Intravenous administration, 10 μCi.
   At specific time intervals following administration of ^{131}I-EB intravenously via coccygeal vein subgroups of rats were killed by exanguination and the pancreas, liver, heart, spleen, lungs, kidneys and thyroid were obtained. All these organs were rinsed with physiological saline to clean their surfaces, followed by a sampling of 1 gram of each organ. (In cases of the tissue weighing less than one gram, the entire tissue was used as a sample.) Each tissue sample was then homogenized with physiological saline to a total volume of 2 ml and the homogenate dispensed in a test tube, 12 mm in calibre. Blood samples, 2 ml per animal, were also obtained. Specific radioactivities of these homogenates and blood samples were determined by means of a scintillation counter, and the values thus obtained recorded in terms of "g Tissue" (or "Total Organ" in the case of organs weighing less than one gram). These values were then converted to "Total Organ" (or "g Tissue" in the case of organs weighing less than one gram) in proportion to gross weights of the organs.
   ii) Intraperitoneal injection, 10 μCi.
   Homogenized tissue and blood samples were prepared after intraperitoneal in-

troduction of ^{131}I-EB into cats and determinations of specific radioactivities made as in i) above.

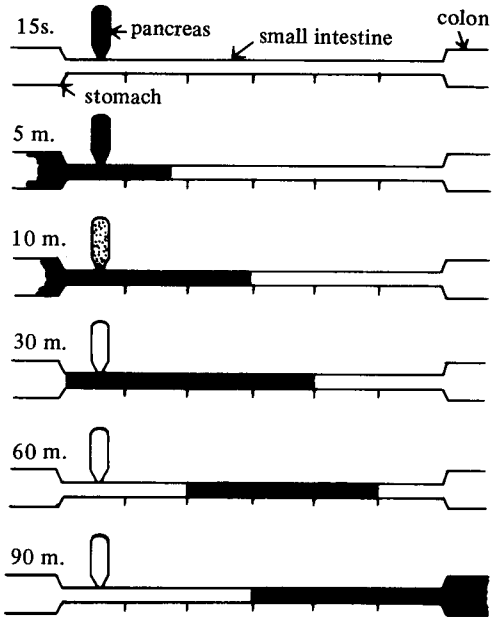

Fig. 5 Iodeosin. I. V. inj.

3. ^{131}I-RB Dosage Group (Rats).

i) Intravenous administration, 5 μCi.

Homogenized tissue and blood samples were prepared and assays for specific radioactivity were carried out as in 2-i) above.

ii) Intraperitoneal administration, 5 μCi.

Homogenized tissue and blood samples were prepared and assays for specific radioactivity were carried out as in 2-i) above.

iii) Application upon laparotmy, 40 μCi.

The experiments from 2-i) through 3-ii) produced results to be described in Results 2 and 3, and indicated active accumulation of intraperitoneally injected tetraiodo-dyes in the pancreas, but they did not yield data adequate for elucidation of the route by which the dyes accumulate in the pancreas. Therefore, experiments 3-iii) through 4-iii) were carried out in association with 3-i) and 3-ii) on the assumption that parenterally introduced dyes could take any of various routes: Circulatorily (vascular), lymphatically or physicochemically (intake from the visceral surface), yield such high intrapancreatic concentrations. 3-iii) was performed to examine the circulatory (vascular) or physicohcemical route possibilities.

a) Dropping onto the surface of pancreas.

Dye solutions were dropped directly onto the surface of the pancreas of rats laparotomized under nembutal anesthesia, followed by preparation of tissue homogenate samples and assays for specific radioactivity.

b) Dropping onto tissues remote from the pancreas.

In laparotomized rat, dye solutions were dropped onto tissues remote from the pancreas, followed also by preparation of tissue homogenate samples and assays for specific radioactivity. Care was taken to avoid direct contact of the dyes to the surface of the pancreas in applying the solutions onto remote organs.

iv) Intramuscular injection, 10 μCi.

This segment of experiments was perfomed to examine the possible circulatory (vascular) route. Dye solutions were injected into the femoral muscles whereupon tissue samples were obtained at specific time intervals for radioactivity assays.

