Asthma—Kennedy and Thursby-Pelham

BRITISH MEDICAL JOURNAL 1021

observations it was found that the immediate effect of the adrenergic drugs was similar.

To obtain a measure of the duration of effect of the different inhalants, serial assessments were continued for three and a half hours after each inhalant therapy on two groups of asthmatic subjects containing 12 subjects in each group. From these observations it was found that the inhalants gave distinct time-response curves.

The duration of isoprenaline was shortest; its action had been completely lost by 90 minutes. Adrenaline bitartrate and adrenaline hydrochloride combined with benzocaine were similar: a peak effect occurred at 15 minutes and was maintained up to 90 minutes, after which response gradually waned. Atropine methonitrate was found to have some immediate effect; the response reached a maximum at 90 minutes and was usually maintained throughout the three and a half hours of observation. The inhalation of isoprenaline in combination with atropine methonitrate showed substantial advantages over the other drugs tested. At 15 minutes the response was as good as the best isoprenaline response; it continued to improve for 120 minutes, after which it was

maintained at this level during the three and a half hours of observation.

It is recommended that the frequency of administration of atropine methonitrate with or without adrenergic inhalants should be strictly controlled, especially in acute asthma.

We are indebted to the staff of the Department of Respiratory Physiology for carrying out the investigations described in this report, especially Mr. James Booth, S.R.N., Mr. Peter Wilkes, S.R.N., Mr. Norman Curnock, S.R.N., Mrs. Sheila Clarke, S.R.N., Mrs. K. Tattersfield, who prepared the graphs, and also Mrs. E. Turner and Mrs. E. C. Wright for the analyses.

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Use of Krypton-85 in the Study of Hypoxia in Porto-pulmonary Bilharziasis (Schistosomiasis)


Porto-pulmonary bilharziasis often presents as hepatosplenomegal and cor pulmonale (Zaky, 1952; Zaky et al., 1959). The haemodynamic changes in this disease have already been discussed (Foda, 1959; Zaky et al., 1962). We found that in about 10% of these cases hypoxia of less than 94% was present. This hypoxia could not be corrected by 100% O2 inhalation.

When the alveolar CO2 tension was matched simultaneously against the arterial CO2 tension either at rest or on moderate exercise, a significant gradient was found between the alveolar PACO2 and the arterial PACO2, the latter being raised from 2 to 7 mm. Hg. Studies of pulmonary function in these cases revealed almost normal findings (Ashba, 1959), particularly the minute alveolar ventilation and the helium-mixing time. These findings can only mean a veno-arterial admixture either inside the lung from pre-capillary pulmonary-artery/pulmonary-vein shunting or from the portal-vein blood to the pulmonary vein. In order to elucidate the above findings it was decided to carry out further investigations using the gas krypton-85.

Materials and Methods

Krypton-85 is a very interesting gas in that it is cleared by the alveoli to the extent of 95-99% in one circulation. We followed the method described by Fritts et al. (1960) to investigate the problem of a pre-capillary pulmonary-artery/pulmonary-vein shunting. By this method a gas solute is injected with a known quantity of a blue dye into the superior vena cava and both are recovered from the brachial artery within the period of one circulation. The concentration of dye is obtained from spectrophotometer readings, while the radioactivity is read on the scaler. The percentage of shunt is calculated from the formula:

$$\frac{\text{Kr counts in integrated radial}}{\text{conc. of dye injected mg/l}} \times 100 \text{ Kr counts integrated conc. of dye in integrated radial mg/l.}$$

The pulmonary-artery concentrations after injection into the superior vena cava were calculated from the radiological size of the heart after the method of Hanson (1961), and the ratio of the right to the left cavities was considered to be 55-45%. This gave the cardiac volume in which the dilution of superior-vena-cava injection could have taken place.

To investigate the problem of portal-vein/pulmonary-vein shunting, the same amount of krypton-85 was injected into the splenic pulp in bolus form; the bilharzial spleen lends itself admirably for the purpose as it is easily accessible and firm. We had no trouble while using this route in our cases apart from a moderate degree of pain after the injection. Samples were collected simultaneously from the pulmonary artery and the radial artery at approximately 10-second intervals for the first minute after the injection and at every 30 seconds for the next three to five minutes. The samples were then sealed in mica cuvettes and counted through an appropriate G.M. tube for five minutes.

