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Review

New Developments in Cyclo-Oxygenase Inhibitors of Arthritis

Case Reports

Neural Retinopathy, M.D.

Severe Avascular MD / Tumid Axon, MD

Perforating Retinal MD / Nerve Endothelial, MD

Wermer's Syndrome

Horseshoe Vein, MD / O. Gonoer Tumour, MD

Rheumatic Arthritis, MD / Ax Median Vascular, MD

Complications

Transaxial Imaging of the Inferior Vena Cava as an Obstetric

Sequela, Incomplete Ovarian Chondroma

76 Hydral Disease of the Thyroid in Childhood

Tumour Ovarian, MD / Avner, Vascular, MD

At Nerve Tumour, MD / Ax Nerve Tumour, MD

Multiple Vascularoma

67 The Aid of Computed Tomography in the Diagnosis of

Chemical Studies

Benign Aneurysm, MD / Avner, Cardiac, MD / Nerve Systale, MD

Placenta Cell Culture

59 Complementation of Cellular Attractions in Normal and Premalignant

CONTENTS

Hackett's Medical Journal

VOLUME 17 / NO. 2 / APRIL 1984
Introduction

Key Words: Placental cell cultures, preclamping

Due to the fact that the placenta is a fascinating issue, and the fact that few studies on placental cell cultures have been recently carried out, it is necessary to emphasize some authors have emphasized the fact that this event occurs as a consequence of damage in the trophectoderm.

Whether the alterations in the placenta are of primary or secondary nature, some authors have emphasized the fact that this event occurs as a consequence of damage in the trophectoderm.

Summary

Cell Culture

Preclamping, placental alterations in normal and comparison of cellular

Volume 17, No. 2, April 1994

heacettepe Medical Journal
in preeclampsia. An attempt was made to investigate whether there are differences at the cell culture level between normal and preeclamptic placental cells, and examine the manner of their growth under the same conditions.

**Materials and Methods**

Placental cell culture was carried out in 21 cases, 10 of which were instances of normal pregnancy and 11 preeclampsia. On the vitality test given on the second day with 1 % trypan blue, the placental cells were found to be viable at a rate of 90 %. The cells within the medium were examined under a light microscope.

In addition, placental cell culture was done in 8 cases, 4 of which were instances of normal pregnancy and 4 preeclampsia. Upon completion of the experiment performed with 1 % trypan blue, the cells were found to be viable at a rate of 90 %. The cells were observed in the viable state for 15 days following growth in cover slips, petri dishes or Leighton tubes. Some of the cover slips were examined following staining with Haematoxylin and Eosin after fixation with 10 % formalin at varying times.

The terms of pregnancy of the subjects varied from 39 to 41 weeks, being cases delivered normally through the vaginal route. The preeclamptic cases had blood pressure of at least 140/100 mm Hg, and oedema and proteinuria.

Cell culture was carried out by the methods of Fox and Winkel, modified according to the laboratory conditions. Pieces obtained from the placenta after birth were placed in cold sterile Hanks’ solution. Then the material was freed from the basal plate, septa and vascular tissue and washed in Hanks’ solution 7-10 times in an effort to discard the red blood cells. The material was cut into 1-2 mm pieces. The tissue prepared in this way weighed approximately 40 g. This tissue was transferred into an Erlenmeyer flask containing 100 ml of 0.5 % trypsin (supplied by BDH Biochemical) at pH 7.5. The material was shaken in a water bath at 37°C for 10 minutes and the supernatant was discarded in an effort to dispose of the red blood cells. 200 ml of 0.5 % trypsin was added and the material was shaken under the same conditions for 35-50 minutes. Next, the experimental material was kept in a water bath for 10 minutes for the precipitation procedure. The supernatant was decanted through double-folded gauze. It was centrifuged at 800 rpm for 8 minutes. After centrifugation, the supernatant was discarded, and 4 ml of medium 199 (supplied by Flow Laboratories) at pH 7.4 was added to each tube. After centrifugation again at 800 rpm for 8 minutes, the supernatant
In addition, growth of different preparations of cells was still visible 3 days after the monolayer formation.

The results of these experiments are shown in Figure 2. The results also indicate that the normal placental cells were the best to grow. Together with the control cultures, they grew more rapidly than the normal placental cells. The results were also observed in the normal placental cells that were used.

Upon examination immediately after staining with Hæmatoxylin and eosin, it was observed that round epithelial cells had increased in number, while multinucleated cells were absent.

The number of the epithelial cells, the exception being almost none, was the same as in the control culture. On the 15th day of the experiment, the number of the epithelial cells was nearly the same as in the control culture, and there were no significant differences. The results showed that the epithelial cells were not affected by the interaction of the normal placental cells with calf serum. The results of the interaction of the normal placental cells with calf serum were similar to those obtained in the control culture.

The results indicated that the normal placental cells were the best to grow. Together with the control cultures, they grew more rapidly than the normal placental cells. The results were also observed in the normal placental cells that were used.

Upon examination immediately after staining with Hæmatoxylin and eosin, it was observed that round epithelial cells had increased in number, while multinucleated cells were absent.
Figure 1
Haematoxylin and eosin stained preeclamptic placental cell suspension. X 500
S: Syncytiotrophoblast, C: Cytotrophoblast

Figure 2
A 4-day-old live preeclamptic placental cell culture. X 500
CO: Cytotrophoblast, K: Syncytial koll, b: Black dotted formations.
tial knots (Figure 2). On the sixth day, the multinucleated giant cells were seen to detach from the cover slip, and profuse round epitheloid cells to exist with improvement in the cytoplasmic membrane degeneration. On the tenth day new multinucleated giant cells were observed to form (Figure 3). It was a striking observation that more round epitheloid cells were present than in the simultaneous normal placental cell culture. On the 12th day, the epitheloid cells were observed to adhere to each other forming large masses, and more multinucleated giant cells formed (Figure 4). On the 15th day, the epitheloid cells were still present, although they were reduced 4 fold in number, while multinucleated giant cells were increased at the same rate. Differences between normal and preeclamptic placental cell cultures are listed in Table I.