4. Observation of Influences of Esberiven and Gascon Administered along with Intraperitoneal ^{131}I-RB (Rats).

i) Intraperitoneal injection of ^{131}I-RB, 10 μCi, plus intravenous administration of esberiven.

Esberiven, a lymph flow accelerator, was injected intravenously as a drug suitable for promoting circulatory intrapancreatic accumulation of dyes, concomitantly with intraperitoneal injection of ^{131}I-RB.

ii) Intraperitoneal injection of ^{131}I-RB, 10 μCi, plus intraperitoneal administration of esberiven.

For the same purpose as 4-i), a mixture of ^{131}I-RB and esberiven was administered into the intraperitoneal cavity.

iii) Intraperitoneal injection of ^{131}I-RB, 10 μCi, plus intraperitoneal administration of Gascon.

Gascon, a surfactant, was administered in combination with ^{131}I-RB intraperitoneally for the purpose of aiding intrapancreatic accumulation of the radioactive dye by the physicochemical route.

RESULTS

1. 8% EB Dosage Group.

i) Radiographic observation following intravenous injection, 20 ml (Adult dogs).

At any time interval after injection of the dye, the pancreas was not demonstrable on X-ray.

ii) Macroscopic observation following intravenous injection, 0.1 ml (Rats).

As can be seen from Figure 5, the pancreas was found to be stained red 15 seconds after injection, followed by dissipation to reddish color at 10 minutes and practically completely faded at 30 minutes. The dye was excreted into the duodenal lumen and thereafter moved toward the anus along with the intestinal content.

2. ^{131}I-EB Dosage Group (Rats).

i) Intravenous administration, 10 μCi.

Intrahepatic accumulation was overwhelmingly greater up to one hour following intravenous introduction of the dye in the kidney, whereas the pancreas showed only a modest peak in 5 minutes after injection, hence no significant accumulation. While no other tissue exhibited significant dye accumulation, a very small amount of free ^{131}I was found to have been taken up by the thyroid (Fig. 6).

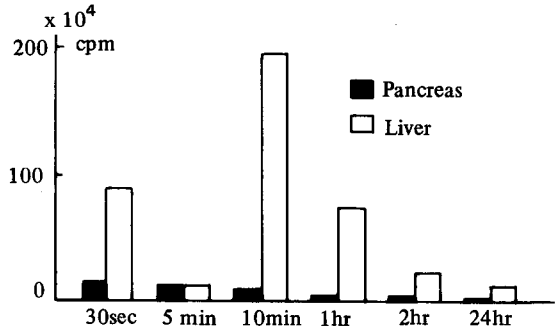

Fig. 6 Radioactivity per g tissue after i. v. injection of IB.

ii) Intraperitoneal administration, 10 μCi.

In contrast to the response to intravenous injection, the pancreas displayed a markedly active deposit of the dye during the period from 5 to 120 minutes after intraperitoneal injection, the concentration (per gm of tissue weight) being roughly 5 to 9 times that in the liver (Figs. 7, 8).

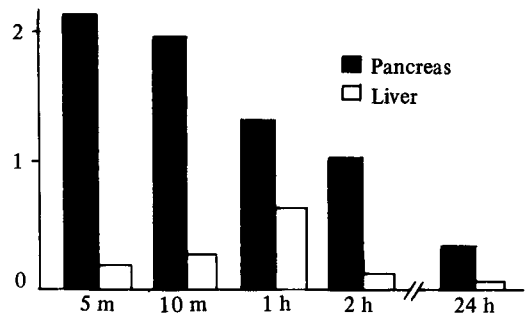

Fig. 7 Radioactivity per g tissue after intraperitoneal injection of ^{131}I-IB (EB).
I*-IB: I. P. inj. g tissue.