Results

The first experiment, when the krypton-85 solute and the blue dye were injected into the superior vena cava, showed the

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absence of shunting between the pulmonary artery and the pulmonary vein (see Table). The shunt did not exceed 5.7% except in two cases (Nos. 1 and 5) in which it was 10%.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Arterial O₂ Saturation %</th>
<th>Conc. of Dye in Injected Solution (g./l.)</th>
<th>Conc. of Dye in Integrated Radial Solution (mg./l.)</th>
<th>Conc. of #Kr in Injected Solution</th>
<th>Conc. of #Kr in Integrated Radial</th>
<th>Pulm-art./Pulm-vein Shunt %</th>
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</thead>
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<tr>
<td>1</td>
<td>90</td>
<td>220</td>
<td>90460</td>
<td>211</td>
<td>10</td>
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<tr>
<td>2</td>
<td>93</td>
<td>190</td>
<td>253703</td>
<td>100</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>93</td>
<td>100</td>
<td>249450</td>
<td>51</td>
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<tr>
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<td>93</td>
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<td>487</td>
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<tr>
<td>5</td>
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<td>232100</td>
<td>220</td>
<td>3.5</td>
<td></td>
</tr>
</tbody>
</table>

When we examined the radial-artery samples after splenic injections we found that the degree of krypton concentration was almost equal to or even higher than that obtained in the same artery after injection into the superior vena cava (Fig. 1). When we considered the pulmonary-artery levels responsible for these radial-artery concentrations, we found that after splenic injection the pulmonary-artery concentrations were markedly lower than those after the superior vena cava injection. Another finding was that radioactivity was present in the brachial artery in plateau form for about three minutes; then it started to decline (Fig. 1). In one case (Fig. 2) radioactivity was still present in the brachial artery 30 seconds after it had disappeared from the pulmonary artery. Another finding, in seven cases, was that the krypton concentrations in the pulmonary artery attained a high peak in the first 10 seconds after the splenic injection (Fig. 1).

**Discussion**

Of our 15 cases of hypoxia, 10 showed portal-vein/pulmonary-vein shunting, two showed pulmonary-artery/pulmonary-vein shunting, and three could not be explained by either route. Our data from the second experiment indicate that direct communications exist between the portal system and the pulmonary venous system, contributing to a veno-arterial admixture. The rapid high concentration in the pulmonary artery could not have arrived along the normal portal circulation, as this usually takes 25–30 seconds. The primary peak presumably represents a short-circuit either to the superior vena cava via the vena cavae as well as other intercostophrenic veins (Fig. 3) or short veins communicantes to the inferior vena cava. The splenic pressure was high in the cases that showed the primary peak in the pulmonary-artery concentration, the pressure ranging from 25 to 33 mm. Hg. The fact that krypton-85 may stay as long as five minutes suggests that the degree of pooling in the overdistended portal system is enormous. In one case (Fig. 3) the multiple peaks in the pulmonary-artery samples suggested various short-circuits of different lengths, velocities, and magnitudes at different levels.

As was mentioned earlier, our bilharzial cirrhotic cases could not be fully saturated by inhalation of 100% oxygen. On inhalation of 100% O₂, normally the blood plasma is capable...
of carrying a further 1.8 vol.% in solution at 600 mm. Hg of alveolar-oxygen tension. It is presumed that the oxygen saturation can be raised a further 8% or so provided all the cardiac output flows over the alveoli. In bilharzial cirrhosis it rises

![Image 1](image1.png)

**Fig. 4.**—X-ray film of oesophagus with barium showing extensive varicose veins in a case of porto-pulmonary bilharziasis. (By courtesy of Dr. Fachal.)

acetylsalicylic or acetylsalicylic esterase (which is believed to be low (El-Hawari, 1958) in cirrhosis of liver) is an important factor. Either some unknown substance exists which operates only inside the body and prevents the red cell from oxygen saturation in the brief interval it crosses the alveoli, in addition to the portal-vein/pulmonary-vein shunting, or the latter really attains a much higher magnitude than is at present conceived.

In Fig. 6 we tried to sum up the various shunts that occur in porto-pulmonary bilharziasis. It incorporates splenic shunts (Zaki et al., 1962), oesophageal and other intercostophrenic veins to the vena azygos, or short venae communicantes to the inferior vena cava; all these contribute to a diastolic overloading of the right ventricle. Bronchopulmonary shunts increase the systolic work of the right ventricle. Repetitive showers of schistosoma ova that lodge in the branches of the pulmonary artery create further occlusive angiitis, which increases the total pulmonary arteriolar resistance. The large size of the pulmonary arteries is therefore due to an increase in flow, pressure, and resistance in competition with each other.

The hypoxia in most cases is contributed to by portal-vein/pulmonary-vein shunting. Few cases have precapillary pulmonary-artery/pulmonary-vein shunting, but full explanation of the remaining factors, particularly the problem of bronchial-vein/pulmonary-vein shunting, still awaits further investigation.

**Summary**

Hypoxia of a degree less than 94% appears in porto-pulmonary bilharziasis in about 10% of cases.

Fifteen cases have been studied, using the gas krypton-85, to elucidate the presence of veno-arterial admixture, either in the lungs between the pulmonary artery and the pulmonary vein or in the portal circulation between the portal vein and the pulmonary vein.

Injection of krypton-85 into the superior vena cava with a dye and the recovery of both from the radial artery in one circulation revealed the absence of shunts in the lungs except in two cases.

Injection of krypton-85 into the spleen and taking simultaneous samples from the pulmonary artery and the radial artery revealed the presence of shunts between the portal vein and the pulmonary vein.