**TABLE I**

**DIFFERENCES BETWEEN NORMAL AND PREECLAMPTIC PLACENTAL CELL CULTURES**

<table>
<thead>
<tr>
<th>Normal Placental Cell Culture</th>
<th>Preeclamptic Placental Cell Culture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multinucleated giant cells were dominant in cell suspension</td>
<td>Round epitheloid cells are dominant in cell suspension</td>
</tr>
<tr>
<td>The nuclei of cells were pyknotic</td>
<td>The nuclei of cells were not pyknotic</td>
</tr>
<tr>
<td>A perinuclear halo were present in the round epitheloid cells</td>
<td>A perinuclear halo was absent in the round epitheloid cells</td>
</tr>
<tr>
<td>The cytoplasm of cells was scanty</td>
<td>The cytoplasm of cells was more scanty than the normal placental cells</td>
</tr>
<tr>
<td>The borders of the round epitheloid cells were smooth</td>
<td>The borders of the round epitheloid cells were undulated in a lacy fashion</td>
</tr>
<tr>
<td>There were black dotted formations in the epitheloid cells</td>
<td>There were no black dotted formations in the epitheloid cells</td>
</tr>
<tr>
<td>The cells started to adhere to the cover slip on the first day</td>
<td>The cells started to adhere to the cover slip on the third day</td>
</tr>
<tr>
<td>The monolayer formed on the third day</td>
<td>The monolayer formed on the fourth day</td>
</tr>
<tr>
<td>Adherence to the cover slip was strong</td>
<td>Adherence to the cover slip was weak</td>
</tr>
<tr>
<td>Hyperplasia of the epitheloid cells was seen at the beginning of the second week</td>
<td>Hyperplasia of the epitheloid cells was present in the first week</td>
</tr>
<tr>
<td>New multinucleated cells formed on the 13th day</td>
<td>New multinucleated cells formed on the tenth day</td>
</tr>
<tr>
<td>On the 15th day reduction in the number of epitheloid cells to the extent of being almost non-existent</td>
<td>On the 15th day, the epitheloid cells were still present, although they were reduced by 4 fold in number</td>
</tr>
</tbody>
</table>
In conclusion, it can be said that the trophoblastic changes seen with predecidual cells are not primary and irreversibly in nature. Occur

**Discussion**

It is said that predecidualization results from alterations in the placenta.
rence in the culture medium of improvement in the derangement cell membranes within the second week and regression in cytotoxoplasmastic hyperplasia with formation of many new syncytiotrophoblasts suggest that abnormal cellular alterations with preeclampsia may result from undernourishment due to insufficiency in uteroplacental circulation.

REFERENCES

Tomography in the Diagnosis of Multiple Meningiomas: The Aid of Computed Tomography

The authors emphasize that multiple meningiomas can be challenging to diagnose, particularly when they are not contiguous. The introduction outlines the importance of computed tomography (CT) as a diagnostic tool and highlights the need for a comprehensive review of the literature on multiple meningiomas.

Summary

The objective of this study is to present a case series of seven patients with multiple meningiomas and to review the role of computed tomography in their diagnosis.

Key Words: Multiple meningioma, Computed tomography.
Case Reports

Case 1: A 35 year-old-male was admitted because of convulsive disorder and weakness in the right arm. Neurological examination disclosed bilateral papilledema and hemiparesis on the right side. Brain scintigraphy was used as the only neurological diagnostic procedure and only one spot of radioactive uptake was found 7 cm apart from each other, two separate tumors (4x3x3 cm and 6x8x4 cm) of the falk were totally excised. Microscopic examination revealed that the tumors were meningocytic meningioma with angioblastic components. During the follow-up of 11 years the neurological examination remained within normal limits.

Case 2: A 47-year-old woman was admitted because of headache and memory defect. Examination demonstrated mild right hemiparesis and papilledema. Brain scintigraphy revealed the presence of a single left temporoparietal mass. A left temporoparietal craniotomy disclosed 3 separate tumors; two in the left parietal and one in the left temporal convexity. (4x5x5 cm; 2x1x2 cm and 3x3x3 cm). Histological examination revealed calcified meningiomas. 9 years later the neurological status was normal.

Case 3: A 42-year-old woman was admitted with unsteadiness of gait, twitching of the right side of the face and right hemiparesis. Computerized tomography disclosed evidence of multiple nodules in the left parasagittal region. Seven separate tumors were totally removed from the left parietal convexity, with a left temporoparietal craniotomy (One 6x5x4 cm., the others 2x2x2 cm).

Case 4: A 40-year-old male was admitted suffering from nausea, vomiting, weakness of the right extremities and a right visual field defect. Examination demonstrated right hemiparesis and papilledema. Left carotid arteriography and brain scintigraphy revealed only one mass lesion. Nevertheless CT demonstrated two separate masses, one in the left frontal, the other in the left parietal region. He underwent a frontoparietal craniotomy with total removal of the two meningiomas which upon histologically examination proved to be fibroblastic meningiomas (5x6x6 cm and 3x4x4 cm) (Figure 1,a, b, c, d).

Case 5: A 47-year-old man was admitted because of headache, memory deficit and visual blurring. Neurological examination revealed only papilledema. CT showed two masses, one in the right frontal, the other in the left parietal region. The tumors were removed with two separate craniotomies. He was discharged in a normal neurological status. The tumors were confirmed histologically to be meningocytic and fibroblastic meningiomas (Figure 2).
Figure 1 a, b

Figure 1a and Figure 1b show angiography of Case 4's angiography reveals a single mass.
Radioisotope brain scanning of the same case reveals a huge mass localized in frontoparietal region (Fig. 1c). CT revealed two separate meningiomas (Fig. 1d).
All of the patients are still alive and show no stigma of von Reck–Hippel's disease.

Case 7: A 26-year-old woman was admitted with right sided localising signs. Neurological examination disclosed a right homonymous hemianopia and papilloedema. 7 years before the admission a retroperitoneal meningioma had been removed. An arteriogram of the left common carotid revealed a large mass in the left temporo-pontine region. The brain radionuclide scanning demonstrated also only one spot of radionuclidean uptake in the same region. An surgery for a separate mass (6x5cm and 3x2.5cm) was performed.

Case 8: A 51-year-old woman had headache, disorientation and local motor seizures on the right side. Examination demonstrated papilloedema.

CT of case 2 shows two separate meningiomas with enhancement.

Figure 2
Discussion

Meningiomas, known as benign tumors, comprise 13.4-19 % of all brain tumors. Cushing and Eisenhart applied the term “Multiple Meningioma” to a condition in which a patient has more than one meningioma. Meningiomas and meningiomatosis associated with von Recklinghausen’s neurofibromatosis are not included in this definition. Reports on multiple meningiomas are rare. The first report on this subject was by Amstímov and Blumenau in 1889. In the literature not only intracranial meningiomas but also others that were in various neuroaxial locations have been reported. There are also cases in which meningiomas were found with other intracranial tumors. Multiple meningiomas have been reported as 1.3-5.9 % of all intracranial meningiomas. The seven cases that we present here constitute 1.95 % of our meningioma cases which had surgical intervention during the same period. Inclination to unilateral localization which is reported as an interesting feature of multiple meningiomas in the literature is also one of the characteristics of our cases, except one (Case 5).
Two separate masses could not be distinguished.

Ich could angiography vertex a parasagittal meningioma (Fig. 3c and Fig. 3d).

Figure 3c, d
The reason for multiplicity is still uncertain today. The possibilities include multicentric foci, spreading along the cerebrospinal fluid pathways and venous transmission. Another possibility may be hereditary factors. According to this thesis, a disorder of the formation in mesodermal germ layers would be the factor in multiple meningioma pathogenesis. 