PANCREATIC UPTAKE OF TETRAIODO-DYE

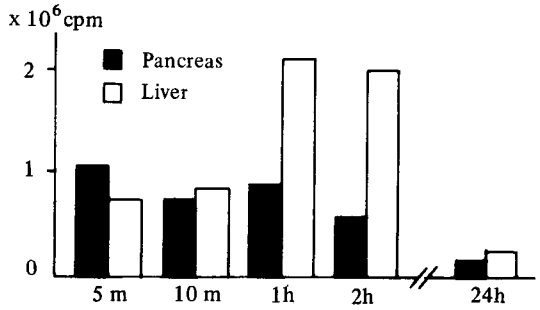

Fig. 8 Radioactivity of total organ after intraperitoneal injection of ^{131}I-IB (EB). I*-IB: I. P. inj. total organ.

Total content of the dye in the pancreas also exceeded that in the liver at 5 minutes after administration. The liver exhibited a peak concentration per gm of tissue at one hour after injection, amounting to half to that for the pancreas, and the total dye content of the liver was three times as much as that of the pancreas at 2 hours. Nevertheless, dissipation from the liver being apparently faster than from the pancreas, the difference in dye concentration from the liver thereafter reincreased. None of the remaining tissues showed significant deposit of the dye.

3. ^{131}I-RB Dosage Group (Rats).

i) Intravenous administration, 5 μCi.

This segment of experiments was conducted for comparison with the intraperitoneal injection, although the procedure is rather clinically common as in the case of ^{198}Au-colloid scintigrams. The results were practically the same as those obtained with ^{131}I-EB, only a modest peak being observed immediately after injection.

ii) Intraperitoneal injection, 5 μCi.

Accumulation in the pancreas and its duration were made prominet by intraperitoneal administration of the radioactive dye as well as by ^{131}I-EB. Maximum accumulation occurred at 30 minutes post injection and the concentration at any given time between 5 and 60 minutes after injection accounted for not less than 70% of the maximum value; furthermore, the values over the ensuing 120 minutes were of more than 50% of the maximum value. In addition, the uptake by the liver was slower than in the case of ^{131}I-EB, demonstrating a peak concentration at 2 hours post administration. The intrapancreatic concentration per gm of tissue amounted to ten-odd times the intrahepatic concentration 5 minutes after injection. Total dye content of the pancreas consistently exceeded that of the liver over the initial 60 minutes (Fig. 9).

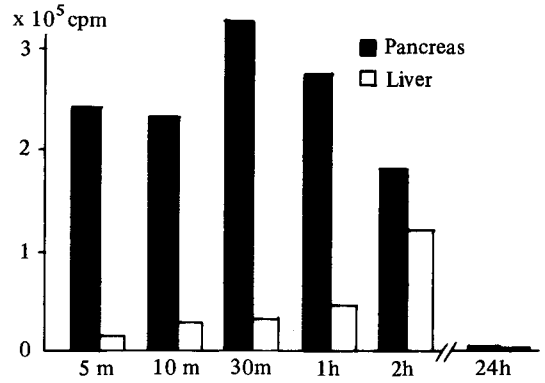

Fig. 9 Radioactivity per g tissue after intraperitoneal injection of ^{131}I-RB.
I*-RB: I. P. inj. g tissue.

iii) Application upon laparotomy, 40 μCi.

Intrapancreatic accumulation was prominent. At 5, 10 and 30 minutes after application, the concentration in pancreas of animals receiving dye solutions dropped onto the surface consistently exceeded by more than 100% that in pancreas of animals receiving solutions dropped onto remote organs. Figure 10 shows a comparison of concentrations per gm of tissue at 5 minutes after application.

There was no significant difference between the two with respect to accumulation rate, but distributions in organs other than the pancreas and liver were fairly low (Fig. 10).

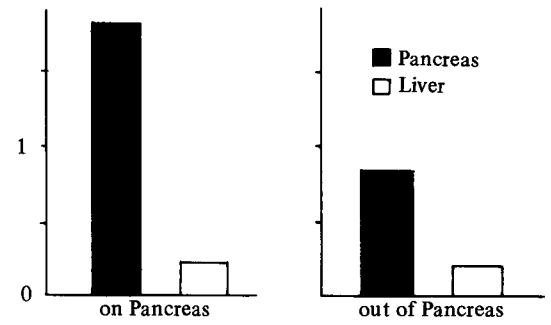

Fig. 10 Application upon laparotomy, per g tissue of ^{131}I-RB (5 min).
I*-RB: Laparotomy g tissue (5 min).

iv) Intramuscular injection, 10 μCi.