In seven cases high concentrations of krypton-85 in the pulmonary artery within 10 seconds indicated a short-circuit from the portal circulation to the superior vena cava.
presumably takes place via the vena azygos through oesophageal
and other intercostophrenic veins or short venae communicantes to
the inferior vena cava.

The krypton injected into the spleen as a bolus could be
recovered from the radial artery as late as five minutes after-
wards, indicating marked overdistention and retardation in the
portal pool.

A summary of the various haemodynamic shunts in porto-
pulmonary bilharziasis is presented in Fig. 6.

We are grateful to the National Research Council and Dr. S.
Hashish, whose active co-operation in the nuclear physics depart-
ment made the work with krypton possible.

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Spontaneous Intraperitoneal Haemorrhage During Pregnancy:
Report of Three Cases


Spontaneous intraperitoneal haemorrhage during pregnancy or
the puerperium, although relatively rare, may be due to a
variety of causes and may originate from any intra-abdominal
artery or vein, or a blood-filled viscus. Rupture of a splenic-
artery aneurysm is perhaps the best-known source of such
bleeding, but the basic features and principles of management
are similar whether the site of bleeding is in the upper or the
lower abdomen. It is evident from the literature that there is
still often a considerable delay in diagnosis, which adversely
affects the results of treatment. Three cases treated in Ban-
bridge Hospital and Lurgan and Portadown Hospital, and
reported below, illustrate different sources of haemorrhage.
Obstetrical cases in these two neighbouring hospitals are under
the overall care of the one consultant, although in Banbridge
Hospital general practitioners look after their own normal cases.
Both hospitals have a combined emergency surgical duty rota.

Case 1

A married woman aged 27, gravida-2, para-0, was admitted to
Banbridge Hospital on 1 April 1961 when 23 weeks pregnant. Her
first pregnancy in 1960 had ended in abortion at 10 weeks. She
had awakened from sleep with severe abdominal pain and had called
her doctor, who found her blood-pressure to be 90/50 mm. Hg but
without tachycardia. There was generalized abdominal tenderness
and the uterus corresponded in size to a 22-weeks pregnancy. The
foetal heart could be heard. Immediate admission to hospital was
arranged.

On arrival at hospital the patient's colour was good, the pulse
rate 100, and the systolic pressure had risen to 120 mm. Hg. The
terine fundus was at the level of the umbilicus and the foetal
heart was audible. There was generalized abdominal tenderness, maximum
in both iliac fossae, with guarding and rebound tenderness.
A provisional diagnosis of intraperitoneal bleeding, possibly from a
splenic-artery aneurysm, was made, blood transfusion was started
and arrangements were made for laparotomy.

At operation the abdomen was entered through a left paramedian
incision and the peritoneal cavity was found to contain 2 pints (1,140
ml.) of blood and blood clot. The site of bleeding was a vein on the
anterior surface of the uterus and a small tear was present in the
peritoneum overlying the bleeding-point. The bleeding was con-
trolled by suturing the area with interrupted catgut sutures over gel
foam soaked in thrombin. Blood and blood clot were cleared from
the peritoneal cavity and the abdomen was then closed in layers
without drainage. A total of 2 pints (1,140 ml.) of blood was given
before and during operation and the patient's post-operative condi-
tion was satisfactory. Recovery afterwards was uneventful and she
was discharged home on 15 April.

The remainder of her pregnancy was normal, and on 29 June
she had a normal delivery of a living child weighing 7 lb. 5 oz.
(3,315 g.). Subsequent inquiry from another hospital in which she
had been curedretted after her previous abortion showed that there had
been no complications at that time and nothing to suggest perfora-
tion of the uterus at operation. No history of trauma during the
present pregnancy could be obtained, and it must be presumed that
the intraperitoneal bleeding was spontaneous.

Case 2

A married woman aged 38, gravida-6, para-5, collapsed at home
with sudden severe left-sided abdominal pain on 26 June 1961. She
was then 10 days past her expected date of confinement and had
been feeling well until one week previously, when she had developed
a cough and slight continuous pain in the left loin. Her previous
pregnancies and labours had been normal.

The obstetric flying squad was called, and on arrival found the
patient to be severely shocked, pale, cold, and cyanosed, with stertor-
ous breathing. The pulse was thready, rate 140, and the systolic
pressure was 65 mm. Hg. Crepitations were heard at both lung
bases. The uterus corresponded in size to a term pregnancy and
was contracting. The presentation was vertex with the head
engaged, and the foetal heart could be heard. There was no
tenderness over the uterus, but tenderness was marked in the left
flank. There was no revealed vaginal bleeding.

Blood transfusion was started immediately and 2 pints (1,140 ml.)
of blood was given rapidly, after which the blood-pressure rose to
115/75 mm. Hg and the pulse rate dropped to 120. A third pint
(570 ml.) of blood was begun and the patient was transferred to the
Lurgan and Portadown Hospital, 7 miles (11 km.) distant. During
the journey the blood-pressure started to fall again and on admission
to hospital the systolic pressure was 75 mm. Hg. Further blood
was transfused and the patient's condition improved. By this time
the foetal heart was no longer audible.

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