In recent years, with the increasing use of CT scanning in neurosurgery, important steps have been taken in the diagnosis of multiple meningiomas. Although the value of cerebral angiography cannot be denied, the accuracy of meningioma diagnosis for even single nodular meningiomas is 83 %. The accuracy rate in cases with more than one nodule is quite low. As a matter of fact in our case 4, carotid angiography demonstrated only a single mass in the left parietal region (Figure 1a and Figure 1b), and two separate masses were visualized with CT scanning (Figure 1d). Also in case 7, a single nodule in the left temporoparietal region is demonstrated with left carotid angiography, but two nodules were excised during the surgical intervention. The possibility of correct diagnosis of meningiomas is only 31 % with the aid of radioisotop brain scintigraphy. In the four cases (1,2,4,7) in which we used brain scintigraphy, only one area of radioactive uptake could be shown.

Meningioma cases are diagnosed with 84.5 % accuracy with the aid of CT scanning. This percentile reaches 96.3 % with contrast enhancement. This point is especially important in multiple meningiomas. Meningiomas in our cases which could not be diagnosed with other neuroradiological methods were visualized by CT.

Five of our cases (72 %), were diagnosed after the use of CT in our institution began in 1976. This also supports the view that the incidence of the diagnosis of multiple meningiomas has increased through the use of CT.

This review of our cases has shown that the use of CT in diagnosing multiple meningiomas is much more effective compared to other neuroradiological procedures. Therefore meningioma cases should be carefully investigated with CT for the evidence of more than one mass.

REFERENCES

Hydatid Disease of the Thyroid in Childhood

Mehmet Ali Altun, M.D.* / Akgün Hiçsönmez, M.D.**
Nebil Büyükpamukçu, M.D.**

Summary

The localisation of hydatid cyst in the thyroid gland is rare and even rarer in childhood. In the literature, only 155 adult cases are reported, and not more than 10 cases in childhood. 4 out of our 77 thyroid patients requiring surgical treatment are diagnosed to have hydatid cysts.

The most accurate method for determining the nature of the thyroid nodule is by ultrasonography. We believe this is the way to obtain a definite diagnosis for this disease preoperatively.

Key Words: Hydatid cyst, Thyroid gland.

Introduction

Hydatid cyst disease is seen all over the world but it is in countries of the Mediterranean and South America that this entity is most often diagnosed. In a review of the literature the organ selection of hydatid cyst in descending order of preference is found to be the liver, lungs, abdomen, spleen, cranium, bone, muscle and thyroid gland.

Hydatid cyst is rarely seen in thyroid tissue. Among the 77 thyroid patients operated on between 1970-1982 in Hacettepe University Pediatric Surgery Department, 4 were found to have hydatid cysts peroperatively. Childhood hydatid disease of the thyroid is discussed and compared with the literature.

Clinical Data

Case 1: A girl 8 years old was admitted to the hospital because of a cervical mass that had existed for a long time and had recently begun to enlarge.

* Instructor, Department of Pediatric Surgery, Hacettepe University Medical School
  Ankara, Turkey.
** Professor, Department of Pediatric Surgery, Hacettepe University Medical School.
The patient was operated with a cystic diagnosis of nodular goitre.

There was a mobile mass 3X4 cm in size between the two lobes of the thyroid.

CASE 1: A girl 9 years old was admitted with a complaint of a mass in her cervical region existing for 4 months.

When operated, the patient was found to have a hydatid cyst in the left lobe of the thyroid scintigraphically.

The left and right lobes were normal; there was a hydropoelastic nodule in the left lobe.

There was a mobile mass 5X6 cm. in the left thyroid region.

CASE 2: A boy 6 years old was admitted because of a left cervical mass.

An operation of excision and cystic diagnosis was performed, without any pericapsular extension. The mass was found to be cystic. Hydatid cyst was diagnosed and a hydropoelastic nodule in the right lobe of the thyroid scintigraphically.

Physical examination showed a mobile mass 5X5 cm. in the right cervical region. The other systems were normal.

Physical examination showed a mobile mass 5X5 cm. in the right cervical region.
TABLE I
ANALYSIS OF CLINICAL AND LABORATORY FINDINGS

<table>
<thead>
<tr>
<th>Case</th>
<th>Symptom</th>
<th>Sign</th>
<th>Preop Dx.</th>
<th>Thyroid Scan</th>
<th>Postop. Dx</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cervical mass</td>
<td>3x4 cm. right lobe</td>
<td>Noduler goitre</td>
<td>Hypoactive nodule</td>
<td>Hydatid cyst</td>
</tr>
<tr>
<td>2</td>
<td>Cervical mass</td>
<td>3x4 cm. left lobe</td>
<td>Noduler goitre</td>
<td>Hypoactive nodule</td>
<td>Hydatid cyst</td>
</tr>
<tr>
<td>3</td>
<td>Cervical mass</td>
<td>5x6 cm. left lobe</td>
<td>Noduler goitre</td>
<td>Hypoactive nodule</td>
<td>Hydatid cyst</td>
</tr>
<tr>
<td>4</td>
<td>Cervical mass</td>
<td>3x4 cm. isthmus</td>
<td>Noduler goitre</td>
<td>Hypoactive nodule</td>
<td>Hydatid cyst</td>
</tr>
</tbody>
</table>

Discussion

The thyroid gland is a rare localisation for hydatid disease in children. In review of the literature it is noticed that the disease was first reported in 1704 by Liteaud and soon after this there came Oser’s and Descercac’s 12, Shalkeas’ and Sechas’ 12, von Eiselberg’s 21 cases in series.¹ The total number of cysts of the thyroid gland reported does not exceed 155, most of which are adults in South American countries.²

The first case of hydatid cyst in childhood was reported by Gattiin 1913.³ There are not more than 10 cases reported in the literature of hydatid disease localised in thyroid in children.

Nacif and Perinetti reported a rate of 0.38 % for a hydatid cyst to be located in the thyroid gland.⁴ In our series this rate is 3.4 % of thyroid operations performed at our center. This high rate is most probably due to our country being an endemic area for this disease.

Enlargement of the thyroid gland in childhood has a spectrum of 1-6%⁵ in regions of endemic goitre, this number increases.⁶ Hydatid disease in the thyroid is very rare. We can explain the etiology of implantation of hydatic cysts in thyroid tissue by the life cycle of Echinococcus Granulosus. This parasite can settle in the thyroid gland passing the liver and lungs. The blood flow rate in thyroid tissue is high, 6 ml/gr of thyroid tissue per minute. This amount is 50 times the flow rate of other parts of the human body.⁷ But it is hard to correlate this high amount of blood flow with such a small number of incidence. This could be explained by lodging of the parasite in the liver and the lungs.

When the clinical data is overviewed, the common finding is a solitary cervical mass in the thyroid gland.
REFERENCES

LITERATURE

2. Figure 9, a propos, in the en face view of the fundus. This de
3. Figure 10, a propos, in the en face view of the fundus. This de
4. Figure 11, a propos, in the en face view of the fundus. This de
5. Figure 12, a propos, in the en face view of the fundus. This de
6. Figure 13, a propos, in the en face view of the fundus. This de
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8. Figure 15, a propos, in the en face view of the fundus. This de
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10. Figure 17, a propos, in the en face view of the fundus. This de
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12. Figure 19, a propos, in the en face view of the fundus. This de
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19. Figure 26, a propos, in the en face view of the fundus. This de
20. Figure 27, a propos, in the en face view of the fundus. This de


University, Ankara, Turkey.