Intramuscularly introduced dye yielded a tissue distribution virtually that seen following intravenous injection, although the former required much longer to reach

maximum distribution. Values at 1 and 2 hours after intramuscular injection correspond respectively to those seen at 10 and 60 minutes following intravenous injection.

4. Effect of Esberiven and Gascon Administered along with Intraperitoneal ^{131}I-RB.

i) Intraperitoneal injection of ^{131}I-RB, 10 μCi, plus intravenous administration of esberiven.

While only a slight increase in pancreatic uptake of the dye was observed with animals receiving esberiven concomitantly, there existed evidence of a marked acceleration of the uptake with the peak value emerging in 15 minutes following injection. Excretion of the dye was also faster (Fig. 11).

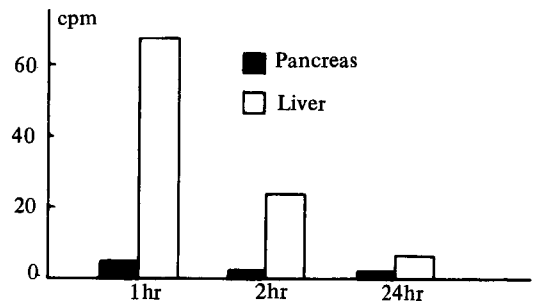

Fig. 11 Radioactivity per g tissue after intramuscular injection of ^{131}I-RB.

ii) Intraperitoneal injection of ^{131}I-RB, 10 μCi, plus intraperitoneal administration of esberiven.

Intrapancreatic concentration peaked in 10 minutes in the group of animals to which esberiven had been given just as in the case of observation i) above. In addition, a substantial increase in dye uptake (by 100–200%) was also in evidence. The animals, however, displayed retardation in excretion of the dye compared with those in i) above (Fig. 12).

iii) Intraperitoneal injection of ^{131}I-RB, 10 μCi, plus intraperitoneal administration of gascon.

Animals receiving the surfactant displayed a decrease in pancreatic dye uptake by about 50%. However, significant acceleration of dye uptake was seen with peak concentration after about 5 minutes (Fig. 13).

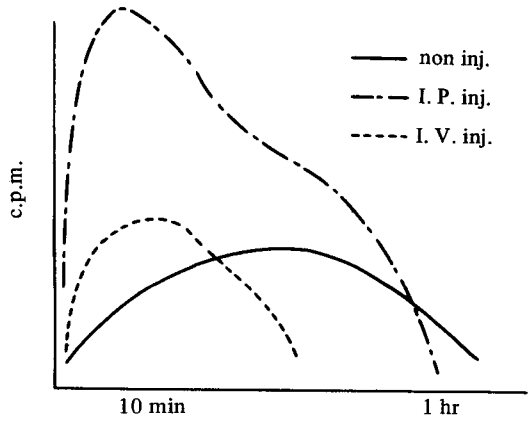

Fig. 12 Effect of esberiven.

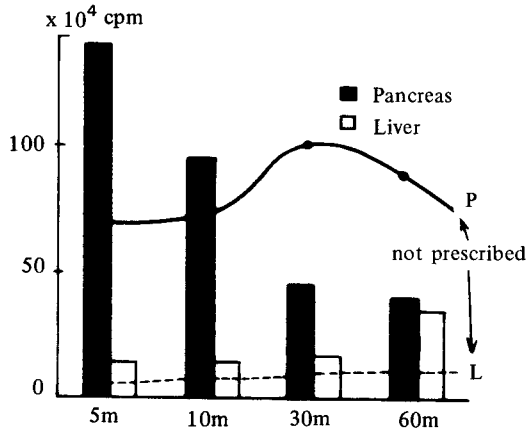

Fig. 13 Intraperitoneal injection of ^{131}I-RB plus gascon (silicone).