Associate Professor in the Department of General Surgery, Faculty of Medicine, Hacettepe University, Ankara, Turkey.

1 - Absence of symptomatic Granulomatous disease.

2 - Absence of portal hypertension in liver biopsy.

3 - Absence of primary biliary cirrhosis as determined by liver biopsy.

4 - No evidence of primary biliary cirrhosis as determined by Liver function tests.

5 - No prior biliary tract surgery.

I. Absence of biliary stones.

Criteria have been proposed as a practical guide for diagnosis. The diagnostic approach includes a liver biopsy and recurrent chromatiditis. Following the demonstration of a narrow section of the liver biopsy, the symptoms resemble obstructive jaundice or jaundice because the symptoms are seen in patients with primary sclerosing cholangitis. It has been empirically unclassified variety of segmental sclerosing cholangitis. If this has been empirical unusual variety of sclerosing cholangitis. It has been empirically

Introduction

Key Words: Sclerosing cholangitis.

condition were discussed. The condition was considered and an appropriate treatment of this rare disease was directed towards the surgical intervention. Pathologically, the condition involved the obliterated segment involving about 1.5 cm of the proximal bile duct with acinar abdulacinar and ficollicular cholangiographic changes.

Summary

This is a case report of a 26-year-old female who presented with acute abdominal pain and jaundice. Operative cholangiogram demonstrated changes consistent with intrahepatic bile duct obstruction. The patient underwent a cholecystectomy and exploratory laparotomy.

Volume 17 / No. 2 / April 1998 / pp. 81 - 86

Aliyu E. Barii, M.D., Ph.D. / Vahmez Sanges, M.D.
This case report demonstrates the complete surgical and roentgenologic properties of segmental sclerosing cholangitis.

Case Report

GK, a 26-year old woman, was admitted to the Department of Surgery of Hacettepe University Hospital on 16 April 1974, with a 15-day history of jaundice and right upper quadrant abdominal pain. She had noticed the presence of dark urine and light stools. There was no past history pertinent to biliary tract or gastrointestinal disease. Abdominal examination revealed mild tenderness without rigidity in the right upper quadrant. The liver was palpable 3 cm below the right costal margin with a sharp nontender edge. Her total bilirubin level was 17.5 mg. percent with a 14.5 mg percent direct component. The tentative diagnosis was obstructive jaundice secondary to choledocholithiasis.

On April 16th, the patient underwent emergency abdominal exploration. Exploratory laparotomy revealed an obliterated segment involving about 1.5 cm of the proximal common hepatic bile duct. The smallest Bakes dilator could barely be passed into the right and left hepatic ducts because of extreme stenosis. There was no evidence of calculi in the extrahepatic biliary system. A cholecystectomy was performed and a small T-tube was inserted into the opened common bile duct. The proximal limb of the tube was successfully placed into the stenotic segment. Operative cholangiogram showed an abnormal dilatation of the biliary system above the obliterated common hepatic duct (Figure 1A and B). E. coli was isolated from bile and she received large doses of ampicillin and chloramphenicol.

The patient had an uneventful postoperative period and serum bilirubin and alkaline phosphatase returned to normal levels within 34 days. The liver biopsy taken during surgery revealed cholangitis. The patient was discharged on prednisone 10 mg daily. She did well for the next five months during which time she was entirely asymptomatic and the T-tube was left in place.

On 24 October 1974, she was readmitted to the Hacettepe Hospitals with a one week history of right upper quadrant pain and jaundice. The liver function tests showed serum bilirubin of 4.5 mg per cent and alkaline phosphatase of 21.7 K. A. u. T-tube cholangiogram revealed some narrowing of the common hepatic and left hepatic ducts (Figure 2). Pyocyanus was isolated in the bile culture and she was treated with large doses of gentamycin and penicillin. With the continued lack of improvement in her condition (Figure 3), a cholangiojejunostomy was performed at a point where, the right hepatic duct appeared normal in the interlobar
function. Suggested explanation is essential for the diagnosis and treat- 
examination of the liver and the systemic segment of the hepatic duct 
measurement of the lesion by operative cholangioscopy and pathologic 
our patient's. The definite diagnosis in our case was made by careful door- 
the serious carcinoma of the bilary system is also similar to other 
high risk group of bile ducts, The clinical picture of the slow-grow- 
the stenosing strictures, but most frequently occurs proximal to a me-

Marred discrimination is rare in diffuse stenosing cholangitis due to 
"classical" possibilities, hepatic cirrhosis and pancreatitis. 

However a similar appearance of the high level bile duct with 
areas of high cholangiopidore were quite distinctive in our case. The type of a-
this radiologic picture was quite distinctive in our case. Therefore all-
where it enters an operative cholangioscopy is done under high pressures. 
all bile ducts are obstructed bilary lumen and adequate pharynx without marked 
showing dilated bilium and additional pharyngeal obstruction. The distal bile ducts are indistinguishable from the operative bile ducts. The symptoms of severe bile duct obstruction may be obstructive, some initial bilary symptoms occur with-
GeneSec of stenosing cholangitis remains obscure. Although a 

**Discussion**

of additional liver failure and death.

Operative period. The patient became moreicteric, showed evidence 
She developed cardiopulmonary failure in the immediate post-

Cholangiops...
will be dead on arrival at the hospital and 34 to 57 per cent of the patients who reach the hospital alive and are surgically treated will subsequently die. Penetrating and blunt abdominal trauma can be responsible for these serious injuries. We recently dealt with a case which can be regarded as an obstetrical complication. Since we have not encountered such an interesting obstetrical complication in the literature, we wish to report this case.

Case Report

A twenty-two year old female entered the emergency room on April 10, 1983 in the middle of the night, complaining of generalized weakness, dizziness, nausea and vomiting. Since she had a cloudy consciousness, information was given by her husband about her recent history. He stated that she had delivered a term infant normally and spontaneously at the Manisa Maternity Hospital approximately 10 hours before the admission and had not had excessive postpartum vaginal bleeding. Two hours after the delivery she had begun to feel ill, anxious, faint and pale. Primary care including 1000 cc of dextran solution had been given at the Manisa Maternity Hospital because of her reduced and clouded consciousness and decreased systolic blood pressure. However, she had not improved and was sent to the Aegean University Medical Faculty Hospital for further investigation and treatment.

On arrival at the obstetrics and gynecology clinic her systolic blood pressure was 50 mm Hg, and pulse was filiform. Her axillary temperature and respiration rate were 36 °C and 48 per minute respectively. She looked ill and pale, and her skin was covered with cold sweat. Her extremities were cold and pale. Breathing sounds were equal bilaterally but tachypneic. Abdominal examination revealed that the fundus of the uterus was two centimeters below the umbilicus and contracted. On the right side and behind the uterus there was a hard mass which extended to the right upper quadrant of the abdomen. On admission hematocrit was 20 per cent. Large caliber intravenous cannulas were immediately placed bilaterally to the upper extremities and Ringer's lactate solutions were administered. At the same time blood was sent for type and cross match. The uterine cavity was investigated manually to rule out uterine rupture and found to be intact. After surgical consultation we decided to perform exploratory laparotomy. She was given 4 units of compatible whole blood before the operation. At surgery she was found to have an extensive retroperitoneal hematoma especially at the right side of the columna vertebrales; the hematoma extended posteriorly from the pelvis up to the level of the costal margin. There was no pulse
Blood loss is influenced by preoperative complications, but also significantly to the overall morbidity of associated infarcts. This, in turn, can increase postoperative complications and further influence survival rates. Increased morbidity and mortality rates are associated with a decreased flow to the affected area.

Injury was at the inferior vena cava region, where the traditional plan for management would be surgical repair. However, preoperative planning and staging is essential. Immediate and prompt evaluation of the patient's clinical status is necessary to determine the extent of the injury. In some cases, a detailed anatomic study of the cava region may be necessary to determine the exact location of the injury and plan the appropriate surgical repair.

**Discussion**

The initial concern is the potential for hemorrhage, which may be significant and life-threatening. The presence of significant blood loss in the emergency room, as well as the rapidity of the hemorrhage, may require immediate intervention. The patient's condition, as well as the extent of the hemorrhage, will determine the appropriate course of action.

For minor hemorrhages, observation and conservative management may be sufficient. However, for significant hemorrhages, surgical intervention may be necessary. The surgical approach will depend on the location and extent of the hemorrhage, as well as the patient's overall condition.

In conclusion, the management of hemorrhage in the inferior vena cava region requires a multidisciplinary approach, including prompt evaluation, accurate diagnosis, and timely intervention. The outcome of such cases is highly dependent on the rapidity and efficacy of the treatment.
An interesting point of our case was that this injury occurred at delivery probably as a result of excessively and wrongly performed Kristeller maneuver by the midwife, as there was no vascular abnormality seen upon surgery. Because the perivascular connective tissues and intact abdominal wall potentially were able to provide a significant tamponade effect, she stayed alive after the injury up to the operation. This tamponade effect was suddenly lost when anesthesia or laparotomy was begun, and ischemic cardiac arrest occurred.

The present study reviews the factors that appear critical to patient survival. Hopefully results in the future will be better than we have been able to report at this time.

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A 26-year-old man was referred to us for evaluation of ulcers and neoplasms.

Case Report

A 26-year-old man was referred to us for evaluation of ulcers and neoplasms.

Introduction

Key Words: Werner’s syndrome, character, malignancy.

A case of Werner’s syndrome is presented and the pertinent literature surveyed.

Werner’s Syndrome

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losed that he had been suffering from these lesions for the last ten years. He had been hospitalized on several occasions and treated under the diagnosis of scleroderma. Three years ago cataract of the left eye was removed.

One sister, 36 years old, was of short stature, and appeared prematurely aged.

On physical examination the patient appeared to be prematurely aged. Blood pressure was 140/130 mm Hg, pulse rate 96 beats/minute. His weight was 42 kg, height 1.65 m. There was poor muscle development of the extremities.

There was pronounced atrophy of the skin of the face, as well as pseudoexophthalmos. The nose was sharp, the lips were thin and tightly stretched. There was polyosis. The subcutaneous tissues and muscles were underdeveloped. Armpit and pubic hairs were sparse. The testes were of prepubertal size. On the dorsal aspect of both feet, the skin was smooth and tightly bound to the underlying structures. There were atrophic ulcers, and hyperkeratosis in the ankle regions. The toenails were dystrophic. The skin temperature of the toes was 35.1°C. Ophthalmological examination disclosed cataract of the right eye (Figures 1, 2, 3).
Röntgenographic survey of the bones revealed osteoporosis and neurotrophic changes in the bones of the feet. The maxillary bone scan disclosed increased osteoblastic activity. Chest X-ray showed calcifications. Left ventricular hypertrophy was detected on electrocardiographic examination. The erythrocyte sedimentation rate was 30 mm/hour. The fasting glucose level was 110 mg/dL, the 30-minute glucose level 210 mg/dL, the 60-minute glucose level 256 mg/dL, and the 120-minute glucose level 225 mg/dL.

The results of the following laboratory examinations were all normal or negative: complete blood cell counts, serum electrolyte levels, blood urea nitrogen, total plasma proteins, urinalysis, liver function tests, total serum lipids, cholesterol, uric acid, serologic test for syphilis, intravenous pyelogram, gastrointestinal tract series with barium, scans of liver, spleen, and thyroid, and T₃-T₄ levels.

Histologic examination of the skin biopsy specimen demonstrated epidermal atrophy and lack of rete ridges, increased melanin pigment in the basal layer and sclerosis of the collagen bundles in the dermis.

Discussion

Our patient presented with pseudoxoophthalmos, beaked nose, scleroderma-like skin changes, ulcers, cataract, diabetes mellitus, testicular atrophy, and osteoporosis. On the basis of our clinical and laboratory findings, this case can be diagnosed as Werner’s syndrome.

In 1904, Werner described this rare, autosomal recessive connective-tissue disorder.¹ Consanguinity among parents is common and more than one sibling may be affected.

Cessation of physical growth begins between 10 and 18 years of age, resulting in small size and thin limbs. The most consistent features are short stature, acromicria, aged-appearance of the face, high-pitched voice, beaked-shaped nose, diabetes mellitus, premature atherosclerosis, metastatic calcifications, osteoporosis, osteomyelitis, vascular calcifications, gonadal atrophy, premature cavities and baldness.⁴⁻⁵

Cutaneous changes are more severe toward the acral points of the face, forearms and hands, and especially the legs and feet. On bony prominences hyperkeratosis and ulcers may develop. The sclerotic skin is restrictive of the motion of joints, and may cause deforming of digits.¹ The nails are remarkable for dystrophic changes.

Other features of Werner’s syndrome are posterior cortical and subcapsular cataracts, keratoconjunctivitis, chorioretinitis, blue sclera, proptosis, nystagmus, and retinitis pigmentosa.
Death in these patients of the associated malignant tumors which contribute to a common cause of death.

Recognized as a syndrome with certain diagnostic features that differentiate it from so-called carcinomatous, lymphoid, neuroendocrine, and mixed tumors, the syndrome of Werner is characterized by certain distinctive features, such as:

- Progressive manifestations of the disease, including:
  - Symptomatic neuroendocrine, lymphoid, and mixed tumors
  - manifestations of the disease, including:
  - Symptomatic neuroendocrine, lymphoid, and mixed tumors
  - Symptomatic neuroendocrine, lymphoid, and mixed tumors

In Werner's syndrome, the DNA repair function is reportedly impaired, which may also be present.

The syndrome has been associated with certain immunologic abnormalities, such as decreased levels of CD10 and CD21 in the bone marrow of patients with Werner's syndrome. DNA repair function is reportedly impaired in Werner's syndrome, which may also be present.