I*-RB & silicone: I. P. inj. g tissue.

DISCUSSION

Leodoux-Lebard and his associates reported in 1967 that maximum intrapancreatic accumulation of erythrosin B was observed at one hour after intravenous administration of dye, whereas the data obtained from this study indicate only a modest peak concentration in about five minutes following intravenous injection. The coloring agent which stained the pancreas is promptly excreted into the intestinal tract as pancreatic juice and

the agent is then conveyed together with the intestinal content toward the rectum, thereby rendering pancreatography extremely difficult. In addition, considerably large doses are required for the use of erythrosin B as a contrast medium, i.e., 1 to 3 ml per kg of body weight, and at these dose levels, the dye stains practically all tissues including the skin, and marked edema of the mucosa was seen as an adverse side effect. These disadvantages disqualify the dye from clinical use as a contrast medium for radiographic demontration of the pancreatic parenchyma.

A practical advantage of radioisotope-labelled compounds, such as ^{131}I-EB, is free from such side reactions, because a small amount of the radioactive iodine-labelled erythrosin B for adults (about 0.01 ml per kg of body weight, 300 μCi) is sufficient for scintigraphic demonstration of the pancreas. Skin-reddening and mucosal edema never result from the administration of the dye in such low dosage. However, ^{131}I-EB uptake of the pancreas was greatly exceeded by that of the liver, when the radioactive dye was injected by intravenous route; hence scintigraphic demonstration of the pancreas was difficult. The extremely low deposit of intravenously administered ^{131}I-EB (^{131}I-iodeosin B) in the pancreas as compared to its intrahepatic accumulation was reported by Kato and Takashima[12] as well.

In view of these, other possible routes of administration for pancreatic scintigraphy were explored in this study. Intraperitoneal administration was found to yield very high intrapancreatic concentration of the radioisotope-labelled erythrosin B, and the dye, unlike intravenously injected ^{131}I-EB, was retained in the organ for a much longer period (more than 60 minutes), thus suggesting adequacy of the radioactive dye for use in the scintigraphic scanning of the pancreas. Concerning the visualization of scintigraphy of the pancreas and the liver, the superimposition of both organs is a problem to be solved.

The ratio of specific radioactivity per gm of pancreas to that of liver is approximately 2.5:1 at peak concentrations in the case of ^{75}Se-selenomethionine which has been conventionally used clinically in scintigraphic diagnosis, whereas in the case of ^{131}I-EB the ratio was found in this investigation to be 11:1. The ratio of total specific radioactivity of the pancreas to that of the liver was similarly found to be 1:3 in the case of ^{75}Se-selenomethionine and, conversely, to be 1.4:1 in the case of ^{131}I-EB. The findings indicate that the use of ^{131}I-EB in place of ^{75}Se-selenomethionine simplifies the procedure for discerning the pancreas from the liver.

As a result of our search for a readily obtainable and inexpensive substitute for ^{131}I-EB, a trial product and not generally available, we fortunately came upon ^{131}I-RB. Figure 3 depicts the similarity of ^{131}I-RB to ^{131}I-EB. It is an established clinical principle that intravenously administered ^{131}I-RB is secreted selectively from the liver cells to permit scintigraphic recording of the liver, whereas accumulation of the radioactive dye in the pancreas scarcely occurs. In contrast, when the radioisotope-labelled dye was injected intraperitoneally, the dye peak distribution (accumulation) ratio between pancreas and liver was found to be 15:1 as concentration per gram of tissue, as against 11:1 for intraperitoneally injected ^{131}I-EB, and to be 1.7:1 as total content in tissue. While a prompt excretion from the pancreas and early onset of uptake by the liver

occur with ^{131}I-EB, ^{131}I-RB is retained longer in the pancreas and its uptake by the liver is fairly slow. There is adequate demonstration of safety and lack of serious side effects in the case of ^{131}I-RB. From these observations it follows that the latter is more advantageous than the former for use in preparation of scintigrams of the pancreas.