In about 10% of patients with Werner's syndrome, malignant tumors may develop which are distinctly uncommon and include malignant lymphomas, neuroendocrine, and mixed tumors, as well as certain other malignancies, including malignant lymphomas, neuroendocrine, and mixed tumors.

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Acid
Metabolites of Arachidonic
Cyclo-oxygenase
New Developments In

R. Kazim Turner, M.D.*
PGs are not stored; in response to different stimuli (mechanical, chemical, nerve), they enter to the extracellular space upon synthesis which is reflected in elevated levels in plasma and other biological fluids. After cessation of the these stimuli, PG levels rapidly reduce as a result of metabolism in the biological environment.² ³ ¹² ²¹ ²⁴ ³² ³⁸ PGs are derived from 20-Carbon polyunsaturated fatty acids, eicosatrienoic, eicosatetraenoic and eicosopentaenoic acids.³¹ ³⁹ ⁴⁰ Eicosatetraenoic acid (arachidonic acid) is the most abundant and usually found in low concentrations as a free acid but mainly in bound form to cell membrane phospholipids. This precursor is brought about by a group of enzymes, acylhydrolases, such as phospholipase A₂ and triglyceride lipase.³¹ ⁴¹ ⁴² Many stimuli including some hormones, antigen challenge, thrombin and collagen cause the release of PGs by stimulating acylhydrolases which liberates AA in first step from its bound form in cell membrane phospholipids. Among tissue hormones, kinin-peptides and angiotensin-peptides are well known PG-releasers, so far described, which promote PG-synthesis.⁵ ⁶ ²¹ ²⁴ ³⁷ ⁴⁴ Besides phospholipase A₂, other enzymes can also cause the release of AA from membrane phospholipids. In the ovary the presence of high concentration of cholesterol arachidonate, can cause the liberation of AA by cholesterol esterase stimulated by LH leading an increase of PG-synthesis.⁴⁵ Another cascade enzymatic mechanism may be involved in the release of AA from platelet membrane by the stimulation of thrombin. An alternative mechanism is based on the initial stimulation of phospholipase C with subsequent phosphorylation of diglycerides resulting in the formation of phosphatidic acid. Phosphatidic acid is the potent activator of phospholipase A₂ which liberates AA in platelet⁶⁶ as well as in kidney and vascular wall.⁴⁷

The conversion of AA into stable and unstable PGs occurs in two steps. In the first step AA is catalysed by cyclooxygenase (PG-synthetase) which is present in all mammalian cells. This results in oxygenation and cyclization of AA, forming the unstable intermediates, the cycloendoperoxides.⁴⁸ In the second step the catalyzation occurs by tissue specific enzymes, TXA₂-synthetase in platelets and prostacyclin synthetase in blood vessels.²⁰ ²⁴ ⁴⁹ ⁵³ PG-synthetase has partially been purified in many tissues which converts AA to PGG₂ and PGH₂.²⁰ ²⁰ ³⁰ PGG₂, PGH₂ and PGE₂ are formed variably depending on the tissue, physiological states and pathological conditions. Number of adjacent cells can influence the generation of one of these metabolites. A particular type of cell has been studied indicating that the rate of formation of PGI₂ by the sinusoidal cells of the liver can be influenced by contiguous parenchymal cells, hepatocytes, through an effect on cyclic nucleotid levels in the sinusoidal cells.⁵⁴
vascular thrombosis

vascular thrombosis and therefore should be considered non-enzymatic for the prevention of thrombosis, can inhibit cyclooxygenase in both platelet and vascular wall. However, these results of extensive clinical studies indicate that the dose of aspirin is about 700 mg every 12 hours sufficient to suppress platelet aggregation by about 90%. The higher doses of aspirin, formation of TXA2 by more than 90%, the higher dose of platelet cyclooxygenase is due to the high and rapid synthesis of new pro-
yag. The antithrombotic effect by aspirin on the extent of the lesion by platelet aggregation is due to the cyclooxygenase inhibitor. 

very low doses of aspirin are used to inhibit TXA2 formation by platelet cyclooxygenase. ed by aspirin-like drugs than that of the platelet is less affected. has been shown that production of PG2 in the vascular wall is less affected. In this respect, PG2 is a potent antiplatelet agent. As well as PG2 a potent antiaggregating agent, a major portion of TXA2 is present in the platelet. The extent of platelet aggregation is due to TXA2, aspirin, and other antiplatelet drugs. In this context, aspirin-like drugs are largely investigated for the prevention of the generation of these metabolites of TXA2. TXA2, PG2 in thromboxane and prostacyclin, respectively. The role of unstable PG2 (TXA2, PG2) in thromboxane and prostacyclin is decreased generation of the stable products, stable and unstable PG2s. Prostacyclin s is the main product. Important and pursuit of PG2 research, therefore, focus on the discovery of new prostacyclin. The discovery of the inhibitory role of cyclooxygenase, antiplatelet drugs, and the inhibitory role of cyclooxygenase. Similar inhibition has been observed with aspirin. 

Cyclooxygenics reduce the formation of PG2 by inhibiting phospho-
that it might be possible to modify the development of vascular diseases through diet.\textsuperscript{53-59} An important difference between Greenland Eskimos and Danes has been observed in the incidence of atherosclerosis and myocardial infarction. Eskimos have an extremely low incidence in thromboembolic diseases when compared with Danes. The clinical studies clearly indicate that the principal polyunsaturated fatty acid in the lipid fraction of Eskimos blood is eicosapentaenoic acid while it is AA in Danes. Eicosapentaenoic acid differs from AA (eicosatetraenoic acid) gives rise to products having thece double bonds as designated by the subscript TXA\textsubscript{2} and PGI\textsubscript{2}.\textsuperscript{39, 40, 53} TXA\textsubscript{2} unlike TXA\textsubscript{2} which arises from AA, has been observed to be unable to cause platelet aggregation.\textsuperscript{31} However, the vascular unstable metabolite of eicosapentaenoic acid, PGI\textsubscript{2}, possesses potent antiaggregatory activity. It has been shown that eicosapentaenoic acid is readily incorporated into platelet phospholipids and released simultaneously with AA by acylhydrolases. Although eicosapentaenoic acid is a poor substrate for cyclooxygenase, it competes effectively with AA for metabolism by this enzyme, resulting in a reduced formation of TXA\textsubscript{2} in the platelet.\textsuperscript{40-53} In addition, eicosatrienoic acid (dihomo-gammalinoeleic acid) again has been considered as a diet factor or a provitamin which generates the production of PGE\textsubscript{2}. This stable PG has anti-aggregatory and vasodilator actions therefore should be beneficial for the prevention and treatment of vascular thrombosis.\textsuperscript{28, 59}

**Thromboxanes and Prostacyclin**

It should be noted that biological techniques and bioassay have contributed a lot to the development of the field of PGs.\textsuperscript{56} Both TXA\textsubscript{2} and PGI\textsubscript{2} have been first determined depending on their biological activities before their chemical identifications. Without given a detailed information I just would like to emphasize in this review the importance of "blood bathed assay organ techniques" for the identification and discovery of the unstable metabolites of AA.\textsuperscript{64} Some sophisticated chemical methods, such as gas chromatography and mass spectrophotometry have been developed later for the detection and quantification of PGs.

The first exciting observation was the release of an unknown substance by antigen from isolated artificial salt solution-perfused sensitized guinea-pig lung which causes a powerful contractile effect on the isolated venous return superfused spirally cut rabbit aorta.\textsuperscript{58} This unknown substance has been called "Rabbit aorta Contracting Substance" = RCS which also has a powerful aggregating activity.\textsuperscript{58} The half life of this substance was about 1 min. After many years, a non-PG metabolite of PGG\textsubscript{2} or PGH\textsubscript{2} have been identified and called TXA\textsubscript{2}.\textsuperscript{30, 50} The half
Cyclo-oxygenase metabolites of arachidonic acid
synthetase having an IC₅₀ value of 10⁻¹⁰ M. However, this compound also has an inhibitory effect on PGI₂-synthetase in vascular wall having an IC₅₀ value of 8.4 x 10⁻⁷ M indicating its peculiarity as a non-beneficial drug for the treatment of vascular thrombosis. A convenient therapeutic value has been obtained with 2-isopropyl-3-(1-imidazolmethyl) indol and 3-(1-imidazolmethyl)indol which showed a complete selectivity against TXA₂-synthetase in vascular wall.⁶⁶ 5-methyl-7-diethylaminol S-trie(1,5-a)pyrimidine (Trapidil) is also a potent inhibitor of TXA₂-synthetase.⁶⁷ An interesting compound has also been synthesized having a chemical structure of 4-(2-(1-imidazole-1-yl)benzoic acid, Dazoxiben, as the most promising novel candidate for clinical development.⁶⁸

A series of experiments was started in England in 1975 which based upon the biological activity of an unknown substance (PGX) generated in vascular wall incubated with cyclic-endoperoxides or AA.²⁸ ³¹ ⁵⁶ ⁶⁹ Later, it has been established that in vitro incubation of AA or PGH₂ with arterial slices produces a substance which causes the relaxation of isolated vascular strips and vasodilatation when given intravenously.⁹¹ In addition, a potent anti-aggregating effect of this unknown substance has also been described.⁵³ The chemical structure of PGX is further elucidated and renamed as prostacyclin with abbreviation of PGI.⁵³ ⁵⁶ PGI₂ is the main metabolite of AA in all vascular tissues.²⁸ ³¹ ⁵⁶ Large vessel wall synthesizes PGI₂ especially at the intimal surface and progressively decreases toward the adventitia.⁵³ The effective production of PGI₂ by vascular endothelial cells is also shown in tissue cultures.³¹ ⁵³ ⁵⁶ The enzyme which causes the transformation of cyclic-endoperoxides to PGI₂ has been shown to be localized in the microsomal fraction of blood vessels endothelial cells.³¹ ⁵⁶ The ability of blood vessels to produce PGI₂ seems to be essential in prevention of platelet aggregation and deposition in endothelial surfaces. This mechanism might be an important event for the prevention of vascular thrombosis and atherosclerosis.²⁹ ⁵³ ⁵⁶ ⁷⁰ In some regional vascular areas PGI₂ might also be an endogenously occurring humoral vasodilator for vascular tone.⁵⁶

It has been described that fetal blood vessels have the greatest capacity to produce PGI₂, a property that might be related to the low peripheral resistance of the fetal circulation.⁴⁹ ⁵⁴ ⁷¹ PGI₂ is also a major metabolite of AA in utero-placental tissues and its deficiency should be the cause of hypertension during pregnancy.⁷² PGI₂ is an extremely labile metabolite of AA in vascular wall having one minute half-life in the biological environment. Spontaneous hydrolysis of PGI₂ forms 6-keto-PGF₁α which differs from 6-keto-PGE₁ in the substituent at C-9. The enzyme, 9-hydroxyprostaglandin dehydrogenase is probably
Glycogen phosphorylase, a key regulator of glycogen metabolism, is activated by the phosphorylation of its regulatory subunit, G6Pase.

The activation of G6Pase is controlled by the phosphorylation of its regulatory subunit, G6Pase. This phosphorylation event is triggered by the binding of glucose 6-phosphate (G6P) to the enzyme, leading to its activation.

Phosphorylation of G6Pase by cAMP-dependent protein kinase (蛋白激酶A) is a critical step in the activation of the enzyme. This process is mediated by a variety of signaling pathways, including the activation of extracellular signal-regulated kinases (ERK) and the activation of mitogen-activated protein kinases (MAPK).

G6Pase activation is also regulated by the levels of G6P, glucose, and ATP in the cell. These factors control the enzyme's activity by modulating its phosphorylation status. The balance between the activation and deactivation of G6Pase is critical for maintaining glucose homeostasis and energy metabolism.

In summary, the activation of G6Pase is a complex process that involves multiple regulatory mechanisms. Understanding these mechanisms is crucial for the development of strategies to modulate carbohydrate metabolism and treat diseases associated with altered glucose homeostasis.
from infarcted myocardium.\textsuperscript{7b-78} It has also a beneficial effect against endotoxin shock and improves the pertubated splanchnic circulation during the shock.\textsuperscript{55-58} An interesting effect of PGI\textsubscript{2} on platelet viability has been described. It has been shown that platelet in normal intravital conditions shows for about 6 hours functional activity. However, when prepared with the addition of PGI\textsubscript{2} they remain functional for more than 72 hours.\textsuperscript{52-57, 60-69} In vitro long-lasting viability of platelets in the presence of PGI\textsubscript{2} is not accompanied by a prolonged increase in cAMP level. This clearly indicates that increase in functional viability of platelet by PGI\textsubscript{2} is not related with its antiaggregant activity.\textsuperscript{28, 52-60}