As for pathways of dye accumulation in the pancreas following intraperitoneal administration, three different routes were deemed possible: Physicochemical, lymphatic and hematogeous. The results of the segments of experiments 3-iii) and 3-iv) indicate that the intraperitoneally administered dye is mostly taken in by the physicochemical route or from the visceral surfaces, and partly by the lymphgenous route.

A conclusion can be drawn from the data obtained that esberiven affects the intraperitoneally injected ^{131}I-RB uptake by the pancreas in two distinct ways: acceleration of intake and increase in uptake. Esberiven shows the acceleration and the increasing effects, when injected by intraperitoneal route along with ^{131}I-RB, whereas when administered intravenously, it shows only the accelerating effect. Promotion of excretion from the pancreas occurs, when the uptake is accelerated. Therefore, esberiven may advisably be injected intravenously for rapid progress of scanning, but concomitant injection with ^{131}I-RB by intraperitoneal route is more preferable for pancreatic scintigraphy. Meanwhile, the experiments demonstrate involvement of the lymphogenous pathway in the dye uptake by the pancreas. It has been found that gascon is inferior to esberiven in increasing pancreatic ^{131}I-RB uptake, but is superior in hastening the dye intake. If a surfactant with an adequate safety factor for intraperitoneal introduction in man was obtainable, its simultaneous administration by this route prior to scintigraphic scanning of the pancreas would substantially reduce the interval between the injection of ^{131}I-RB and subsequent initiation of the examination. It is probable that the efficient intake of the dye from the entire pancreatic surface is due to the ability of the surface-active agent to aid diffusion of ^{131}I-RB in the abdominal cavity. However, the injected surfactant gives rise to diffusion of the dye not only to the surface of the pancreas but also to the surfaces of other organs which eventually hastens the dye intake, whereas esberiven elevates only the lymphogenous dye uptake (involved also in the intake from the surface).

The proportions of these mechanisms involved in pancreatic dye accumulation are considered to have affected the pancreatic dye uptake rate. The use of the dye is of significance in that the determination of the rate of its excretion from the pancreatic duct into the duodenum provides measurement of pancreatic function (external secretion), and that the use of a radioisotope-labelled dye will lead to advancement of technical progress towards simultaneous diagnostic recording of both morphologic and functional changes of the pancreas. There exists, in this context, the possibility of developemnt of this scintigraphic method to permit simultaneous diagnosis of pancreatic function, by seeking thorough elucidation of the mechanism whereby the intraperitoneally injected dye behaves until excretion from the pancreatic duct, as well as by persevering in our efforts toward success in making the scanning technique clinically practicable.

SUMMARY AND CONCLUSION

1. In a series of experiments in rats, intraperitoneal administration of ^{131}I-rose bengal was found to be superior to the conventional intravenous injection of ^{75}Se-selenomethionine to obtain satisfactory pancreatic scintigrams. This report documents the results of the experiments.

2. After injection of ^{131}I-erythrosin B (^{131}I-iodeosin B) by the intravenous route, the liver exhibited an overwhelming uptake of the dye in the first hour, followed by a gradual increase in intrarenal concentration, whereas the pancreas showed only a modest peak intake immediately following the injection (5 minutes), whereafter practically no intrapancreatic accumulation of the dye. In contrast, intraperitoneally administered dye was markedly accumulated in the pancreas during the period from 5 to 120 minutes post injection, with a peak concentration per gram of tissue approximately ten times greater than that of the liver.

3. ^{131}I-rose bengal, when injected by intraperitoneal route, was found to be accumulated more actively in the pancreas, showing a peak concentration per gram of tissue some fifteen times higher than that of the liver, and also significant intrapancreatic deposit of the dye was long sustained.

4. These pancreatotropic tetraiodo-dyes, when administered intraperitoneally, yield pancreatic concentrations approximately four to six times those usually produced by the conventional intravenous injection of ^{75}Se-selenomethionine.

5. With respect to safety and economy the results stress greater practical usefulness of intraperitoneal ^{131}I-rose bengal than the conventional ^{75}Se-selenomethionine for pancreatic scintigrams.

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