As cited above, lipid peroxides, such as 15-HPAA, are potent and selective inhibitors of the generation of PGI\textsubscript{2} in the vascular wall.\textsuperscript{59-61, 53-54, 63-64} It has also been shown that lipid peroxides tremendously increase in atherosclerotic vascular lesions.\textsuperscript{28-59} The increased lipid peroxidation has been observed in vitamin E deficiency, ageing process and hyperlipidemia accompanying atherosclerosis.\textsuperscript{56-75} Deposition of lipid peroxides (15-HPAA) in atheromatous plaque could predispose to thrombus formation because of its inhibitory effect against the generation of PGI\textsubscript{2} without altering that of TXA\textsubscript{2}.\textsuperscript{31-53} Human atheromatous plaques do not produce PGI\textsubscript{2}.\textsuperscript{53} This has also been described in experimental atherosclerotic rabbits.\textsuperscript{28-53} In normal rabbits PGI\textsubscript{2} formation in aorta is abolished by de-endothelization and progressively recovers with re-endothelization over a period of about 70 days. However, this recovery does not occur when the rabbits are made hypercholesterolemic by diet.\textsuperscript{23-53, 69} All these findings clearly indicate that there is a close relation between atherosclerosis and PGI\textsubscript{2} formation in arterial wall. Lipid peroxides, as a potent and selective inhibitor of PGI\textsubscript{2} formation, should have a very important role in the development of atherosclerosis. On the other hand, these findings have opened up a new approach for the prevention and treatment of atherosclerosis. Since the inhibition of the generation of 15-HPAA might result in an increase in the biosynthesis of PGI\textsubscript{2} in vascular wall. Vitamin E acts as an antioxidant and perhaps its empirical use in arterial diseases in the past,\textsuperscript{56} had, in fact, a biochemical rational.\textsuperscript{56} After the discovery of TXA\textsubscript{2} and PGI\textsubscript{2} and their functional homeostatic role in cardiovascular regulation, the explanation of the disorders related with this system became understandable and many therapeutic approaches are raised. It is very clear that the inhibition of the biosynthesis of PGI\textsubscript{2} may cause the initiation of atherosclerotic cardiovascular diseases. It should be learned whether or not all drugs used in therapeutics have any effect on PGI\textsubscript{2} and TXA\textsubscript{2} generations and how these drugs can influence the ratio of TXA\textsubscript{2}/PGI\textsubscript{2}. In
enhance the action of heparin by as much as 100%. This slight increase in the bioavailability of heparin in vivo, however, would be of little or no significance since the anticoagulant effect of heparin in vitro is due to its interaction with an anticoagulant substance which reduces the anticoagulant effect of heparin in vivo. Further, it is not known whether the anticoagulant effect of heparin is due to its interaction with this anticoagulant substance.

In practice, the presence of a heparin-like factor in the medium, which could be termed the "anticoagulant factor," is observed. This factor is also present in the blood of patients with a history of heparin administration. In addition, the anticoagulant factor of heparin is also present in the blood of patients with a history of heparin administration. In this case, the anticoagulant factor has been shown to be due to the presence of heparin in the medium. In conclusion, the anticoagulant factor is a heparin-like substance which could be termed the "anticoagulant factor."
vitro observations support the beneficial effect of PGI₂ in extracorporeal circulation. Long term use of heparin in the therapy is complicated in some patient by thrombocytopenia and thromboembolic episodes. It is worthy to note here that heparin-induced platelet aggregation is not inhibited by cyclooxygenase inhibitors, such as aspirin, but inhibited by substances which elevate plasma cAMP level.⁵⁵-⁵⁹

Many antihypertensive and vasodilator drugs, partially act through the increased biosynthesis of PGI₂ in tissues. A series of exciting observations have been published recently indicating PGI₂ releasing effect of propranolol, a non-selective beta-adrenoceptor blocker. It has recently been described that cyclooxygenase inhibitors such as aspirin lessened the fall in blood pressure induced by propranolol in hypertensive patients suggesting that the antihypertensive effect of the drug may be associated with PGs.⁹⁰ Recently the evidences have been presented indicating that propranolol can cause the release of PGI₂ from kidney which may contribute to a direct antihypertensive action of this beta adrenoceptor blocking agent.⁸⁵ An antiarrhythmic effect of PGI₂ has also been described in different arrhythmias models.⁷⁹-⁸⁰ It is highly possible that the antiarrhythmic effect of propranolol might be partially mediated through the increase of the biosynthesis of PGI₂ in myocardium.⁷⁹

So far, PGI₂ is the most potent inhibitor of all forms of aggregation, and potent vasodilator. This fact clearly suggests that the future of anti-thrombotic and vasodilator therapy lies in the development of compounds with "PGI₂" type of action, long acting and orally active.

During last six years PGI₂ (Epoprostenol⁹) has been available experimental studies in humans and it has been tested in a wide range of disorders. Its beneficial effect is established in extracorporeal circulation such as cardiopulmonary bypass, charcoal haemoperfusion and haemodialysis.⁵⁹-⁹¹ Other application for this compound include peripheral arterial diseases,⁸² acute and chronic artery insufficiency,⁹² haemolytic uremic syndrome,⁵⁹-⁸² thrombotic thrombocytopenic purpura,⁵⁶-⁸² hypertension in pregnancy,⁹² pulmonary hypertension,⁵³-⁵⁶,⁵⁹ Raynaud’s disorder and persistent foetal circulation.⁹² A few side effects have been reported during the therapy with Epoprostenol. Facial flushing, headache, tachycardia and decrease in diastolic pressure are the most common side effects. Erythema over the venous infusion site, sudden bradycardia, palor and sweating are rarely reported side effects seen during Epoprostenol therapy. In addition, restlessness, abdominal discomfort, nausea and drowsiness are reported in a few cases.⁹¹
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Citril

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Atherosclerosis

A should be considered another subject of a review article.

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V and Beaded Polysaturated fatty acids are also metabolized

End of PDF, so far described.

observations, ZK 36 37 4 is proposed to be the most effective stable analog.

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V and Beaded Polysaturated fatty acids are also metabolized

Continuous infusion of ZK 36 37 4 at the dose of 20 ng/kg/min

Blocking effect of ZK 36 37 4 has also been described. 99

agrees closely with the reduced vascular contractile force seen in the 99

indicates that this compound also has a potent antithrombotic effect

in various pharmacological studies with ZK 36 37 4 has been found to be more potent and long-lasting when

compared with PGF 2 across in vivo. ZK 36 37 4 has also been shown to have a profound effect similar to natural PGF 2

Most recently a new chemically stable analog of PGF 2 has been

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- Reduction in gastro-oesophageal reflux disease (GERD) symptoms in achondroplastics.
- Reduced expression of COX-2 and TXA2 receptors in achondroplastic patients.
- Increased collagen synthesis and reduced matrix metalloproteinase activity in achondroplastic bone.
- Enhanced osteoclast activity in achondroplastic bone, leading to increased bone resorption.
- Decreased bone mineral density in achondroplastics compared to normal controls.
- Reduced bone turnover markers in achondroplastics, indicating decreased bone remodeling.
- Increased fibrosis and decreased bone vascularity in achondroplastic bone.
- Reduced bone matrix protein synthesis in achondroplastic bone.
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1. Manuscripts, letters and editorial correspondence should be sent to "The Editor, Hackette Medical Journal, Hackette University, School of Medicine, Dean's Office, Akrara-Tunkey, by first-class mail (airmail for overseas)."

2. Submissions considered for publication are received with the understanding that no part of the submission has previously appeared elsewhere in any other publication.

3. Manuscripts should be typed double-spaced on standard-size type.

4. Number pages consecutively in order and place author(s) name, title, and two highly-quality copies of the manuscript should be submitted.

5. Hackette Medical Journal invites papers on original research.

6. Original articles and research papers should normally be divided into following sections:

   a. Introduction
   b. Methods
   c. Results
   d. Discussion
   e. References

7. References must be typed in double spacing and numbered.

8. Fewer than two pages of more than 200 words must be included at the beginning of the paper.

9. Results (g) Discussion and (7) References.

10. Key Words and Methods.

II. For reviews, for case reports and 1 for letters.

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   (g) Discussion

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   (h) Introduction

   (i) Key Words

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   (k) Case Reports

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